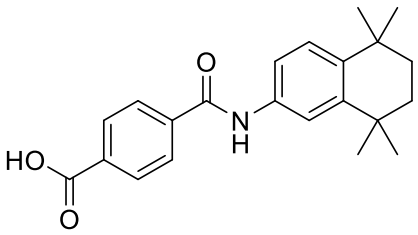
Product data sheet

MedKoo Cat#: 202780 Name: Tamibarotene CAS#: 94497-51-5 Chemical Formula: $C_{22}H_{25}NO_3$ Exact Mass: 351.18344 Molecular Weight: 351.44	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
Tamibarotene, also known as SY-1425, is an orally active, synthetic retinoid, developed to overcome all-trans retinoic acid (ATRA) resistance, with potential antineoplastic activity. As a specific retinoic acid receptor (RAR) alpha/beta agonist, tamibarotene is approximately ten times more potent than ATRA in inducing cell differentiation and apoptosis in HL-60 (human promyelocytic leukemia) cell lines in vitro. Due to a lower affinity for cellular retinoic acid binding protein (CRABP), tamibarotene may show sustained plasma levels compared to ATRA.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	17.57	50
Ethanol	17.57	50

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	2.85 mL	14.23 mL	28.45 mL
5 mM	0.57 mL	2.85 mL	5.69 mL
10 mM	0.28 mL	1.42 mL	2.85 mL
50 mM	0.06 mL	0.28 mL	0.57 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Lv XR, Zheng B, Li SY, Han AL, Wang C, Shi JH, Zhang XH, Liu Y, Li YH, Wen JK. 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. doi: 10.1042/BJ20130418. PMID: 23992409.

2. Jin Y, Wang L, Liu D, Lin X. Tamibarotene modulates the local immune response in experimental periodontitis. Int Immunopharmacol. 2014 Dec;23(2):537-45. doi: 10.1016/j.intimp.2014.10.003. Epub 2014 Oct 14. PMID: 25448496.

In vivo study

1. Toyama T, Asano Y, Akamata K, Noda S, Taniguchi T, Takahashi T, Ichimura Y, Shudo K, Sato S, Kadono T. Tamibarotene Ameliorates Bleomycin-Induced Dermal Fibrosis by Modulating Phenotypes of Fibroblasts, Endothelial Cells, and Immune Cells. J Invest Dermatol. 2016 Feb;136(2):387-398. doi: 10.1016/j.jid.2015.10.058. Epub 2015 Nov 18. PMID: 26967475.

2. Kitaoka K, Shimizu N, Ono K, Chikahisa S, Nakagomi M, Shudo K, Ishimura K, Séi H, Yoshizaki K. The retinoic acid receptor agonist Am80 increases hippocampal ADAM10 in aged SAMP8 mice. Neuropharmacology. 2013 Sep;72:58-65. doi: 10.1016/j.neuropharm.2013.04.009. Epub 2013 Apr 23. PMID: 23624141.

7. Bioactivity

Biological target:

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

In vitro activity

To further investigate the effect of Am80 on apelin promoter activity, VSMCs were co-transfected with GFP‐KLF5 expression plasmids and apelin promoter‐reporter constructs containing various 5′-deletion fragments. As shown in Figure 4(C), KLF5 overexpression significantly elevated the activities of the apelin promoter of the three different constructs. When Am80 was added, the relative activity of the different constructs further increased. To assess whether the TCE sites in the apelin promoter region were required for Am80-induced apelin expression, the promoter constructs in which the different TCE sites were mutated were co-transfected, respectively, with KLF5 expression plasmid GFP–KLF5. The luciferase activity assay results showed that mutation of site-2 or site-3 did not affect apelin promoter activity and that only the mutation of site-1 blocked the activation of the apelin promoter by KLF5 (Figure 4D). To investigate whether KLF5 bound directly to the TCE sites in Am80-stimulated VSMCs, an oligonucleotide pull-down assay was carried out. As shown in Figure 4(E), KLF5 was bound only to TCE site-1 of the apelin promoter, and Am80 treatment increased its binding. Furthermore, no KLF5 bands were detected when probes containing site-2 or site-3 were used. These results suggest that KLF5 activated apelin transcription by directly binding to site-1 of the apelin promoter.

Reference: Biochem J. 2013 Nov 15;456(1):35-46. https://portlandpress.com/biochemj/article-lookup/doi/10.1042/BJ20130418

In vivo activity

Dermal thickness of lesional skin sections was greater in BLM-treated mice than in phosphate-buffered saline (PBS)-treated mice on day 28 but was comparable on day 7. Of note, Am80 significantly attenuated BLM-induced dermal thickness on day 28 (Figure 1a). Consistent with this finding, Am80 treatment significantly reduced collagen content and mRNA expression of the Col1a1, Col1a2, Col3a1, and Col5a1 genes while promoting that of the Mmp13 gene in the lesional skin of BLM-treated mice (Figure 1b and c). Becasue transforming growth factor (TGF)-β1 and connective tissue growth factor (CTGF) are enough to induce experimental dermal fibrosis and their elevated expression is the hallmark of SSc dermal fibroblasts, the expression of these growth factors was examined. As expected, the decrease in mRNA expression of the Tgfb1 and Ctgf genes was noted in BLM-treated mice exposed to Am80 (Figure 1d), which was also confirmed at protein levels by immunohistochemistry (Figure 1e). To further elucidate the antifibrotic effect of Am80 on tissue fibrosis, TSK1 mice were employed, another widely accepted murine SSc model characterized by increased hypodermal thickness. In line with the results of BLM-treated mice, Am80 significantly ameliorated hypodermal thickness and collagen content in the back skin of TSK1 mice (Figure 1f and g). These findings suggest that Am80 exerts a potent antifibrotic effect on dermal fibrosis by reducing the production of collagen, promoting its degradation, and regulating expression of various soluble factors in SSc murine models.

Reference: J Invest Dermatol. 2016 Feb;136(2):387-398. https://linkinghub.elsevier.com/retrieve/pii/S0022-202X(15)00059-7

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.