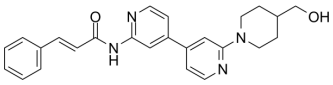
BPA-B9

Cat. No.:	HY-149086
Molecular Formula:	$C_{25}H_{26}N_4O_2$
Molecular Weight:	414.5
Target:	RAR/RXR; Apoptosis; PARP; Bcl-2 Family
Pathway:	Metabolic Enzyme/Protease; Vitamin D Related/Nuclear Receptor; Apoptosis; Cell Cycle/DNA Damage; Epigenetics
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

BPA-B9 is a RXRα ligand and antagonist targeting the pRXRα-PLK1 interaction. BPA-B9 has excellent RXRα-binding affinity (K_D=39.29 ± 1.12 nM). BPA-B9 inhibits the proliferation of cancer cells by inducing mitotic arrest and cell apoptosis[1].

IC_{50} & Target			
	PARP	Bcl-2	Mcl-1

In Vitro

BPA-B9 (0-250 nM, 24 h) induces a dose-dependent increase of apoptotic cells in MDA-MB-231 cells[1].
BPA-B9 (0-125 nM, 12 h) inhibits the cell cycle of A549 in the G2/M phase[1].
BPA-B9 (0-500 nM, 0-24 h) induces a dose- and time-dependent increase in the expression of cleaved PARP, and anti-apoptosis proteins Bcl-2 and Mcl-1 were reduced dose-dependently[1].
BPA-B9 shows excellent anti-proliferative activity against TNBC cell line MDA-MB-231 (IC_{50}=16 ± 3 nM, SI > 3), and displays potent activities against HCC1937, A549, H460, HepG2, and HeLa cells with IC_{50} values of 0.561 μM, 0.201 μM, 0.253 μM, 0.128 μM, and 0.077 μM, respectively[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Apoptosis Analysis[1]

Cell Line:	MDA-MB-231 cells and A549 cells
Concentration:	0, 31.25, 62.50, 125, and 250 nM
Incubation Time:	24 h
Result:	Induced a dose-dependent t (0, 31.25, 62.50, 125, and 250 nM) increase (7.96, 16.94, 28.30, 30.40, 40.40%) of apoptotic cells in MDA-MB-231 cells.

Cell Cycle Analysis[1]

Cell Line:	MDA-MB-231 cells and A549 cells
Concentration:	0, 15.625, 31.25, 62.50, and 125 nM
Incubation Time:	12 h
Result:	Inhibited the cell cycle of A549 in the G2/M phase. After incubation with BPA-B9 at 62.50 nM and 125 nM, the percentage of A549 cells in the G2/M phase reached 12.89% and 46.49%, respectively, compared to 8.62% in untreated cells.

Western Blot Analysis[1]

Cell Line:	MDA-MB-231 cells
Concentration:	0, 7.8, 31.3, 125, and 500 nM
Incubation Time:	0, 1, 3, 6, 8, 10, 12, 16, and 24 h
Result:	Induced a time-dependent increase in the expression of cleaved PARP. Moreover, cleaved PARP was elevated, and anti-apoptosis proteins Bcl-2 and Mcl-1 were reduced dose-dependently.

In Vivo

BPA-B9 (0-25 mg/kg, IP, once every day for 15 days) has significant anticancer efficacy in vivo with no considerable side effects[1].

BPA-B9 (25 mg/kg, IP or PO, once) displays better pharmacokinetics than the lead XS-060 (HY-149085)[1].

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

Animal Model:	BALB/c mice (aged 4-6 weeks, with injection of MDA-MB-231 cells)[1]
Dosage:	0, 12.5, 25 mg/kg
Administration:	IP, once every day for 15 days
Result:	Inhibited tumor growth by causing mitotic arrest, chromosome aberrations, and DNA-damage response. Significantly reduced the tumor volume and the tumor growth inhibition (TGI) of BPA-B9 was 59.3% at a dosage of 25.0 mg/kg/day, but a slight difference was shown at the dose of 12.5 mg/kg/day with no statistical significance.

Animal Model:	Sprague-Dawley rats (10-14 weeks, 200-220g)[1]
Dosage:	25 mg/kg
Administration:	Oral absorption (p.o.) and intraperitoneal injection (i.p.), once, (Pharmacokinetic Analysis)
Result:	The oral absorption of BPA-B9 is very poor, while intraperitoneal injection displayed good absorption. Pharmacokinetic Parameters of XS-060 in Sprague-Dawley rats[1].

	BPA-B9 25 mg/kg (i.p.)
T_{max} (h)	0.14 ± 0.10
C_{max} (μg/L)	8083.33 ± 1193.04
$AUC_{0-\infty}$ (μg⋅h/L)	14615.65 ± 5508.77
$T_{1/2}$ (h)	2.23 ± 0.17
CLz/F (L/(h⋅kg))	1.55 ± 0.73
Vd, z/F (L/kg)	5.15 ± 2.78

REFERENCES

[1]. Chen J, et al. Discovery of bipyridine amide derivatives targeting pRXRα-PLK1 interaction for anticancer therapy. Eur J Med Chem. 2023 Apr 6;254:115341.

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