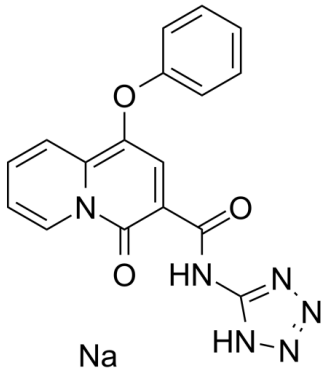
Data Sheet

Product Name:	Quinotolast sodium
Cat. No.:	CS-6569
CAS No.:	101193-62-8
Molecular Formula:	$C_{17}H_{12}N_6NaO_3$
Molecular Weight:	371.31
Target:	Histamine Receptor; Leukotriene Receptor; Prostaglandin Receptor
Pathway:	GPCR/G Protein; Immunology/Inflammation; Neuronal Signaling
Solubility:	DMSO : 115 mg/mL (309.71 mM; ultrasonic and warming and heat to 60°C)



BIOLOGICAL ACTIVITY:

Quinotolast sodium in the concentration range of 1-100 μg/mL inhibits **histamine**, **LTC_4** and **PGD_2** release in a concentration-dependent manner. IC50 & Target: histamine[1]

leukotriene[1] **In Vitro:** Quinotolast inhibits the release of histamine and the generation of leukotriene (LT) C_4 and prostaglandin (PG) D_2 from dispersed human lung cells. Quinotolast (100 μg/mL) significantly inhibits PGD_2 and LTC_4 release. Quinotolast inhibits PGD_2 release by 100% and LTC_4 release by 54%. The inhibitory effect of Quinotolast on histamine release from dispersed lung cells is largely independent of the preincubation period, no tachyphylaxis being observed. Quinotolast shows a significant inhibition of inflammatory mediators from human dispersed lung cells[1]. Quinotolast also shows strong inhibitory effects on histamine and peptide leukotrienes release from guinea pig lung fragments or mouse cultured mast cells. Quinotolast concentration-dependently inhibits pLTs release from cultured mast cells. The IC_{50} value for Quinotolast is 0.72 μg/mL[2]. **In Vivo:** Quinotolast potently inhibits such type I allergic reactions as passive cutaneous anaphylaxis (PCA) and anaphylactic bronchoconstriction in rats by both intravenous and oral dosing. When Quinotolast is given i.v. to rats, Quinotolast, dose-dependently inhibits PCA. The doses of Quinotolast required to inhibit the reaction by 50% (ED_{50}) is 0.0063 mg/kg. Given p.o., Quinotolast inhibits the reaction. ED_{50} value for Quinotolast is 0.0081 mg/kg. Although almost complete inhibition is observed with Quinotolast at a dose of 0.32 mg/kg, its effect is slightly attenuated at a dose of 1 mg/kg[2].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: Quinotolast is dissolved in DMSO (for 1 μg/mL and over) or purified water (for under 1 μg/mL) and diluted with reaction buffers[2].[2]**Mast cells** are obtained after the culture of bone marrow cells from the femurs of female BDF_1 mice in the presence of conditioned medium from WEHI-3 cells containing interleukin 3. The cells are suspended with Tyrode's buffer (137 mM NaCI, 2.7 mM KC1, 1.8 mM $CaCl_2$, 1 mM $MgCl_2$, 0.4 mM NaH_2PO_4, 11.9 mM $NaHCO_3$, 5.6 mM glucose) containing 0.1% gelatin and are sensitized with mouse monoclonal anti-DNP IgE (50 μg/10^6 cells). Then the cells are washed and resuspended with Tyrode's buffer containing 0.25% BSA. The cells (2×10^6 cells) are incubated for 5 min at 37°C and challenged with TNP-BSA (2 ng BSA/mL). **Quinotolast (0.1, 1, 10, 100 ug/mL)** is added to the reaction tube simultaneously with the antigen. Ten minutes later, the reaction is stopped by the addition of EDTA (2.7 mM). pLTs in the cell supernatant sre quantified as immunoreactive leukotriene C_4 ($iLTC_4$) with a leukotriene $C_4/D_4/E_4$[^{3}H] assay system. % Inhibition is calculated in each experiment from the amount of immunoreactive leukotriene C_4 ($iLTC_4$)[2].

Animal Administration: For oral dosing, Quinotolast is dissolved or suspended in 0.5% methylcellulose (Rats)[2].

For i.v. dosing, Quinotolast is dissolved in 0.12 mM Na_2CO_3 and diluted with 0.1 % $NaHCO_2$ containing saline or is dissolved in saline (Rats)[2].[2]Rats [2]

Rats (8 week-old) are used. To study the presence of tachyphylaxis by Quinotolast, **Quinotolast (0.001, 0.01, 0.1, 1,10 and 100**

mg/kg) is given i.v. in a large dose 30 min before challenge, and again at a smaller dose simultaneously with the antigen challenge.

References:

[1]. Okayama Y, et al. Inhibition of histamine and eicosanoid release from dispersed human lung cells in vitro byquinotolast. Jpn J Pharmacol. 1995 Dec;69(4):375-80.

[2]. Kobayashi K, et al. Effects of quinotolast, a new orally active antiallergic drug, on experimental allergic models. Jpn J Pharmacol. 1993 Sep;63(1):73-81.

CAIndexNames:

4H-Quinolizine-3-carboxamide, 4-oxo-1-phenoxy-N-2H-tetrazol-5-yl-, sodium salt (1:1)

SMILES:

O=C(NC1=NN=NN1)C2=CC(OC3=CC=CC=C3)=C4N(C2=O)C=CC=C4.[Na]

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