

## Product Data Sheet

Product Name: Salmeterol xinafoate

Cat. No.: GC11531

### Chemical Properties

Cas. No. 94749-08-3

Chemical Name 2-(hydroxymethyl)-4-[1-hydroxy-2-[6-(4-phenylbutoxy)hexylamino]ethyl]phenol;1-hydroxynaphthalene-2-carboxylic acid

SMILES C1=CC=C(C=C1)CCCCOCCCCCNCC(C2=CC(=C(C=C2)O)CO)O.C1=CC=C2C(=C1)C=CC(=C2O)C(=O)O

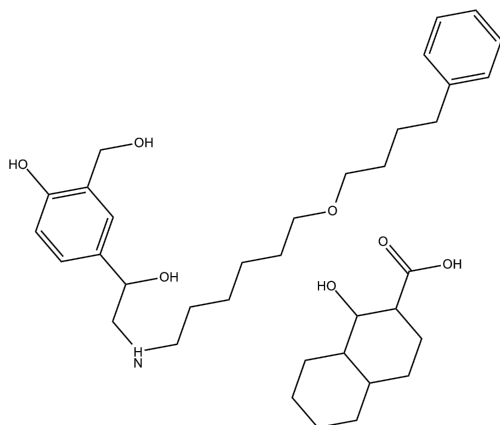
Formula  $C_{36}H_{45}NO_7$  M.Wt 603.75

Solubility  $\geq 30.1875$  mg/mL in DMSO,  $\geq 15.83$  mg/mL in EtOH with ultrasonic and warming Storage Store at  $-20^{\circ}\text{C}$

General tips For obtaining a higher solubility , please warm the tube at  $37^{\circ}\text{C}$  and shake it in the ultrasonic bath for a while.Stock solution can be stored below  $-20^{\circ}\text{C}$  for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure



### Protocol

**Caution: Product has not been fully validated for medical applications. For research use only.**

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**Kinase  
experiment:**

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<sub>2</sub>, and 2 mM EDTA, using 1-5 µg of membrane protein, 50 pM <sup>125</sup>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<sub>2</sub>. Nonspecific binding is determined in the presence of 5 µM (±)-propranolol. The radioactivity on the filters is counted with a γ-counter.

**Animal  
experiment:**

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.

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### References:

- [1]. Sharma M, et al. Salmeterol; A Long Acting  $\beta$ 2-Adrenergic 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.

### Background

$\beta$ 2-adrenergic receptor agonists are a class of drugs acting on the beta2-adrenergic receptor, thereby causing smooth muscle relaxation, which results in dilation of bronchial passages, vasodilation in muscle/liver, relaxation of uterine muscle and release of insulin. Salmeterol xinafoate, as a long-acting beta2-adrenergic receptor agonist, is clinically prescribed for the treatment of asthma, chronic obstructive pulmonary disease (COPD) and other pulmonary disorders. It was previously marketed as a dry powder inhaler in the US and is still available in the UK market.

**In vitro:** In a previous study, it was found that salmeterol could reduce retinal Müller cell death through the inhibition of the phosphorylation of IRS-1(Ser307). In addition, the findings also suggest the importance of IRS-1 in beta-adrenergic receptor signaling in the prevention of cell death in retinal Müller cells [1].

**In vivo:** A previous animal study showed that salmeterol significantly decreased the production of pro-inflammatory cytokines in a model of allergen-challenged mice, which expressed tumor-necrosis factor-alpha, interleukin-1 and interleukin-6. Moreover, it was found that salmeterol could reduce the inflammation caused by lipopolysaccharide in activated murine bone marrow-derived dendritic cells (DCs). Therefore, this study suggested that salmeterol regulated the inflammation of allergen-induced asthma by modulating DCs, providing evidence that DCs were the target immune cells responsible for the action of salmeterol against asthma [2].

**Clinical trial:** In an early clinical investigation, it was found that salmeterol was significantly better than disodium cromoglycate in improving both morning and evening PEF [3]. A recent Phase-2 clinical

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trial, named “Dose-Ranging Study of the Salmeterol Component of Fluticasone/Salmeterol Spiromax Compared to Fluticasone Spiromax and Advair Diskus in Asthma Subjects”, was conducted in the US to evaluate the dose response, efficacy and safety of salmeterol combined with fluticasone for the treatment of persistent asthma.

### *References:*

- [1] Walker RJ, Anderson NM, Bahouth S, Steinle JJ. Silencing of insulin receptor substrate-1 increases cell death in retinal Müller cells. *Mol Vis.* 2012;18:271-9
- [2] Hu Z, Chen R, Cai Z, Yu L, Fei Y, Weng L, Wang J, Ge X, Zhu T, Wang J, Bai C. Salmeterol attenuates the inflammatory response in asthma and decreases the pro-inflammatory cytokine secretion of dendritic cells. *Cell Mol Immunol.* 2012;9:267-75.
- [3] Bousquet J, Aubert B, Bons J. Comparison of salmeterol with disodium cromoglycate in the treatment of adult asthma. *Ann Allergy Asthma Immunol.* 1996;76:189-94.

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