TEI-9647

Cat. No.: HY-12398

CAS No.: 173388-20-0

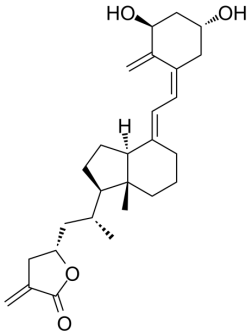
Molecular Formula: $C_{27}H_{38}O_4$

Molecular Weight: 426.59

Target: VD/VDR

Pathway: Vitamin D Related/Nuclear Receptor

Storage: -20°C, protect from light, stored under nitrogen
* In solvent : -80°C, 6 months; -20°C, 1 month (protect from light, stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (234.42 mM; Need ultrasonic)

Preparing Stock Solutions	Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
	1 mM	2.3442 mL	11.7209 mL	23.4417 mL
	5 mM	0.4688 mL	2.3442 mL	4.6883 mL
	10 mM	0.2344 mL	1.1721 mL	2.3442 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: 2.5 mg/mL (5.86 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (5.86 mM); Clear solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: 2.5 mg/mL (5.86 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

TEI-9647, a Vitamin D_3 Lactone analogue, is a potent and specific vitamin D receptor (VDR) antagonist. TEI-9647 inhibits VDR/VDRE-mediated genomic actions of $1\alpha,25(OH)_2D_3$. TEI-9647 inhibits bone resorption and HL-60 cell differentiation induced by of $1\alpha,25(OH)_2D_3$. TEI-9647 has the potential for suppressing the excessive bone resorption and osteoclast formation in Paget's disease[1][2][3].

In Vitro

TEI-9647 (100 nM; 24 hours) treatment clearly suppresses $p21^{WAF1,CIP1}$ gene expression induced by $1\alpha,25(OH)_2D_3$[1].
TEI-9647 (10-1000 nM; 96 hours) dose-dependently blocks the reciprocal changes of CD11b and CD71 expression associated with HL-60 cell differentiation induced by $1\alpha,25(OH)_2D_3$. TEI-9647 completely blocks the increase in CD11b and the decrease

in CD71 expression at 100 nM[1].
TEI-9647 blocks both 1α,25(OH)$_2$D$_3$-mediated HL-60 cell differentiation and also activation of the luciferase reporter in COS-7 cells that has been transfected with the cDNA containing the DRE of the rat 25(OH)D$_3$-24-hydroxylase gene and cDNA of the human vitamin D nuclear receptor[1].
TEI-9647 can not induce cell differentiation even after treatment at 1 μM in HL-60 cell. TEI-9647 alone can not induce activation of NBT-reducing activity or α-NB esterase activity. In contrast, TEI-9647 markedly suppresses the up-regulation induced by 1α,25(OH)$_2$D$_3$ (0.1 nM) in HL-60 cells[1].
TEI-9647 (0.001-1 μM; for 10 days) dose-dependently inhibits bone resorption induced by of 1α,25(OH)$_2$D$_3$ (1 nM). TEI-9647 alone never induces bone resorption even at 1 μM[2].
TEI-9647 (10 nM; 12 h) markedly inhibits TAFII-17 and 25-OH-D$_3$-24-hydroxylase gene expression induced by 1α,25(OH)$_2$D$_3$ (0.1 nM) in bone marrow cells[2].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

RT-PCR[1]

Cell Line:	HL-60 cells
Concentration:	100 nM
Incubation Time:	24 hours
Result:	Clearly suppressed p21^{WAF1,CIP1} gene expression induced by 1α,25(OH)$_2$D$_3$.

REFERENCES

[1]. Miura D, et al. Antagonistic action of novel 1α,25-dihydroxyvitamin D$_3$-26, 23-lactone analogs on differentiation of human leukemia cells (HL-60) induced by 1α,25-dihydroxyvitamin D$_3$. J Biol Chem. 1999 Jun 4;274(23):16392-9.

[2]. Seiichi Ishizuka, et al. Vitamin D antagonist, TEI-9647, inhibits osteoclast formation induced by 1α,25-dihydroxyvitamin D$_3$ from pagetic bone marrow cells. J Steroid Biochem Mol Biol. 2004 May;89-90(1-5):331-4.

[3]. Kazuya Takenouchi, et al. Synthesis and structure-activity relationships of TEI-9647 derivatives as Vitamin D$_3$ antagonists. J Steroid Biochem Mol Biol. 2004 May;89-90(1-5):31-4.

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