JAK1/TYK2-IN-3

Cat. No.: HY-143885

CAS No.: 2734918-37-5

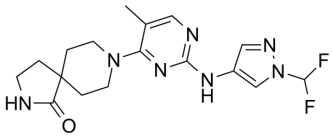
Molecular Formula: $C_{17}H_{21}F_2N_7O$

Molecular Weight: 377.39

Target: JAK

Pathway: Epigenetics; JAK/STAT Signaling; Stem Cell/Wnt

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

JAK1/TYK2-IN-3 is a potent, selective and orally active dual TYK2/JAK1 inhibitor with IC_{50} values of 6 and 37 nM, respectively. JAK1/TYK2-IN-3 also shows selectively relative to JAK2 (IC_{50}=140 nM) and JAK3 (IC_{50}=362 nM). JAK1/TYK2-IN-3 shows anti-inflammatory effect by regulating the expression of related TYK2/JAK1-regulated genes, as well as the formation of Th1, Th2, and Th17 cells[1].

IC_{50} & Target

Tyk2	JAK1	JAK2	JAK3
6 nM (IC_{50})	37 nM (IC_{50})	140 nM (IC_{50})	362 nM (IC_{50})

In Vitro

JAK1/TYK2-IN-3 (compound 48) (10, 20, 30 mg/kg) shows anti-inflammatory effect by regulating the formation of Th1, Th2, Th17 cells[1].

JAK1/TYK2-IN-3 (10, 20, 30 mg/kg) inhibits the NF-κB signaling pathway by inhibits the JAK-STAT pathway, thereby reducing the inflammatory response in ulcerative colitis (UC) mice[1].

JAK1/TYK2-IN-3 (10, 20, 30 mg/kg) dose-dependently inhibits the mRNA expression of TNF-α, IL-1β, IL-12, IL-17A, IL-22, IFN-α, and IFN-β[1].

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

In Vivo

JAK1/TYK2-IN-3 (10, 20, 30 mg/kg; p.o.; twice a day for 12 days) shows a good therapeutic effect on ulcerative colitis (UC)[1].

JAK1/TYK2-IN-3 (5 mg/kg, p.o.) shows 23.7% oral bioavailability in rats[1].

Pharmacokinetic Parameters of JAK1/TYK2-IN-3 in male Sprague-Dawley rats[1].

compd	dose(mg/kg)	Administration	C_{max}(ng/mL)	Cl ($Lh^{-1}kg^{-1}$)	$T_{1/2}$(h)	AUC_{0-t} (ng·h/mL)	F (%)
48	5 mg/kg	p.o.	400.4±55.3	11.3±5.2	2.4±2.1	440.9±157.0	23.7

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

Animal Model:	6-8 weeks, 270-325g male Sprague-Dawley rats[1]
Dosage:	5 mg/kg
Administration:	p.o.

Result:	Showed 23.7% oral bioavailability in rats.

Animal Model:	Six-eight week old male C57BL/6 mice, 20-22 g (2.5% dextran sulfate sodium (DSS)-induced acute UC mouse model)[1]
Dosage:	10, 20, 30 mg/kg
Administration:	p.o., twice a day, 12 days
Result:	Improved the infiltration of inflammatory factors and reduced the damage caused by DSS.

REFERENCES

[1]. Yang T, et al. Identification of a Novel 2,8-Diazaspiro[4.5]decan-1-one Derivative as a Potent and Selective Dual TYK2/JAK1 Inhibitor for the Treatment of Inflammatory Bowel Disease. J Med Chem. 2022; 65(4):3151-3172.

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