上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话：021-61312973　　传真：021-55068248
网址：www.shyuanye.com
邮箱：shyysw@sina.com

产品名称：曲前列尼尔钠
产品别名：Treprostinil sodium； UT-15

生物活性：

Description	Treprostinil sodium is a potent DP1 and EP2 agonist with EC50 values of 0.6±0.1 and 6.2±1.2 nM, respectively.

IC_{50} & Target				
DP/DP1 Receptor	EP_1 Receptor	EP_2 Receptor	EP3 Receptor	EP_4 Receptor
0.6 nM (EC_{50})	285 nM (EC_{50})	6.2 nM (EC_{50})	68.9 nM (EC_{50})	181 nM (EC_{50})
IP Receptor	TP Receptor	EP_2 Receptor	EP_1 Receptor	EP_4 Receptor
1.9 nM (EC_{50})	919 nM (EC_{50})	3.6 nM (Ki)	212 nM (Ki)	826 nM (Ki)
EP3 Receptor	DP/DP1 Receptor	IP Receptor	FP Receptor	
2505 nM (Ki)	4.4 nM (Ki)	32.1 nM (Ki)	4680 nM (Ki)	

In Vitro	Treprostinil has high affinity for the DP1, EP2 and IP receptors (Ki=4.4, 3.6 and 32 nM, respectively), low affinity for EP1 and EP4 receptors and even lower affinity for EP3, FP and TP receptors. Activation of IP, DP1 and EP2 receptors, as with treprostinil, can all result in vasodilatation of human pulmonary arteries[1].Treprostinil inhibits viability of cultured endothelial colony forming cells. Endothelial colony forming cells proliferation is stimulated by conditioned media from Treprostinil pretreated mesenchymal stem cells[5].
In Vivo	Inhaled treprostinil sodium, a prostacyclin analog, is the most recent agent to receive FDA approval for the treatment of a fatal orphan disease: pulmonary arterial hypertension (PAH)[2]. Treprostinil preserves the sinusoidal endothelial cell lining and reduces platelet deposition early post-transplantation compared to placebo. Hepatic tissue blood flow is significantly compromised in the placebo group, whereas treprostinil maintains blood flow similar to normal levels[3].Treprostinil treatment significantly increases the vessel-forming ability of endothelial colony forming cells combined with mesenchymal stem cells in Matrigel implanted in nude mice. Silencing VEGF-A gene in mesenchymal stem cells also blocks the pro-angiogenic effect of Treprostinil[4]. Treprostinil is most efficacious in raising intracellular cAMP levels in murine and human hematopoietic stem and progenitor cells[5]. Treatment with Treprostinil significantly reduces the recruitment of cells compared to normoxic mice. Treprostinil also reduces right ventricular systolic pressure and slightly reduces the vascular remodelling but fails to reverse the right ventricular hypertrophy[6].

In Vitro:

DMSO : ≥ 26 mg/mL (63.03 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	**1 mg**	**5 mg**	**10 mg**
	1 mM	2.4243 mL	12.1215 mL	24.2430 mL
	5 mM	0.4849 mL	2.4243 mL	4.8486 mL
	10 mM	0.2424 mL	1.2122 mL	2.4243 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

Solvent&Solubility	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: ≥ 2.5 mg/mL (6.06 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.06 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 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: ≥ 2.5 mg/mL (6.06 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.06 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 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: ≥ 2.5 mg/mL (6.06 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.06 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 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Whittle BJ, et al. Binding and activity of the prostacyclin receptor (IP) agonists, treprostinil and iloprost, at human prostanoid receptors: treprostinil is a potent DP1 and EP2 agonist. Biochem Pharmacol. 2012 Jul 1;84(1):68-75. [2]. Smadja DM, et al. Treprostinil indirectly regulates endothelial colony forming cell angiogenic properties by increasing VEGF-A produced by mesenchymal stem cells. Thromb Haemost. 2015 Oct;114(4):735-47. [3]. Ferrantino M, et al. Inhaled treprostinil sodium for the treatment of pulmonary arterial hypertension. Expert Opin Pharmacother. 2011 Nov;12(16):2583-93. [4]. Kazemi Z, et al. Repurposing Treprostinil for Enhancing Hematopoietic Progenitor Cell Transplantation. Mol Pharmacol. 2016 Jun;89(6):630-44. [5]. Ghonem N, et al. Treprostinil, a prostacyclin analog, ameliorates ischemia-reperfusion injury in rat orthotopic liver transplantation. Am J Transplant. 2011 Nov;11(11):2508-16. [6]. Nikam VS, et al. Treprostinil inhibits the recruitment of bone marrow-derived circulating fibrocytes in chronic hypoxic pulmonary hypertension. Eur Respir J. 2010 Dec;36(6):1302-14.

实验参考：

Cell Assay	Human or murine hematopoietic stem and progenitor cells are incubated in the presence of vehicle or the combination of 10 μM Treprostinil and 30 μM forskolin at 37°C for 1 hour and 24 hours. After

	washing with phosphate-buffered saline at 4°C, cells are stained for externalized phosphatidylserine with the apoptosis kit[5].
Animal Administration	Rats[3] Male Lewis rats weighing 200-300 g are used in the study. Donor animals receive treprostinil or placebo 24 h before hepatectomy and the corresponding recipient animal receive the similar treatment until the time of sacrifice. The surgeon is blinded to treatment. Recipients are sacrificed at 1, 3, 6, 24 and 48 h post-transplantation to examine the early events after IRI. Treprostinil (100 ng/kg/min) or placebo is administered subcutaneously via an Alzet implantable osmotic pump. This dose is selected to achieve a steady-state plasma concentration in the range of 5-20 ng/mL[3]. Mice[6] Bone marrow transplanted (BMT) mice are divided into five different groups with each group consisting of 6 to 10 mice. One group of mice is exposed to hypoxia (10% inspired oxygen fraction) in a normobaric chamber whereas the second group (control BMT) of animals are placed in a normoxic chamber with a normal oxygen environment (21% inspired O2 fraction) for 28 days. Sham group mice receive saline treatment whereas two other groups of mice receive Treprostinil infusions of different dose levels (14 ng/kg and 70 ng/kg per minitue) and are exposed to hypoxia for 4 weeks. For comparison, human infusion rates in PAH therapy vary from 10 to 60 ng/kg per min[6].
References	[1]. Whittle BJ, et al. Binding and activity of the prostacyclin receptor (IP) agonists, treprostinil and iloprost, at human prostanoid receptors: treprostinil is a potent DP1 and EP2 agonist. Biochem Pharmacol. 2012 Jul 1;84(1):68-75. [2]. Smadja DM, et al. Treprostinil indirectly regulates endothelial colony forming cell angiogenic properties by increasing VEGF-A produced by mesenchymal stem cells. Thromb Haemost. 2015 Oct;114(4):735-47. [3]. Ferrantino M, et al. Inhaled treprostinil sodium for the treatment of pulmonary arterial hypertension. Expert Opin Pharmacother. 2011 Nov;12(16):2583-93. [4]. Kazemi Z, et al. Repurposing Treprostinil for Enhancing Hematopoietic Progenitor Cell Transplantation. Mol Pharmacol. 2016 Jun;89(6):630-44. [5]. Ghonem N, et al. Treprostinil, a prostacyclin analog, ameliorates ischemia-reperfusion injury in rat orthotopic liver transplantation. Am J Transplant. 2011 Nov;11(11):2508-16. [6]. Nikam VS, et al. Treprostinil inhibits the recruitment of bone marrow-derived circulating fibrocytes in chronic hypoxic pulmonary hypertension. Eur Respir J. 2010 Dec;36(6):1302-14.