产品名称：昔美酸沙美特罗
产品别名：Salmeterol xinafoate；沙美特罗昔萘酸酯 ；GR 33343X xinafoate

生物活性：

Description	Salmeterol xinafoate is a long-acting beta-2 adrenergic receptor (β_2AR) agonist, with K_i of 1.5 nM for WT β_2AR, and used for asthma treatment.
IC_{50} & Target	Ki: 1.5 nM (WT β2AR)[2]
In Vitro	Salmeterol significantly inhibits production of pro-inflammatory mediators by RAW264.7 and THP-1 cells. Salmeterol downregulates PgLPS-mediated phosphorylation of the ERK1/2 and JNK but not p38 MAP kinases (MAP-K). Salmeterol also attenuates the activation of NF-κB via inhibition of nuclear translocation of p65-NFκB, the transcriptional activity of NF-κB and IκBα phosphorylation[1]. Salmeterol shows very high selectivity for the WT β2AR (β1 Ki /β2 Ki ratio of approximately 1500) with Ki of 1.5±0.4 nM[2]. Salmeterol prevents phosphorylation levels of IRS-1Ser307 induced by tumor necrosis factor-α. Salmeterol alone prevents cell death in retinal Müller cells ($p<0.05$ versus 25 mM glucose). Salmeterol in conbination with IRS-1 shRNA shows a significant increase in cell death compared to salmeterol alone. Moreover, salmeterol alone treatment significantly reduces cytochrome C levels, with the effect lessened when salmeterol is combined with IRS-1 shRNA[3]. Salmeterol (100 μM) causes apoptosis of DCs, and can not affect the differentiation and maturation of DCs at 10 μM. Salmeterol (10 μM) decreases the mRNA and protein levels of pro-inflammatory cytokines in LPS-activated DCs and inhibits MAPK and NF-κB activation[4].
In Vivo	The OVA/LPS groups with salmeterol result in a significant decrease in the enhanced AHR in allergic mice in a dose-dependent manner. Salmeterol contends with asthma via regulating the inflammation of the airway of the mice[4].

Solvent&Solubility

In Vitro:

DMSO : ≥ 50 mg/mL (82.82 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6563 mL	8.2816 mL	16.5631 mL
	5 mM	0.3313 mL	1.6563 mL	3.3126 mL
	10 mM	0.1656 mL	0.8282 mL	1.6563 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: ≥ 2.5 mg/mL (4.14 mM); Clear solution

	此方案可获得 ≥ 2.5 mg/mL (4.14 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 (4.14 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.14 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 (4.14 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.14 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]. Sharma M, et al. Salmeterol; A Long Acting β2-Aderenergic Receptor Agonist Inhibits Macrophage Activation by Lipopolysaccharide From Porphyromonas Gingivalis. J Periodontol. 2017 Mar 3:1-17. [2]. Isogaya M, et al. Identification of a key amino acid of the beta2-adrenergic receptor for high affinity binding of salmeterol. Mol Pharmacol. 1998 Oct;54(4):616-22. [3]. Walker RJ, Anderson NM, Bahouth S, Silencing of insulin receptor substrate-1 increases cell death in retinal Müller cells. Mol Vis. 2012;18:271-9. Epub 2012 Feb 1. [4]. Hu Z, et al. Salmeterol attenuates the inflammatory response in asthma and decreases the pro-inflammatory cytokine secretion of dendritic cells. Cell Mol Immunol. 2012 May;9(3):267-75.

实验参考：

Animal Administration	All mice are sensitized on days 0 and 14 by intraperitoneal injection of either PBS or 0.08 mg OVA and 0.1 mL aluminum hydroxide in 0.1 mL of PBS (pH 7.4). After sensitization, animals are exposed to aerosolized PBS-only (negative control), 1% OVS/PBS (acute exposure), 1% OVA/0.01% LPS/PBS (extra LPS exposure) or 1% OVA/0.01% LPS/salmeterol/PBS (sal treatment) for 40 min, once per day for 3 consecutive days (days 24-26). On day 27, the mice are killed and lungs are divided into two groups for analysis: the left lung lobes are lavaged three times with 1 mL of PBS with 1% fetal calf serum and 5 U/mL heparin, and the right halves are fixed by 4% paraformaldehyde for histological analysis. [4]
Kinase Assay	The cells are rinsed twice with ice-cold phosphate-buffered saline and mechanically detached in ice-cold buffer containing 10 mM Tris·HCl, pH 7.4, 5 mM EDTA, 10 μg/mL benzamidine, 10 μg/mL soybean trypsin inhibitor (type II-S), and 5 μg/mL leupeptin (lysis buffer). The lysate is centrifuged at 45,000 ×g for 10 min at 4°C. The pellet is rehomogenized in lysis buffer, with a Potter-type homogenizer, and stored at −80°C until use. The competition binding assays are performed in buffer containing 75 mM Tris·HCl, pH 7.4, 12.5 mM $MgCl_2$, and 2 mM EDTA, using 1-5 μg of membrane protein, 50 pM ^{125}I-CYP, and 0-100 μM unlabeled ligand in the presence of 100 μM GTP, for 60 min at 37°C. The binding reaction is terminated by dilution and rapid filtration through Whatman GF/C filters; the filters are washed three times with solution containing 25 mM Tris·HCl, pH 7.4, and 1 mM $MgCl_2$. Nonspecific binding is determined in the presence of 5 μM (±)-propranolol. The radioactivity

	on the filters is counted with a γ-counter. [2]
References	[1]. Sharma M, et al. Salmeterol; A Long Acting β2-Aderenergic Receptor Agonist Inhibits Macrophage Activation by Lipopolysaccharide From Porphyromonas Gingivalis. J Periodontol. 2017 Mar 3:1-17. [2]. Isogaya M, et al. Identification of a key amino acid of the beta2-adrenergic receptor for high affinity binding of salmeterol. Mol Pharmacol. 1998 Oct;54(4):616-22. [3]. Walker RJ, Anderson NM, Bahouth S, Silencing of insulin receptor substrate-1 increases cell death in retinal Müller cells. Mol Vis. 2012;18:271-9. Epub 2012 Feb 1. [4]. Hu Z, et al. Salmeterol attenuates the inflammatory response in asthma and decreases the pro-inflammatory cytokine secretion of dendritic cells. Cell Mol Immunol. 2012 May;9(3):267-75.