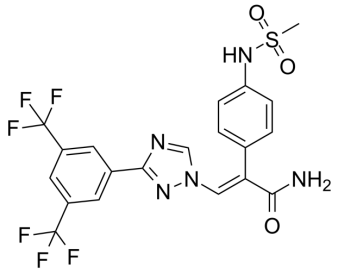
XPO1-IN-1

Cat. No.:	HY-144763
Molecular Formula:	$C_{20}H_{15}F_6N_5O_3S$
Molecular Weight:	519.42
Target:	Apoptosis
Pathway:	Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	XPO1-IN-1 (compound D4) is an orally active and potent XPO1 inhibitor, with an IC_{50} of 24 nM in MM.1S cell. XPO1-IN-1 can efficiently induce cell apoptosis and cell cycle arrest. XPO1-IN-1 displays favorable metabolic stability and pharmacokinetic properties. XPO1-IN-1 can be used for multiple myeloma (MM) research[1].
IC_{50} & Target	XPO1

In Vitro

XPO1-IN-1 (compound D4) (24 h) shows high anti-proliferation efficacy in MM.1S cell and lymphomatous cell lines[1].
XPO1-IN-1 (0-10 μM, 24 h) induces cancer cell cycle arrest[1].
XPO1-IN-1 (0-10 μM, 48 h) induces apoptosis of MM.1S cell[1].
XPO1-IN-1 (0-10 μM, 2 h) inhibits XPO1-dependent nuclear export[1].
XPO1-IN-1 shows the good metabolic stability, with more than 80% intact compound remained over rat plasma (2 h), and around 85% intact compound remained in liver microsomes (1 h)[1].

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

Cell Proliferation Assay

Cell Line:	MM.1S, Mino, VAL, Rael, Namaiwa, Mutu, H9, JB6, and YT[1]
Concentration:	
Incubation Time:	24 h
Result:	Showed high anti-proliferation efficacy in MM.1S cell and lymphomatous cell lines (Mino, VAL, Rael, Namaiwa, Mutu, H9, JB6, and YT), with IC_{50} values of 24, 80.2, 189.1, 201.8, 77.7, 158.2, 101.1, 154.1, and 75.4 nM, respectively.

Cell Cycle Analysis

Cell Line:	MM.1S cell[1]
Concentration:	0, 0.1, 1, 5, and 10 μM
Incubation Time:	24 h
Result:	Induced cancer cell cycle arrest in high concentration (>100 nM), increased the population of cells arrested in G2 to 37.3% in 5 μM.

Apoptosis Analysis

Cell Line:	MM.1S cell[1]
Concentration:	0, 0.1, 1, and 10 μM
Incubation Time:	48 h
Result:	Induced apoptosis, significantly increased the apoptotic cell rate to 64.7% (10 μM) when compared to the sample with negative control (6.7%).

Immunofluorescence

Cell Line:	MM.1S cell[1]
Concentration:	0, 0.1, 1, and 10 μM
Incubation Time:	2 h
Result:	Inhibited XPO1-dependent nuclear export.

In Vivo

XPO1-IN-1 (compound D4) (Sprague Dawley rats; 10 mg/kg, IG; 1 mg/kg, IV; once) shows a good pharmacokinetic properties [1].Pharmacokinetic Parameters of XPO1-IN-1 in SD rats[1].

Parameters	i.g. (10 mg/kg)	i.v. (1 mg/kg)
T_{max} (h)	2.17 ± 1.76	0.08
$T_{1/2}$ (h)	2.12 ± 0.16	2.32 ± 0.17
C_{max} (ng/mL)	1391.27 ± 586.77	1239.08 ± 152.54
AUC_{0-t} (ng/mL·h)	5774.13 ± 1461.41	1668.03 ± 229.48
$AUC_{0-\infty}$ (ng/mL·h)	6387.17 ± 1637.18	1791.40 ± 236.56
CL (mL/h/kg)	1638.65 ± 431.97	565.30 ± 80.40
F (%)	34.6	

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Animal Model:	Sprague Dawley rats[1]
Dosage:	10 mg/kg (IG), 1 mg/kg (IV)
Administration:	Oral gavage (IG), IV, once (Pharmacokinetic Analysis)
Result:	Showed a good pharmacokinetic properties, with relatively long half-life of 2.12 h (IG) and 2.32 h (IV), respectively, and decent bioavailability F (%) of 34.6%.

REFERENCES

[1]. Qu B, et al. Design, synthesis and biological evaluation of sulfonamides inhibitors of XPO1 displaying activity against multiple myeloma cells. Eur J Med Chem. 2022;235:114257.

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