Aplaviroc hydrochloride

Cat. No.: HY-17450A

CAS No.: 461023-63-2

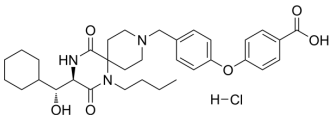
Molecular Formula: $C_{33}H_{44}ClN_3O_6$

Molecular Weight: 614.17

Target: CCR; HIV

Pathway: GPCR/G Protein; Immunology/Inflammation; Anti-infection

Storage: 4°C, sealed storage, away from moisture
* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 200 mg/mL (325.64 mM; Need ultrasonic)
H_2O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	1.6282 mL	8.1411 mL	16.2821 mL
5 mM	0.3256 mL	1.6282 mL	3.2564 mL
10 mM	0.1628 mL	0.8141 mL	1.6282 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: ≥ 12.5 mg/mL (20.35 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 12.5 mg/mL (20.35 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 12.5 mg/mL (20.35 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Aplaviroc (AK 602) hydrochloride, a SDP derivative, is a CCR5 antagonist, with IC_{50}s of 0.1-0.4 nM for HIV-1_{Ba-L}, HIV-1_{JRFL} and HIV-1_{MOKW}.

IC_{50} & Target

HIV-1_{Ba-L}	HIV-1_{JRFL}	HIV-1_{MOKW}	CCR5
0.4 nM (IC_{50})	0.1 nM (IC_{50})	0.2 nM (IC_{50})	

In Vitro

Aplaviroc exerts potent activity against three wild-type R5 HIV-1 strains (HIV-1_{Ba-L}, HIV-1_{JRFL} and HIV-1_{MOKW}) with IC_{50} values of 0.1 to 0.4 nM. Aplaviroc is substantially more potent than two previously published CCR5 inhibitors, E921/TAK-779

and AK671/SCH-C. Aplaviroc suppresses the infectivity and replication of two HIV-1_{MDR} variants, HIV-1_{MM} and HIV-1_{JSL}, at extremely low concentrations (IC_{50} values of 0.4 to 0.6 nM). Aplaviroc binds to CCR5 with high affinity. The K_d values thus determined for Aplaviroc, E913, E921/TAK-779, and AK671/SCH-C are 2.9±1.0, 111.7±3.5, 32.2±9.6, and 16.0±1.5 nM, respectively. Aplaviroc potently blocks rgp120/sCD4 binding to CCR5 with an IC_{50} value of 2.7 nM. These results suggest that the potent activity of Aplaviroc against R5 HIV-1 stems from its binding to ECL2B and/or its vicinity with high affinity, resulting in inhibition of gp120/CD4 binding to CCR5[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

The concentration of Aplaviroc (AK602) reached the maximal concentration immediately after intraperitoneal administration and decreased rapidly[2].

Aplaviroc (AK602, 60 mg/kg, bid, daily) suppresses R5 HIV-1 viremia in hu-PBMC-NOG mice[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	hu-PBMC-NOG mice[2].
Dosage:	60 mg/kg.
Administration:	Single intraperitoneal administration, bid, daily.
Result:	The numbers of $CD4^+$ cells/μL in saline-treated mice were significantly less than those of AK602-treated, ddI-treated, or uninfected mice.

REFERENCES

[1]. Maeda K, et al. Spirodiketopiperazine-based CCR5 inhibitor which preserves CC-chemokine/CCR5 interactions and exerts potent activity against R5 human immunodeficiency virus type 1 in vitro. J Virol. 2004 Aug;78(16):8654-62.

[2]. Hirotomo Nakata, et al. Potent anti-R5 human immunodeficiency virus type 1 effects of a CCR5 antagonist, AK602/ONO4128/GW873140, in a novel human peripheral blood mononuclear cell nonobese diabetic-SCID, interleukin-2 receptor gamma-chain-knocked-out AIDS mouse model. Virol. 2005 Feb;79(4):2087-96.

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