

Product Data Sheet

Product Name: AM580
Cat. No.: GC13664

Chemical Properties

Cas. No. 102121-60-8

SMILES O=C(C1=CC=C2C(C)(C)CCC(C)(C)C2=C1)NC3=CC=C(C(O)=O)C=C3

Formula C₂₂H₂₅NO₃ M.Wt 351.44

Solubility ≥ 14.3mg/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.

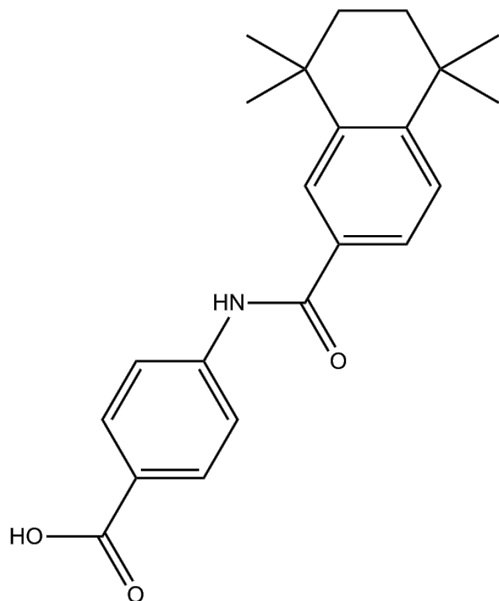
Caution: Product has not been fully validated for medical applications. For research use only.

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Structure



Protocol

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- Kinase experiment:** Approximately 1×10^6 NB4, HL-60, and APL fresh leukemic cells or CML neutrophils are harvested, pelleted 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 MgCl₂, 1 mM CaCl₂, 20 mM ZnCl₂, 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.
- Cell experiment:** MCF-10A (2×10^4) control cells or overexpressing RAR γ 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-RAR γ expression vector, using the same antibodies described for the IHC analysis.

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Animal experiment: 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 RAR α 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.

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 RAR α agonist AM580. *Oncogene*. 2010 Jun 24;29(25):3665-76.
- [3]. Bosch A, et al. Reversal by RAR α agonist Am580 of c-Myc-induced imbalance in RAR α /RAR γ expression during MMTV-Myc tumorigenesis. *Breast Cancer Res*. 2012 Aug 24;14(4):R121.

Background

AM580 is a selective agonist of retinoic acid receptor α (RAR α) with IC₅₀ and EC₅₀ values of 8 nM and 0.36 nM, respectively [1].

RAR α is ubiquitously expressed. It is important for retinoid response during growth and differentiation of epithelial cells. RAR α have functions in the inhibition of cell and mammary tumour growth, increase in tumour latency, induction of cell cycle arrest, stimulation of cell death, and up-regulation of RAR α and RAR γ mRNA [1, 2]. In addition, RAR α is involved in the production of human T cell activation and type 2 cytokine [3].

In SK-BR-3 and T47D breast cancer cell lines, treatment with AM580 at concentrations of 1 nM and

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10 nM for 7 days resulted in the decrease in the number of cells [1]. AM580 at a concentration of 200 nM, enhanced the anti-proliferative effect shown by the knockdown of RAR- γ in MCF-10A breast epithelial and MCF-7 cell lines [2].

When 200 nM AM580 was applied to MMTV-Myc female mice for 96 hours, this led to impaired cell proliferation capacity. Furthermore, combination of AM580 with 100 nM CD437 and SR11253 resulted in strong growth inhibition, clearly demonstrating the ability of AM580 to reduce the tumour growth in MMTV-Myc tumour model [2].

References:

- [1]. Schneider S, Offterdinger M, Huber H, et al. Activation of Retinoic Acid Receptor α Is Sufficient for Full Induction of Retinoid Responses in SK-BR-3 and T47D Human Breast Cancer Cells. *Cancer Res*, 2000, 60(19):5479-87.
- [2]. Bosch A, Bertran S, Lu Y, et al. Reversal by RAR α agonist Am580 of c-Myc induced imbalance in RAR α /RAR γ expression during MMTV-Myc tumorigenesis. *Breast Cancer Res*, 2012, 14(4):R121.
- [3]. Dawson H, Collins G, Pyle R, et al. The Retinoic Acid Receptor- α mediates human T-cell activation and Th2 cytokine and chemokine production. *BMC Immunol*, 2008, 9:16.

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