Tamibarotene

Cat. No.: HY-14652

CAS No.: 94497-51-5

Molecular Formula: $C_{22}H_{25}NO_3$

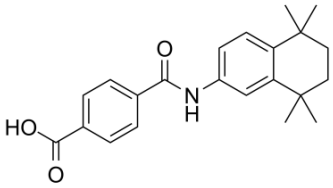
Molecular Weight: 351.44

Target: RAR/RXR; Autophagy; Apoptosis

Pathway: Metabolic Enzyme/Protease; Autophagy; Apoptosis

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 25.5 mg/mL (72.56 mM; Need ultrasonic and warming)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.8454 mL	14.2272 mL	28.4544 mL
	5 mM	0.5691 mL	2.8454 mL	5.6909 mL
	10 mM	0.2845 mL	1.4227 mL	2.8454 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 (7.11 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (7.11 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.11 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Tamibarotene is a retinoic acid receptor α/β (RARα/β) agonist, showing high selectivity over RARγ.

IC_{50} & Target

RARα/β[1]

In Vitro

Tamibarotene (20, 40 μM) down-regulates expression of cell cycle gene in T-cell lymphoma cells. Tamibarotene (5 μM) increases RARE activity in RARA-overexpressing cells to a much greater degree than in RARAlow cells. Moreover, RARAwt overexpression augments the degree of CDK2, CDK4, and CDK6 inhibition caused by Tamibarotene treatment[1].

	Tamibarotene directly reverses the profibrotic phenotype of transforming growth factor-β1-treated dermal fibroblasts, suppresses ICAM-1 expression in endothelial cells, and promots M1 macrophage differentiation in vitro[2]. Tamibarotene (4 μM) up-regulates apelin mRNA and protein levels dose-dependently in VSMCs. Upon Tamibarotene stimulation, the RARα (retinoic acid receptor α) is recruited to the apelin promoter by interacting with KLF5 and Sp1 prebound to the TCE site of the apelin promoter to form a transcriptional activation complex, subsequently leading to the up-regulation of apelin expression in VSMCs. KLF5 and Sp1 co-operatively mediate Tamibarotene-induced apelin expression through their direct binding to the TCE on the apelin promoter[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Tamibarotene (1 mg/kg/day) significantly attenuates dermal and hypodermal fibrosis in bleomycin (BLM)-treated mice and tight skin 1 mice, respectively. Consistently, Tamibarotene significantly suppresses the expression of various molecules related to tissue fibrosis, including transforming growth factor-β1, connective tissue growth factor, IL-4, IL-10, IL-13, IL-17A, tumor necrosis factor-α, IFN-γ, and monocyte chemotactic protein 1 in the lesional skin of BLM-treated mice. Furthermore, Tamibarotene decreases the proportion of effector T cells, while increasing that of naive T cells among $CD4^+$ T cells in the draining lymph nodes of BLM-treated mice[2]. Tamibarotene (2.5 mg/kg, p.o.) does not result in any significant alteration of the AST, ALT, or ALP serum levels in periodontitis-challenged mice compared with that in untreated mice. Tamibarotene ameliorates alveolar bone resorption, significantly reduces the number of P. gingivalis-induced osteoclasts in mice. Tamibarotene measurably increases the percentage of $CD4^+$ $Foxp3^+$ Treg cells as compared to those in EPD mice. Tamibarotene is also effective in reducing the expression of $CD4^+$ROR-$γt^+$ (Th17) cells in P. gingivalis-infected gingival tissues and CLNs[3]. Tamibarotene (1 mg/kg, p.o.) increases apelin expression in balloon-injured arteries of rats, consistent with the results from the cultured VSMCs[4]. In aged SAMP8 mice, hippocampal ADAM10 levels improve after Tamibarotene (1 mg/kg/day) administration. Hes5 and Ki67 are restored and spatial working memory also improves after Tamibarotene administration[5]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	The CellTiter Aqueous Non-Radioactive Cell Proliferation Assay Kit is used to assess cell growth. Briefly, 10,000 cells per well are seeded in a 96-well plate and cultured in RPMI containing 2% charcoal-stripped FBS and indicated retinoid concentrations for 72 hours. At the end of the treatment period, the MTS reagent is added, cells are incubated an additional 2-4 hours, and absorbance is measured at 490 nanometers. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	For the infection, mice are given sulfamethoxazole and trimethoprim in an oral suspension at 10 mL of deionized water ad libitum for 10 days to reduce the native flora and to support colonization of P. gingivalis W83. Four days after the antibiotic therapy finishes, periodontal infection is established through oral inoculation using 1010 colony-forming units of P. gingivalis suspended in 100 μL 4% carboxymethyl cellulose (CMC) for 7 days. The mice are euthanized 4 weeks after the first oral inoculation. Tamibarotene (2.5 mg/kg) is suspended in a 0.5% carboxymethyl cellulose solution. The drug is orally gavaged into the esophagus daily in a volume of 0.1 mL/10 g body weight. Tamibarotene is administered 1 h before the induction of periodontitis and then given daily per the protocol until day 28. Control mice with periodontal disease receive the same volume of 0.5% carboxymethyl cellulose solution. The body weight of each mouse is measured every 3 days. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Pharmacol Res. 2020 Aug 18;105149.

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REFERENCES

[1]. Wang X, et al. Retinoic acid receptor alpha drives cell cycle progression and is associated with increased sensitivity to retinoids in T-cell lymphoma. Oncotarget. 2017 Apr 18;8(16):26245-26255.

[2]. Toyama T, et al. Tamibarotene Ameliorates Bleomycin-Induced Dermal Fibrosis by Modulating Phenotypes of Fibroblasts, Endothelial Cells, and Immune Cells. J Invest Dermatol. 2016 Feb;136(2):387-98.

[3]. Jin Y, et al. Tamibarotene modulates the local immune response in experimental periodontitis. Int Immunopharmacol. 2014 Dec;23(2):537-45.

[4]. Lv XR, et al. Synthetic retinoid Am80 up-regulates apelin expression by promoting interaction of RARα with KLF5 and Sp1 in vascular smooth muscle cells. Biochem J. 2013 Nov 15;456(1):35-46.

[5]. Kitaoka K, et al. The retinoic acid receptor agonist Am80 increases hippocampal ADAM10 in aged SAMP8 mice. Neuropharmacology. 2013 Sep;72:58-65.

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