Pranlukast

Cat. No.: HY-B0290

CAS No.: 103177-37-3

Molecular Formula: $C_{27}H_{23}N_5O_4$

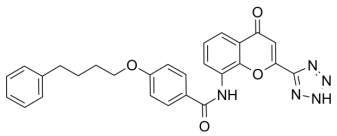
Molecular Weight: 481.5

Target: Leukotriene Receptor; Endogenous Metabolite

Pathway: GPCR/G Protein; Metabolic Enzyme/Protease

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 33.33 mg/mL (69.22 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0768 mL	10.3842 mL	20.7684 mL
5 mM	0.4154 mL	2.0768 mL	4.1537 mL
10 mM	0.2077 mL	1.0384 mL	2.0768 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.75 mg/mL (5.71 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.75 mg/mL (5.71 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Pranlukast is a highly potent, selective and competitive antagonist of peptide leukotrienes. Pranlukast inhibits [^{3}H]LTE_4, [^{3}H]LTD_4, and [^{3}H]LTC_4 bindings to lung membranes with K_is of 0.63±0.11, 0.99±0.19, and 5640±680 nM, respectively.

IC_{50} & Target

LTE_4	LTD_4	LTC_4
0.63 nM (Ki)	0.99 nM (Ki)	5640 nM (Ki)

In Vitro

In the radioligand binding assay, Pranlukast (ONO-1078) inhibits [^{3}H]LTE_4, [^{3}H]LTD_4, and [^{3}H]LTC_4 bindings to lung membranes with K_is of 0.63±0.11, 0.99±0.19, and 5640±680 nM, respectively. The antagonism of Pranlukast against [^{3}H]LTD_4 binding is competitive. In functional experiments, Pranlukast shows competitive antagonism against the LTC_4- and LTD_4-

	induced contractions of guinea pig trachea and lung parenchymal strips with a pA_2 range of 7.70 to 10.71. In the presence of an inhibitor of the bioconversion of LTC_4 to LTD_4, Pranlukast also antagonizes the LTC_4-induced contraction of guinea pig trachea (pA_2=7.78). Pranlukast significantly reverses the LTD_4-induced prolonged contraction without effect on the KCl- and $BaCl_2$-induced contractions of guinea pig trachea[1]. Oxygen-glucose deprivation (OGD)-induced nuclear translocation of $CysLT_1$ receptors is inhibited by pretreatment with the $CysLT_1$ receptor antagonist Pranlukast (10 μM). Pranlukast protects endothelial cells against ischemia-like injury. The effects of the $CysLT_1$ receptor antagonist Pranlukast and the 5-lipoxygenase inhibitor Zileuton on translocation are also assessed. The results show that Pranlukast, but not Zileuton, inhibits the translocation of the $CysLT_1$ receptor 6 h after OGD[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Carrageenan (CAR, 5 mg per mouse) is injected i.p. 24 h before LPS (50 p,g per mouse) is injected i.v. Various doses of Pranlukast (ONO-1078; 40, 20, and 10 mmol/kg), AA-861 (20, 10, and 5 mmol/kg), Indomethacin (40 mmollkg), and the controls are injected s.c. into mice 30 min before they are challenged with 50 p,g of LPS. The maximum soluble doses are 0.6 mmol/mL in 10% DMSO for AA-861 and 1.2 mmol/mL in 10% ethanol for Pranlukast. These solutions are used as the maximum doses for the treatments. The mortality of mice is significantly decreased in AA-861- Pranlukast-treated mice relative to that in the control mice. Pretreatment with CAR (5 mg i.p.) renders the mice more sensitive to the effect of LPS. Although the survival rate of mice treated with each solvent is 20% at 72 h after LPS (50 p,g per mouse) administration, s.c. treatment with AA-861 (20 mmol/kg) or Pranlukast (40 mmol/kg) significantly increases the survival rate after the LPS administration (AA-861, $P<0.001$; Pranlukast, $P<0.01$)[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	EA.hy926 cells are cultured in Dulbecco's modified Eagle's medium (DMEM), supplemented with 10% heat-inactivated fetal calf serum, Penicillin (100 U/mL) and Streptomycin (100 mg/mL). Experiments are conducted 24 h after cells are seeded. OGD is performed. Briefly, the original medium is removed; the cells are washed twice with glucose-free Earle's balanced salt solution (EBSS) and placed in fresh glucose-free EBSS. Cultures are then placed in an incubator containing 5% CO_2 and 95% N_2 at 37°C for 2 to 8 h. Control cultures are maintained in glucose-containing EBSS under normal conditions. 10 μM Pranlukast, 10 μM Zileuton, a 5-LOX inhibitor or 10 μM Pyrrolidine dithiocarbamate (PDTC), is added to the culture 30 min before OGD exposure and maintained during OGD[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Mice[3] Male ddY mice are used. All mice used are 7 to 8 weeks of age. Endotoxin shock is induced in mice. In brief, CAR (5 mg in 0.5 mL of physiological saline) is injected intraperitoneally (i.p.) as a priming agent 24 h before LPS challenge. LPS (50 p,g in 0.5 mL of physiological saline) is injected intravenously into the tail vein as an inducing agent. The indicated doses of AA-861, Pranlukast (40, 20, and 10 mmol/kg), saline, DMSO, or ethanol are administrated subcutaneously (s.c.) in a volume of 1 mL into the backs of mice 30 min before the LPS provocation. Both drugs are injected s.c., because CAR i.p. pretreatment caused peritonitis. To examine the role of endogenous TNF in CAR pretreated mice, 2×10^5 U of rabbit anti-TNF-a antibody or normal serum of rabbit in 0.2 mL is injected intravenously (i.v.) before the LPS challenge[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- J Neurosci. 2016 Oct 12;36(41):10560-10573.

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REFERENCES

[1]. Obata T, et al. In vitro antagonism of ONO-1078, a newly developed anti-asthma agent, against peptide leukotrienes in isolated guinea pig tissues. Jpn J Pharmacol. 1992 Nov;60(3):227-37.

[2]. Fang SH, et al. Nuclear translocation of cysteinyl leukotriene receptor 1 is involved in oxygen-glucose deprivation-induced damage to endothelial cells. Acta Pharmacol Sin. 2012 Dec;33(12):1511-7.

[3]. Ogata M, et al. Protective effects of a leukotriene inhibitor and a leukotriene antagonist on endotoxin-induced mortality in carrageenan-pretreated mice. Infect Immun. 1992 Jun;60(6):2432-7.

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