JH-XVII-10

Cat. No.: HY-144614

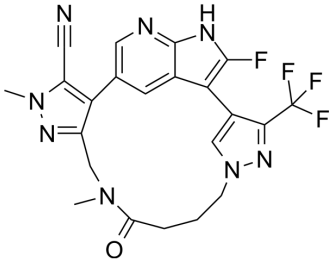
Molecular Formula: $C_{22}H_{18}F_4N_8O$

Molecular Weight: 486.42

Target: DYRK; Apoptosis

Pathway: Protein Tyrosine Kinase/RTK; Apoptosis

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



BIOLOGICAL ACTIVITY

Description

JH-XVII-10 is a potent, selective and orally active DYRK1A and DYRK1B inhibitor with IC_{50}s of 3 nM and 5 nM for DYRK1A and DYRK1B, respectively. JH-XVII-10 shows antitumor efficacy in neck squamous cell carcinoma (HNSCC) cell lines[1].

IC_{50} & Target

DYRK1A	DYRK1B
3 nM (IC_{50})	5 nM (IC_{50})

In Vitro

JH-XVII-10 (compound 10) (1 μM; CAL27 cells) shows active against JNK1 (IC_{50}=1130 nM), JNK2 (IC_{50}=1100 nM), JNK3 (IC_{50} =>10 000 nM), FAK (IC_{50}=90 nM), RSK1 (IC_{50}=82 nM), RSK2 (IC_{50}=80 nM), RSK3 (IC_{50}=61 nM)[1].

JH-XVII-10 (10 μM; 72 h) decreases cell proliferation by ~45%, and ~40% for CAL27 and FaDu cells, respectively[1].

JH-XVII-10 (1, 10 μM; 24 h) induces apoptosis in CAL27 cells[1].

JH-XVII-10 (0.5, 1, 5, 10 μM; 24 h) shows inhibitory effects on pro-tumor signaling in CAL27 cells[1].

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

Cell Proliferation Assay[1]

Cell Line:	CAL27, FaDu, HEK293FT cells
Concentration:	10 μM
Incubation Time:	72 h
Result:	Decreased cell proliferation by ~45%, and ~40% for CAL27 and FaDu cells, respectively.

Western Blot Analysis[1]

Cell Line:	CAL27 cells
Concentration:	0.5, 1, 5, 10 μM
Incubation Time:	24 h
Result:	Showed inhibitory effects on pro-tumor signaling.

Apoptosis Analysis[1]

Cell Line:	CAL27 cells

Concentration:	1, 10 μM
Incubation Time:	24 h
Result:	Induced increases in the proapoptotic marker (cleaved PARP), and decreased the expression of antiapoptotic protein BCL-xL.

In Vivo

JH-XVII-10 (2 mg/kg, i.v.; 10 mg/kg, p.o.) shows oral bioavailability (F=12%)[1].Pharmacokinetic Parameters of JH-XVII-10 in C57Bl/6 male mice[1].

administration	parameters	rat	dog
i.v.	$T_{1/2}$ (h)	1.4±0.3	5.70±1.2
	$AUC_{0-\infty}$ (ng*h/mL)	931.3±95.7	14,830.8±5475.4
	CL (mL/min/kg)	17.6±2.0	149.9±62.5
	V_{ss} (L/kg)	1.7±0.2	828.7±134.2
p.o.	C_{max} (ng/mL)	1661.1±916.6	3979.4±483.5
	T_{max}(h)	0.9±0.8	1.3±0.5
	$T_{1/2}$ (h)	1.4±0.2	4.9±0.6
	$AUC_{0-\infty}$ (ng*h/mL)	5044.9±1061	23,109.9±7752.2
	F (%)	54.2	31.8

C57Bl/6 male mice; 2 mg/kg, i.v.; 10 mg/kg, p.o.[1]

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

Animal Model:	C57Bl/6 male mice[1]
Dosage:	
Administration:	2 mg/kg, i.v.; 10 mg/kg, p.o.
Result:	Showed oral bioavailability (F=12%).

REFERENCES

[1]. Powell CE, et al. Selective Macrocyclic Inhibitors of DYRK1A/B. ACS Med Chem Lett. 2022; 13(4):577-585.

Caution: Product has not been fully validated for medical applications. For research use only.

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