KHK-IN-1

Cat. No.: HY-12841

CAS No.: 1303469-70-6

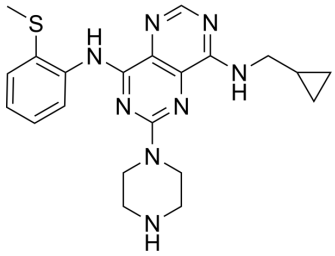
Molecular Formula: $C_{21}H_{26}N_8S$

Molecular Weight: 422.55

Target: Ketohexokinase

Pathway: Metabolic Enzyme/Protease

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



BIOLOGICAL ACTIVITY

Description

KHK-IN-1 (compound 8) is a selective and cell membrane permeable ketohexokinase (KHK) inhibitor (IC_{50}=12 nM; F=34%). KHK-IN-1 inhibits the production of F1P in HepG2 cell lysates (IC>sub>50=400 nM). KHK-IN-1 has potential for the study of diabetes and obesity[1].

IC_{50} & Target

IC50=12 nM (KHK)[1].

In Vitro

KHK-IN-1 stable in human and rat liver microsome preparations (88 and 72% remaining at 10 min) and do not significantly inhibit cytochrome P450s from human liver microsomes (1A2, 2C19, 2D6, 2C9, and 3A4)[1].

KHK-IN-1 (0-10 μM; incubate 30 min, then add to 15 mM fructose and incubate for another 3 h) inhibits production of F1P in HepG2 cell lysates with an IC_{50} value of 400 nM[1].

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

Cell Viability Assay[1]

Cell Line:	HepG2 cells
Concentration:	0-10 μM
Incubation Time:	Incubate 30 min, then add to 15 mM fructose and incubate for another 3 h
Result:	Exhibited inhibition of F1P production in HepG2 cell lysates (IC_{50}=400 nM).

In Vivo

KHK-IN-1 (10 mg/kg; p.o.; single) shows oral bioavailability of 34% in rats[1].

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

Animal Model:	Male Sprague-Dawley rats (~250 g)[1].
Dosage:	10 mg/kg
Administration:	Oral gavage; single
Result:	Exhibited reasonable oral bioavailability in rats (F=34%; oral $t_{1/2}$=4 h), but had a high volume of distribution (Vd_{ss}= 32 L/kg) and a high rate of clearance (CL=160 mL/min/kg).

REFERENCES

[1]. Maryanoff BE, et al. Inhibitors of Ketohexokinase: Discovery of Pyrimidinopyrimidines with Specific Substitution that Complements the ATP-Binding Site. ACS Med Chem Lett. 2011 Apr 18;2(7):538-43.

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