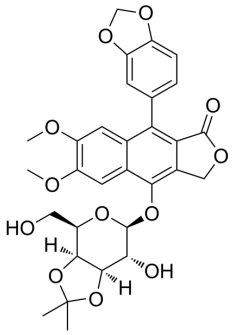
PHY34

Cat. No.:	HY-122650
CAS No.:	2130033-55-3
Molecular Formula:	$C_{30}H_{30}O_{12}$
Molecular Weight:	582.55
Target:	Autophagy
Pathway:	Autophagy
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	PHY34 is an inhibitor that inhibits ATP6V0A2 and CAS thereby inhibiting autophagy, and has a nanomolar effect. PHY34 inhibits cancer cell growth by inducing apoptosis and inhibits tumor growth in xenograft models. PHY34 can be used for research on high grade serous ovarian cancer[1][2].
IC_{50} & Target	ATP6V0A2, cellular apoptosis susceptibility (CAS)[2]

In Vitro

PHY34 (0.001 nM-50 μM, 72 h) inhibits various cancer cells growth with nanomolar potency through activation of apoptosis based on enhanced cPARP levels and has the highest potency in HGSOC cell lines[1].
PHY34 (100 nM, 1 μM; 24 h) blocks the final breakdown of the autolysosomes in OVCAR8 at 100 nM, and in OVCAR3 at 1 μM, respectively[1].
PHY34 (10 nM, 24 h) inhibits the late-stage autophagy that precedes apoptosis induction in OVCAR8[1].
PHY34 (100 nM, 48 h) inhibits the late-stage autophagy that precedes apoptosis induction in OVCAR3[1].
PHY34 (0.01 nM-2 μM, 72 h) induces cell death in the presence of wild-type V0A2, but not V823I mutants in H4 cell[2].
PHY34 (10, 100 nM; 48 h, 72 h) changes subcellular localization of nuclear multiple proteins[2].
PHY34 (20 μM, 1 h) binds specificity with ATP6V0A2 subunit[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1][2]

Cell Line:	OVCAR8, OVCAR3, HT-29, MDA-MB-435, MDA-MB-231, IOSE80, FT33
Concentration:	0.001 nM-50 μM
Incubation Time:	72 h
Result:	Inhibited the growth of various cancer cells with IC_{50} values of 4 nM(OVCAR8, OVCAR3), 43.3 nM(HT-29) , 23 nM(MDA-MB-435) , 5.2 nM(MDA-MB-231). Exhibited no toxicity to IOSE80 and FT33 (IC_{50} >50 μM).

Cell Viability Assay[2]

Cell Line:	H4
Concentration:	0.01 nM-2 μM

Incubation Time:	72 h
Result:	Inhibited mutant cell with an IC_{50} value of 246 pM that was 1000-fold more potent than HTP-013(434 nM). Conferred resistance in V8231 mutation and no impact activity in T216A mutation.

Apoptosis Analysis[1]

Cell Line:	OVCAR8, OVCAR3
Concentration:	10 nM, 100 nM
Incubation Time:	72 h
Result:	Increased the number of cells in early and late apoptosis in OVCAR8 and OVCAR3 at 10 nM and 100 nM, respectively.

Cell Autophagy Assay[1]

Cell Line:	Hela
Concentration:	9.31 fM-20 μM
Incubation Time:	4 h
Result:	Sustained high levels of LC3B puncta with an EC_{50} value of 2 nM. Inhibited autophagy with an EC_{50} value of 3.9 nM.

Cell Autophagy Assay[2]

Cell Line:	OVCAR3
Concentration:	5 nM
Incubation Time:	4 h
Result:	Inhibited autophagy with an ED_{50} value of 6.29 nM, and was more potent than bafilomycin A1 (HY-100558) with an ED_{50} value of 29.1 nM.

Western Blot Analysis[1][2]

Cell Line:	OVCAR8, OVCAR3, OVCAR4
Concentration:	10 nM, 100 nM
Incubation Time:	48 h, 72 h
Result:	Increased cPARP levels in OVCAR8 after 48 h at 10 nM, in OVCAR4 and OVCAR3 after 72 h at 100 nM, respectively. Reversed the conversion of PARP to cPARP combined with RAP (HY-10219) of 1 μM.

Western Blot Analysis[2]

Cell Line:	OVCAR8, OVCAR3, OVCAR4
Concentration:	10 nM
Incubation Time:	24 h, 48 h, 72 h

Result:	Promoted histone H3, LAMP1/2, ACSS2, and PCNA nuclear protein accumulation at 48 h. Reduced expression of KPNA2 (Karyopherin subunit alpha 2) with time-dependent manner. Increased nuclear accumulation of mutant p53 at 48 h.

In Vivo

PHY34 (0.75 mg/kg, i.p., 3 times a week for 3 weeks) inhibits tumor growth and reduces Ki67 expression in tumor tissue in a female nude mouse tumor bearing model constructed by OVCAR8[1].

PHY34 Pharmacokinetics[1]

[redacted][1]

Parameter	Units	IV	IP	PO
Dose	mg/kg	0.6	1.8	75
Dose	nmol	1029.9	3089.8	128742.1
$T_{1/2}$	hr	6.2	8.4	12.3
T_{max}	hr	0.08	0.25	0.25
C_{max}	nmol/L	288.8	519.5	323.6
AUC_{last}	hr*nmol/L	198.8	360.5	599.9
AUC_{inf}	hr*nmol/L	215.8	366.5	663.3
V_z	L/kg	42.7	101.6	3430.3
Cl	L/hr/kg	4.8	8.4	194.1
MRT	hr	6.1	1.9	7.8
F*	%	-	56.6	2.5

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

Animal Model:	OVCAR8-induced xenograft models in female nude mice[1].
Dosage:	0.75 mg/kg, three times a week for three weeks
Administration:	Intraperitoneal injection (i.p.)
Result:	Decreased tumor burden based on average abdominal radiant efficiency with no gross toxicity through analysis of fluorescence imaging.

REFERENCES

[1]. Young AN,et al. Phyllanthusmin Derivatives Induce Apoptosis and Reduce Tumor Burden in High-Grade Serous Ovarian Cancer by Late-Stage Autophagy Inhibition. Mol Cancer Ther. 2018 Oct;17(10):2123-2135.

[2]. Salvi A, et al. PHY34 inhibits autophagy through V-ATPase V0A2 subunit inhibition and CAS/CSE1L nuclear cargo trafficking in high grade serous ovarian cancer. Cell Death Dis. 2022 Jan 10;13(1):45.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA