(Rac)-PF-184 hydrate

Cat. No.: HY-107591A

Molecular Formula: $C_{32}H_{34}ClFN_6O_5$

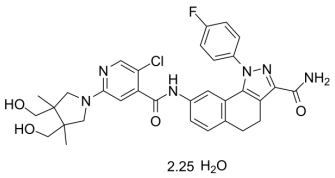
Molecular Weight: 659.64

Target: IKK

Pathway: NF-κB

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



BIOLOGICAL ACTIVITY

Description

(Rac)-PF-184 hydrate is a potent inhibitory factor-κB kinase 2 (IKK-2) inhibitor with an IC_{50} of 37 nM. (Rac)-PF-184 hydrate has anti-inflammatory effects[1].

IC_{50} & Target

IKK-2
37 nM (IC_{50})

In Vitro

(Rac)-PF-184 has slow dissociation kinetics with a $T_{1/2}$ of 6.7 h from rhIKK-2, very low oral bioavailability (5%), high intravenous clearance (59 ml/min/kg), and high P450 metabolism in human liver microsomes[1].
(Rac)-PF-184 binds tightly to endogenous IKK-2 and shows extended inhibition of kinase activity and cytokine production[1].
(Rac)-PF-184 shows a concentration-dependent inhibition on LPS- and IL-1β-induced production of inflammatory mediators in a variety of human disease-relevant cells[1].
(Rac)-PF-184 (0.001-10 μM; 1 h) inhibits IL-1β-induced TNF-α in a concentration-dependent manner with maximal efficacies of 94% and relative potencies of 163 nM[1].
(Rac)-PF-184 inhibits LPS-induced cytokine production from rat alveolar macrophages and blocked p65 nuclear translocation[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

(Rac)-PF-184 (0.3-2.5 mg; i.t.; once) blocks neutrophil infiltration and BAL cell cytokine production[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Fasted male Sprague-Dawley rats (350 g) placed into a chamber connected to a large volume nebulizer filled with 20 ml of 1 mg/mL solution of LPS[1]
Dosage:	0.3-2.5 mg
Administration:	Nano suspension and administered intratracheally in a volume of 100 μL, 60 min before aerosolized LPS
Result:	Resulted in a comparable attenuation of total cell and PMN cell infiltration 4 h after LPS exposure. Dose-dependently inhibited cell infiltration with EC_{50} values of 1 mg. Dose-dependently suppressed BAL fluid TNF- and PGE2 levels comparable with cell infiltration. Inhibited p65 translocation. Showed long-lasting activity.

REFERENCES

[1]. Sommers CD, et al. Novel tight-binding inhibitory factor-kappaB kinase (IKK-2) inhibitors demonstrate target-specific anti-inflammatory activities in cellular assays and following oral and local delivery in an in vivo model of airway inflammation. J Pharmacol Exp Ther. 2009 Aug;330(2):377-88.

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