AM580

Cat. No.: HY-10475

CAS No.: 102121-60-8

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

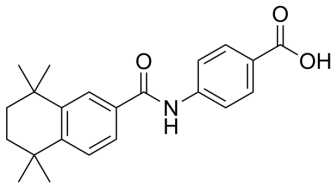
Molecular Weight: 351.44

Target: RAR/RXR; Autophagy

Pathway: Metabolic Enzyme/Protease; Vitamin D Related/Nuclear Receptor; Autophagy

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 45 mg/mL (128.04 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / 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% corn oil
   Solubility: ≥ 2.5 mg/mL (7.11 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

AM580 is a selective RARα agonist with IC_{50} and EC_{50} of 8 nM and 0.36 nM, respectively.

In Vitro

In the presence of G-CSF, AM580 (at 10^{-8} M) produces a remarkable induction in LAP mRNA of NB4 cells. At a concentration of 10^{-5} M, AM580 and ATRA, in combination with G-CSF, induce almost the same level of LAP transcript. AM580 (at 10^{-8} M) leads to an approximately sixfold increase in the steady-state levels of the transcript coding for the G-CSF receptor in NB4 cells[1]. AM580 (50 nM) increases caspase-3 expression in all of the colonies, and in 30% of the colonies induce acinar-like cavitation [2]. Knockdown of RARγ1 in primary Myc cells using shRARγ1 followed by Am580 treatment results in an even higher level of CRBP1 expression, showing that in these cells RARγ has a repressive effect on the RARα target gene CRBP1. Am580 (200 nM)

	enhances the anti-proliferative effect exhibited by RARγ knockdown in the MCF-10A and MCF-7 cell lines but not in the MDA-MB-231 cells[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Am580 (0.3 mg/kg/day) treatment has a more profound effect on tumor-free survival of MMTV-wnt1 mice, the effect being noticeable even in early appearing tumors, and no overt toxicity is found in liver, lungs, kidney, and spleen. Am580 treatment reduces substantially and equally the level of hyperplasia in both transgenic glands[2]. Treatment of MMTV-Myc mice with the RARα-selective agonist Am580 leads to significant inhibition of mammary tumor growth, lung metastasis and extends tumor latency in 63% of mice[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Approximately 1×10^6 NB4, HL-60, and APL fresh leukemic cells or CML neutrophils are harvested, pelletted by centrifugation at 400 g for 10 minutes, washed once with 0.9% NaCl, and centrifuged again. The washed cell pellet is resuspended in homogenization buffer (1 mM $MgCl_2$, 1 mM $CaCl_2$, 20 mM $ZnCl_2$, 0.1 mM NaCl, 0.1% [vol/vol] Triton X-100, 50 mM Tris/HCl, pH 7.4) and disrupted by vigorous pipetting. The homogenate is used for the LAP assay, which is performed with p-nitrophenol phosphate as substrate according to the instructions of the manufacturer. LAP activity is normalized for the content of protein in the sample. Proteins are measured according to the Bradford method using BSA fraction V as a standard. One unit of LAP activity is defined as the amount of enzyme capable of transforming 1 nmol of substrate in 1 minute at 25°C. Enzyme assays are performed in conditions of linearity relative to the substrate and to the concentration of proteins. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	MCF-10A (2×10^4) control cells or overexpressing RARγ are seeded in triplicates in 6-well culture dishes. After 24 hrs, cells are washed with PBS, incubated in 2 mL of DMEM-F12 culture medium, detached and counted every 24 hrs. Statistical significance is determined by t-test. pRB and p27 expression is tested by immunofluorescence analysis of control MCF-10A monolayers and monolayers stably transfected with pSG5-RARγ expression vector, using the same antibodies described for the IHC analysis. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Four months old uniparous (1 pregnancy/lactation cycle) MMTV-neu and 6 weeks old nulliparous MMTV-wnt1 female mice (50 mice/group) are treated with the RARα agonist AM580 (0.3 mg/kg body weight per mouse per day) in the diet (Purina 5053) by adding 1.5 mg AM580 per kg of Purina 5053 diet. Mice that develop tumors within the first month of treatment are removed from the study. Mice are palpated twice a week and tumor appearance is recorded. Once palpable, the size of the tumors is measured weekly. Tumor-free survival is calculated from Kaplan-Meier curves and statistical significance is determined by the Log-rank test for the survival studies and t-test for the tumor growth studies. Metastasis is evaluated by removing the lungs of all the anesthetized mice, selecting randomLy 20 mice per group and inspecting the lung surface for lesions using a stereoscope. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- J Hazard Mater. 2022 Aug 5;435:129024.
- Allergy. 2021 Aug 8.
- EMBO J. 2021 Apr 28;e106771.
- J Exp Clin Cancer Res. 2021 Apr 26;40(1):141.
- Cancer Res. 2023 May 15;CAN-22-3977.

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REFERENCES

[1]. Gianní M, et al. AM580, a stable benzoic derivative of retinoic acid, has powerful and selective cyto-differentiating effects on acute promyelocytic leukemia cells. Blood. 1996 Feb 15;87(4):1520-31.

[2]. Lu Y, et al. Mechanism of inhibition of MMTV-neu and MMTV-wnt1 induced mammary oncogenesis by RARalpha agonist AM580. Oncogene. 2010 Jun 24;29(25):3665-76.

[3]. Bosch A, et al. Reversal by RARα agonist Am580 of c-Myc-induced imbalance in RARα/RARγ expression during MMTV-Myc tumorigenesis. Breast Cancer Res. 2012 Aug 24;14(4):R121.

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