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产品名称：西奥骨化醇
产品别名：Seocalcitol；EB 1089

生物活性：

Description	Seocalcitol is a vitamin D analog, binds vitamin D receptor protein from human osteosarcoma MG-63 cells with Kd of 0.27 nM.
IC_{50} & Target	Kd: 0.27 nM (vitamin D receptor)[1]
In Vitro	Seocalcitol (EB 1089) is a stimulators of osteoclast recruitment in murine bone marrow cultures, with EC_{50} at 0.1 nM. Seocalcitol stimulates bone resorption with an estimated EC_{50} at 0.03 nM[1]. Seocalcitol (EB 1089) elicites a dose-dependent induction of 24-hydroxylase mRNA in the kidney (EC_{50}=0.4±0.13). In the kidney, K_d values for Seocalcitol is 0.48±0.04 nM. However, in the intestine, the K_d for Seocalcitol is 1.43±0.19 nM)[2]. Seocalcitol (0.1-10 nM) induces cell differentiation in a dosedependent manner. A higher differentiating activity is observed for 1 nM Seocalcitol (EB 1089) than for 1 nM VD_3.
In Vivo	Seocalcitol (EB1089), a synthetic vitamin D analog, exhibits reduced hypercalcemic activity relative to $1,25(OH)_2VD_3$. In another study, long-term intraperitoneal (IP) administration of Seocalcitol at a dose of 0.5 μg/kg body weight every other day in C3H/Sy mice exertes a very strong inhibitory effect on hepatocellular carcinoma (HCC) development[4]. Seocalcitol (EB 1089) is administered daily to postnatal rats from 4 to 12 days of age (P4 to P12) by intraperitoneal injection at either 0.38 or 1.25 μg/kg body weight (BW)/day. Only the highest dose of Seocalcitol (1.25 μg/kg BW) causes a significant reduction in weight gain when administered alone or in conjunction with Dexamethasone, all-trans retinoic acid (RA), or retinoic acid[5].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 50 mg/mL (109.97 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1993 mL	10.9967 mL	21.9935 mL
	5 mM	0.4399 mL	2.1993 mL	4.3987 mL
	10 mM	0.2199 mL	1.0997 mL	2.1993 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.5 mg/mL (5.50 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.50 mM，饱和度未知) 的澄清溶液。

	以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 2.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (5.50 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.50 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Wiberg K, et al. Studies on two new vitamin D analogs, EB 1089 and KH 1060: effects on bone resorption and osteoclast recruitment in vitro. Bone. 1995 Oct;17(4):391-5. [2]. Roy S, et al. Comparative effects of 1,25-dihydroxyvitamin D3 and EB 1089 on mouse renal and intestinal 25-hydroxyvitamin D3-24-hydroxylase. J Bone Miner Res. 1995 Dec;10(12):1951-9. [3]. Bondza-Kibangou P, et al. Antioxidants and doxorubicin supplementation to modulate CD14 expression and oxidative stress induced by vitamin D3 and seocalcitol in HL60 cells. Oncol Rep. 2007 Dec;18(6):1513-9. [4]. Ghous Z, et al. Inhibition of hepatocellular cancer by EB1089: in vitro and in vivo study. Anticancer Res. 2008 Nov-Dec;28(6A):3757-61. [5]. Ormerod AK, et al. The calcitriol analogue EB1089 impairs alveolarization and induces localized regions of increased fibroblast density in neonatal rat lung. Exp Lung Res. 2008 May;34(4):155-82.

实验参考：

Cell Assay	This fluorescent dye allowed to determine ROS release in HL60 cells, untreated or treated VD3 or Seocalcitol. Briefly, after treatment, HL60 cells are washed and re-suspended at 10^6 cells/mL in RPMI-1640 without FCS and phenol red. Then, 10 μM H_2-DCFDA probe is added to each plate at a final volume of 2 mL. Cells are incubated for 45 min at 37°C in the dark. A second wash is made before the fluorescence analysis using spectrometer at 488 nm intensity excitation λ_{ex} and 516 nm emission λ_{em}. Results, in arbitrary fluorescence units (AFU), are expressed according to the ratio [(AFU-treated cells)/(AFU control cells)]×100[3].
Animal Administration	Mice[4] Six- to eight-week-old male BALB/c NU/Nu mice are inoculated subcutaneously with 10^6 SKHEP-1 cells into the right flank. Twenty-four hours after inoculation, mice are randomly assigned to a control group (n=10) or the treatment groups (n=10), receiving 0.02, 0.1 or 0.5 μg/kg per day of Seocalcitol (intraperitoneal or oral on alternate days). Control animals receive propylene glycol alone. Tumor size is measured using vernier calipers every third day and the volumes are estimated using the formula 0.5×length×$(width)^2$. Animals receive sterile food and water. Rats[5] Newborn Sprague-Dawley rat pups are randomly assigned to 1 of 6 treatment groups, consisting of daily intraperitoneal injections of the vitamin D analogue Seocalcitol (0.38 or 1.25 μg/kg body weight) alone, or in combination with all-trans retinoic acid (RA; 500 μg/kg body weight) and/or Dexamethasone (DEX; 0.25 μg/day) in a 3×2×2 factorial design. Seocalcitol and RA injections are conducted on P3 through P12, whereas Dexamethasone is administered on P4 through P12.

	Seocalcitol is prepared for injections in a quantity sufficient for all injections by dilution from a stock solution (4 mM in isopropanol) into the carrier Solutol HS 15 (BASF). Solutol-diluted Seocalcitol is stored as aliquots in sealed glass vials under nitrogen gas at 4°C, with daily injections conducted with freshly unsealed aliquots of Seocalcitol. Stock solutions of RA (50 mg/mL DMSO are stored under nitrogen at −80°C and prepared for injection by dilution of freshly thawed aliquots into cottonseed oil (2 μg/μL). A Dexamethasone stock solution (10 mg/mL ethanol) is stored under nitrogen at 4°C and prepared fresh for daily injections in 0.9% NaCl (0.25 μg/μL). All rats receive equivalent volumes of the 3 carrier solutions employed (solutol, cottonseed oil, 0.9% NaCl). Seocalcitol and RA are administered as a 2-phase solution via a 10 μL injection using a 20 μL glass-barreled syringe and a 28-gauge needle, whereas Dexamethasone is administered in a separate 10 μL injection.
Kinase Assay	Vitamin D receptor protein is prepared from cultures of human osteosarcoma cell line MG-63. Suspensions of 5×10^7 cells/mL are homogenized, sonicated, and centrifuged at 30,000g for 1 h at 4°C. The presence of the $1\alpha,25(OH)_2D_3$ receptor is verified by sucrose density gradient analysis. The supernatants are adjusted to 2 mg protein/mL and used for binding studies. Samples of 500 μL are incubated with 10,000 dpm $[^3H]1\alpha,25(OH)_2D_3$ (180 Ci/mmol) and increasing concentrations of $1\alpha,25(OH)_2D_3$ or vitamin D_3 analogs are added. After incubation for 60 min at 22°C, bound and free $[^3H]1\alpha,25(OH)_2D_3$ are separated on dextran-coated charcoal. Each compound is tested in three separate experiments[1].
References	[1]. Wiberg K, et al. Studies on two new vitamin D analogs, EB 1089 and KH 1060: effects on bone resorption and osteoclast recruitment in vitro. Bone. 1995 Oct;17(4):391-5. [2]. Roy S, et al. Comparative effects of 1,25-dihydroxyvitamin D3 and EB 1089 on mouse renal and intestinal 25-hydroxyvitamin D3-24-hydroxylase. J Bone Miner Res. 1995 Dec;10(12):1951-9. [3]. Bondza-Kibangou P, et al. Antioxidants and doxorubicin supplementation to modulate CD14 expression and oxidative stress induced by vitamin D3 and seocalcitol in HL60 cells. Oncol Rep. 2007 Dec;18(6):1513-9. [4]. Ghous Z, et al. Inhibition of hepatocellular cancer by EB1089: in vitro and in vivo study. Anticancer Res. 2008 Nov-Dec;28(6A):3757-61. [5]. Ormerod AK, et al. The calcitriol analogue EB1089 impairs alveolarization and induces localized regions of increased fibroblast density in neonatal rat lung. Exp Lung Res. 2008 May;34(4):155-82.