

Product Data Sheet

Product Name: HO-3867

Cat. No.: GC16208

Chemical Properties

Cas. No. 1172133-28-6

Chemical Name (3E,5E)-3,5-bis(4-fluorobenzylidene)-1-((1-hydroxy-2,2,5,5-tetramethyl-2,5-dihydro-1H-pyrrol-3-yl)methyl)piperidin-4-one

SMILES O=C(/C(CN(CC1=CC(C)(C)N(O[H])C1(C)C)C/2)=C/C3=CC=C(F)C=C3)C2=C\C4=CC=C(F)C=C4

Formula C₂₈H₃₀F₂N₂O₂

M.Wt 464.55

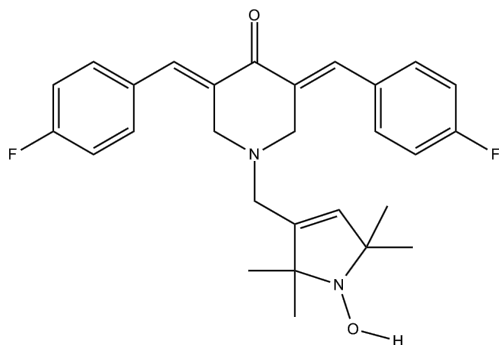
Solubility ≥ 18.15mg/mL in DMSO

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 A2780 human epithelial ovarian cancer cell line, ovarian cancer cell lines used (SKOV3, OVCAR3, A2780R, and OV4)

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Soluble in DMSO. General tips for obtaining a higher concentration: Please Preparation method warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Reacting condition 10 µmol/L, 20 µmol/L, 24 h

Applications HO-3867 was cytotoxic to A2780 and other ovarian cancer cell lines. HO-3867 (20 µmol/L) induced G2 -M cell cycle arrest in A2780 cells. HO-3867 induced apoptosis in A2780 cells. HO-3867 induced apoptosis and inhibited JAK/STAT3 signaling in human ovarian cancer cell lines.

Animal experiment [1,2]:

Animal models Ovarian cancer tumor xenografted mice model

Dosage form Oral gavage, 25, 50, and 100 ppm

Application In ovarian cancer tumor xenografted mice, HO-3867 inhibited the growth of xenograft tumor in mice. HO-3867 inhibited pSTAT3 and downregulated the STAT3-targeting proteins in vivo. HO-3867 (100 ppm p.o.) attenuated left-heart-failure-induced pulmonary hypertension by decreasing oxidative stress and increasing PTEN expression in the lung of rats.

Other notes Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

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References:

[1]. Selvendiran K, Tong L, Bratasz A, et al. Anticancer efficacy of a difluorodiarylidene piperidone (HO-3867) in human ovarian cancer cells and tumor xenografts[J]. Molecular cancer therapeutics, 2010, 9(5): 1169-1179.

[2]. Ravi Y, Selvendiran K, Naidu S K, et al. Pulmonary hypertension secondary to left-heart failure involves peroxynitrite-induced downregulation of PTEN in the lung[J]. Hypertension, 2013: HYPERTENSIONAHA. 111.00514.

Background

HO-3867 is a novel curcumin analog and a selective inhibitor of STAT3. [1]

STAT3 (signal transducer and activator of transcription 3) belongs to the STAT protein family. It mediates various gene expressions for numerous cellular functions, including cell growth, division and apoptosis.

HO-3867 selectively blocked STAT3 phosphorylation, transcription, and DNA binding without inhibiting other STATs proteins. It activated apoptosis in ovarian cancer cells and showed minimal toxicity to healthy cells. [2] HO-3867 also significantly inhibited the proliferation of serum-stimulated SMCs and elevated the phosphorylated and total levels of PTENs in SMCs. [3] By inducing cell cycle arrest and apoptosis, HO-3867 reduced the high levels of pSTAT3 Ser727 in endometrial cancer cells. [4]

In mice tumor xenograft, HO-3867 inhibited the tumor growth without toxic side effects, it also blocked pSTAT3/JAK1 and increased apoptotic marker cleaved Caspase 3/PARP. [2] [5] After rat carotid artery injury, HO-3867 inhibited neointima formation and upregulated PTEN expression. [3]

References:

[1] Tierney BJ, McCann GA, Cohn DE, Eisenhauer E, Sudhakar M, Kuppusamy P, Hideg K, Selvendiran K. HO-3867, a STAT3 inhibitor induces apoptosis by inactivation of STAT3 activity in BRCA1-mutated ovarian cancer cells. *Cancer Biol Ther.* 2012 Jul;13(9):766-75.

[2] Rath KS, Naidu SK, Lata P, Bid HK, Rivera BK, McCann GA, Tierney BJ, Elnaggar AC, Bravo V, Leone G, Houghton P, Hideg K, Kuppusamy P, Cohn DE, Selvendiran K.

HO-3867, a safe STAT3 inhibitor, is selectively cytotoxic to ovarian cancer. *Cancer Res.* 2014 Apr 15;74(8):2316-27.

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[3] Selvendiran K, Kuppusamy ML, Bratasz A, Tong L, Rivera BK, Rink C, Sen CK, Kálai T, Hideg K, Kuppusamy P. Inhibition of vascular smooth-muscle cell proliferation and arterial restenosis by HO-3867, a novel synthetic curcuminoid, through up-regulation of PTEN expression. *J Pharmacol Exp Ther.* 2009 Jun;329(3):959-66.

[4] Tierney BJ, McCann GA, Naidu S, Rath KS, Saini U, Wanner R, Kuppusamy P, Suarez A, Goodfellow PJ, Cohn DE, Selvendiran K. Aberrantly activated pSTAT3-Ser727 in human endometrial cancer is suppressed by HO-3867, a novel STAT3 inhibitor. *Gynecol Oncol.* 2014 Oct;135(1):133-41.

[5] Selvendiran K, Tong L, Bratasz A, Kuppusamy ML, Ahmed S, Ravi Y, Trigg NJ, Rivera BK, Kálai T, Hideg K, Kuppusamy P. Anticancer efficacy of a difluorodiarylidene piperidone (HO-3867) in human ovarian cancer cells and tumor xenografts. *Mol Cancer Ther.* 2010 May;9(5):1169-79.

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