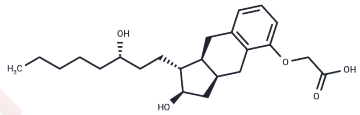
Data Sheet (Cat.No.T5150)

TargetMol

Treprostinil

Chemical Properties



CAS No. : 81846-19-7

Formula: C23H34O5

Molecular Weight: 390.51

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Treprostinil (Orenitram) is a potent DP1, IP and EP2 agonist (EC50: 0.6/1.9/6.2 nM).
Targets(IC50)	Prostaglandin Receptor
In vitro	Treprostinil has a high affinity for the IP, EP2 and DP1 receptors (Ki: 32, 3.6 and 4.4 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 can all result in vasodilatation of human pulmonary arteries[1]. Treprostinil inhibits the viability of cultured endothelial colony forming cells. Endothelial colony forming cells proliferation is stimulated by conditioned media from Treprostinil pretreated mesenchymal stem cells [2].
In vivo	Treprostinil is most efficacious in raising intracellular cAMP levels in murine and human hematopoietic stem and progenitor cells [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]. 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 remodeling but fails to reverse the right ventricular hypertrophy [5].
Cell Research	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 [2].
Animal Research	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 a 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].

Animal Research	. 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 minute) 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[5].

Solubility Information

Solubility	DMSO: 150 mg/mL (384.11 mM),Sonication is recommended. Ethanol: 20 mg/mL (51.22 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (5.12 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.5608 mL	12.8038 mL	25.6075 mL
5 mM	0.5122 mL	2.5608 mL	5.1215 mL
10 mM	0.2561 mL	1.2804 mL	2.5608 mL
50 mM	0.0512 mL	0.2561 mL	0.5122 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

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.
Kazemi Z, et al. Repurposing Treprostinil for Enhancing Hematopoietic Progenitor Cell Transplantation. Mol Pharmacol. 2016 Jun;89(6):630-44.
Ghonem N, et al. Treprostinil, a prostacyclin analog, ameliorates ischemia-reperfusion injury in rat orthotopic liver transplantation.
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.
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.

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