

Product Data Sheet

Product Name: IWR-1-endo

Cat. No.: GC10950

Chemical Properties

Cas. No. 1127442-82-3

Chemical Name 4-((3aR,4S,7R,7aS)-1,3-dioxo-3a,4,7,7a-tetrahydro-1H-4,7-methanoisoindol-2(3H)-yl)-N-(quinolin-8-yl)benzamide

SMILES O=C([C@@]1([H])[C@]2([H])[C@]3([H])C([H])([H])[C@@]1([H])C([H])=C3[H])N(C4=C([H])C([H])=C(C(N([H])C5=C([H])C([H])=C([H])C6=C5N=C([H])C([H])=C6[H])=O)C([H])=C4[H])C2=O

Formula $C_{25}H_{19}N_3O_3$

M.Wt 409.44

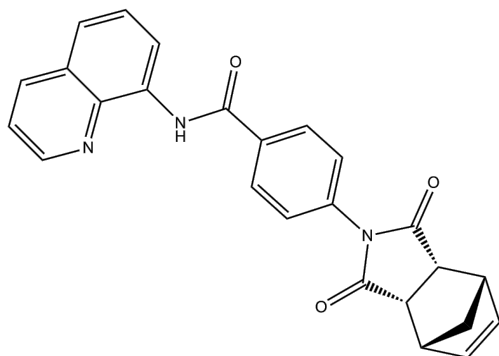
Solubility $\geq 20.45\text{mg/mL}$ in DMSO

Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines HUVEC cell lines

Caution: Product has not been fully validated for medical applications. For research use only.

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Preparation Method The experiment was divided into groups as follow: untreated HUVECs in serum-free culture medium (normal); H/R model (H/R); HUVECs preincubated with IMD for 1 h at 37 °C then changed to culture medium as for the H/R group (H/R + IMD); HUVECs preincubated with IWR-1-endo in incubator for 1 h, then changed to culture medium as for the IMD + H/R group with IWR-1-endo added (H/R + IMD + IWR).

Reaction Conditions IWR-1-endo(10 μ M) ;1h

Applications IWR-1-endo attenuated the protective effect of Intermedin/adrenomedullin-2 and suppressed cell motility and the number of migrating cells.

Animal experiment [2]:

Animal models Entricular apex resection modle

Preparation Method These animals were injected intraperitoneally with 25 μ L of IWR-1-endo (10 μ M in PBS) or DMSO (0.1% in PBS). The injection was performed at 5 dpa and 6 dpa for CM proliferation analysis at 7 dpa. For 30 dpa regeneration analysis, drugs were injected once every two days from 2 dpa throughout 30 dpa.

Dosage form IWR-1-endo (10 μ M , ip, q2d) ; 30days

Applications IWR-1-endo partially rescues cardiomyocyte proliferation defects caused by impaired endocardial Notch signaling

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References:

- [1]. Wang Y, Wu Z, Tian J, Mi Y, Ren X, Kang J, Zhang W, Zhou X, Wang G, Li R. Intermedin protects HUVECs from ischemia reperfusion injury via Wnt/ β -catenin signaling pathway. Ren Fail. 2019 Nov;41(1):159-166.
- [2]. Zhao L, Ben-Yair R, Burns CE, Burns CG. Endocardial Notch Signaling Promotes Cardiomyocyte Proliferation in the Regenerating Zebrafish Heart through Wnt Pathway Antagonism. Cell Rep. 2019 Jan 15;26(3):546-554.e5.

Background

IWR-1-endo is a potent inhibitor of the Wnt response, blocking a cell-based Wnt/ β -catenin pathway reporter response with an IC_{50} value of 180 nM. IWR-1-endo induces Axin2 protein levels and promotes β -catenin phosphorylation by stabilizing the Axin scaffold destruction complex^[1].

IWR-1-endo (10 μ M; 1h) attenuated the protective effect of Intermedin/adrenomedullin-2, inhibited cell motility and the number of migrating cells ^[2]; IWR-1-endo (0.2 μ M; 6 days) reduced the protein expression of ALB, AFP, CYP3A4, β -catenin and TCF1 in the nucleus ^[3]. IWR-1-endo (5-50 μ M; 24h; 48h) reduced the proliferation of HCT116 cells in a dose- and time-dependent manner ^[4].

IWR-1-endo (10 μ M, ip, q2d; 30 days) partially rescued the cardiomyocyte proliferation defect caused by impaired endocardial Notch signaling^[5]. In vivo, IWR-1-endo (5 μ M; 24 h) inhibited zebrafish tail fin regeneration with a minimum inhibitory concentration of 0.5 μ M. The IWR-1-exo diastereoisomer has much lower activity on the Wnt/ β -catenin pathway and has been used as a control^[6].

- [1]. Lu J, Ma Z, Hsieh JC, Fan CW, Chen B, Longgood JC, Williams NS, Amatruda JF, Lum L, Chen C. Structure-activity relationship studies of small-molecule inhibitors of Wnt response. Bioorg Med Chem Lett. 2009 Jul 15;19(14):3825-7. [2]. Wang Y, Wu Z, Tian J, Mi Y, Ren X, Kang J, Zhang W, Zhou X, Wang G, Li R. Intermedin protects HUVECs from ischemia reperfusion injury via Wnt/ β -catenin signaling pathway. Ren Fail. 2019 Nov;41(1):159-166.
- [3]. Gao W, Zhou P, Ma X, Tschudy-Seney B, Chen J, Magner NL, Revzin A, Nolta JA, Zern MA, Duan Y. Ethanol negatively regulates hepatic differentiation of hESC by inhibition of the MAPK/ERK signaling pathway in vitro. PLoS One. 2014 Nov 13;9(11):e112698.

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- [4]. Lee SC, Kim OH, Lee SK, Kim SJ. IWR-1 inhibits epithelial-mesenchymal transition of colorectal cancer cells through suppressing Wnt/ β -catenin signaling as well as survivin expression. *Oncotarget*. 2015 Sep 29;6(29):27146-59.
- [5]. Zhao L, Ben-Yair R, Burns CE, Burns CG. Endocardial Notch Signaling Promotes Cardiomyocyte Proliferation in the Regenerating Zebrafish Heart through Wnt Pathway Antagonism. *Cell Rep*. 2019 Jan 15;26(3):546-554.e5.
- [6]. Lu J, Ma Z, Hsieh JC, Fan CW, Chen B, Longgood JC, Williams NS, Amatruda JF, Lum L, Chen C. Structure-activity relationship studies of small-molecule inhibitors of Wnt response. *Bioorg Med Chem Lett*. 2009 Jul 15;19(14):3825-7.

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