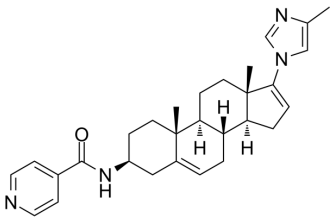
AR antagonist 4

Cat. No.:	HY-151266
CAS No.:	2883447-45-6
Molecular Formula:	$C_{29}H_{36}N_4O$
Molecular Weight:	456.62
Target:	Androgen Receptor
Pathway:	Vitamin D Related/Nuclear Receptor
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	AR antagonist 4 (Compound 67-b) is an orally active androgen receptor (AR) antagonist with an IC_{50} of 246.6 nM against wt-AR, and is also an AR degrader with a DC_{50} of 2.84 μM[1].
IC_{50} & Target	IC_{50}: 208.8 nM (AR(T877A)), 246.6 nM (wt-AR), 268.2 nM (AR (F876L)), 490.2 nM (AR(W741L))[1] DC_{50}: 2.84 μM (AR)[1]
In Vitro	AR antagonist 4 (Compound 67-b) (0-10 μM; 6 days) inhibits LNCaP and 22RV1 cells proliferation[1]. AR antagonist 4 inhibits CYP17A1 with an IC_{50} of 2.59 μM[1]. AR antagonist 4 shows antagonistic activities with IC_{50}s of 490.2, 208.8 and 268.2 nM against AR(W741L), AR(T877A) and AR (F876L), respectively[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	LNCaP and 22RV1 cells
Concentration:	0-10 μM
Incubation Time:	6 days
Result:	Showed antiproliferative activity with IC_{50}s of 246.6 nM and 590 nM against LNCaP and 22RV1 cells, respectively.

Western Blot Analysis[1]

Cell Line:	LNCaP and 22RV1 cells
Concentration:	0, 1, 5, 10 and 20 μM
Incubation Time:	0, 2, 4, 8, 16 and 24 h
Result:	Degraded androgen receptor in a dose- and time- dependent manner.

In Vivo	AR antagonist 4 (Compound 67-b) (20 mg/kg; p.o.; daily for 10 days) inhibits the growth of androgen-sensitive organs (ASOs) under the stimulation of testosterone propionate (TP) in rats[1]. AR antagonist 4 (30 mg/kg; p.o.; daily for 4 weeks) shows antitumor activity in an Enzalutamide (HY-70002)-resistant c4-

2b−ENZ xenograft model in mice[1].

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

Animal Model:	Castrated male Sprague−Dawley rats[1]
Dosage:	20 mg/kg
Administration:	Oral administration, daily for 10 days
Result:	Resulted in statistically significant weight reductions in seminal vesicles (62%, $p < 0.01$) and ventral prostate (66%, $p < 0.01$) versus the testosterone propionate control.

Animal Model:	SPF grade male Babl/c nude male mice, enzalutamide-resistant c4-2b−ENZ xenograft model[1]
Dosage:	30 mg/kg
Administration:	Oral administration, daily for 4 weeks
Result:	Exhibited a remarkable tumor regression with $\Delta T/\Delta C\% = -14\%$ after 4 weeks of treatment.

Animal Model:	Male Sprague−Dawley rats[1]
Dosage:	10 mg/kg
Administration:	Oral administration (Pharmacokinetic Analysis)
Result:	PK Parameters for AR antagonist 4 (Compound 67-b) in Male SD Rats[a][1]

Compound	$T_{1/2}$ (h)	T_{max} (h)	C_{max} (ng/mL)	AUC_{0-t} (ng•h/mL)
AR antagonist 4	2.80	2.17	2670	24 800

[a]Compounds were PO-dosed at 10 mg/kg in a solution of 5% DMSO + 30% PEG400 + 65% water (0.5% MC) in male SD rats. Abbreviations: C_{max}, maximum drug concentration; AUC_{0-t}, area under the curve between 0 and t h; $T_{1/2}$, terminal half-life; T_{max}, the time taken to reach C_{max}.Values are expressed as the mean, n = 3.

REFERENCES

[1]. Wang A, et al. Design, Synthesis, and Biological Evaluation of Androgen Receptor Degrading and Antagonizing Bifunctional Steroidal Analogs for the Treatment of Advanced Prostate Cancer. J Med Chem. 2022 Sep 7.

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