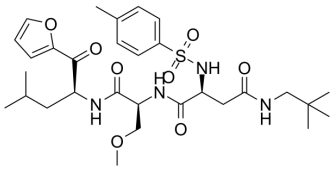
20S Proteasome-IN-2

Cat. No.:	HY-150590
CAS No.:	2028300-31-2
Molecular Formula:	$C_{30}H_{44}N_4O_8S$
Molecular Weight:	620.76
Target:	Proteasome
Pathway:	Metabolic Enzyme/Protease
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

20S Proteasome-IN-2 is a human 20S proteasome inhibitor. 20S Proteasome-IN-2 shows high selectivity to its β5 subunit with the IC_{50} of 0.18 μM. 20S Proteasome-IN-2 displays anti-proliferative effect in vitro and in vivo, and arrests cell cycle at G2/M[1].

IC_{50} & Target

IC50: 0.18 μM (β5 subunit of 20S Proteasome)

In Vitro

20S Proteasome-IN-2 (compoun 11m) inhibits 20S proteasome by forming no irreversible covalent modification on it[1].
20S Proteasome-IN-2 (compoun 11m) (1.56, 3.13, 6.25, 12.5, and 25 μM) shows high binding affinity with purified human 20S proteasome, the equilibrium dissociation constants is 4.8 μM[1].
20S Proteasome-IN-2 (compoun 11m) (0-1.5 μM; 24 hours) inhibits tumor cells in a low concerntration with IC_{50} values of 0.88, 0.77, 0.67, 0.73, 1.3, 0.57, and 0.28 μM for A375, BGC-823, Hela, HT-29, A549, PCM1E8, HCT-116, resepectively[1].
20S Proteasome-IN-2 (compoun 11m) (0-1.5 μM; 24 hours) arrests the cell cycle at G2/M[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Cycle Analysis[1]

Cell Line:	Human colorectal cancer cell line HCT-116 cells
Concentration:	1 μM
Incubation Time:	24 hours
Result:	Arrested the cell cycle at G2/M.

In Vivo

20S Proteasome-IN-2 (compoun 11m) is (i.v.; 5 mg/kg; single injection) rapidly cleared from the plasma with an average terminal plasma half-life of 14 min, thus it exhibits extensive tissue permeability and low clearance rate (CL) of 2.0 L/h/k, and is largely eliminated extrahepatically[1].
20S Proteasome-IN-2 (compoun 11m) (i.v.; 10 mg/kg; twice one week; 4 weeks) shows antitumor efficacy combat solid tumors[1].
Pharmacokinetic parameters of 20S Proteasome-IN-2 (compoun 11m)[1]

Administrations	C_{max} (μg/L)	AUC_{0-t} (μg/L•h)	$T_{1/2}$ (min)	MRT (min)	CL (L/h/kg)	V_{ss} (L/kg)

iv, 5 mg/kg	2007	680	13.83	20.20	2.0	0.66

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Animal Model:	HCT-116 cell xenograft nude mice model[1]
Dosage:	10 mg/kg
Administration:	Intravenous injection; twice weekly for consecutive four weeks
Result:	Inhibited tumor growth in vivo and was well tolerated.

REFERENCES

[1]. Sun Q, et al. Design and synthesis of tripeptidyl furylketones as selective inhibitors against the β5 subunit of human 20S proteasome. Eur J Med Chem. 2020 Apr 15. 192:112160.

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