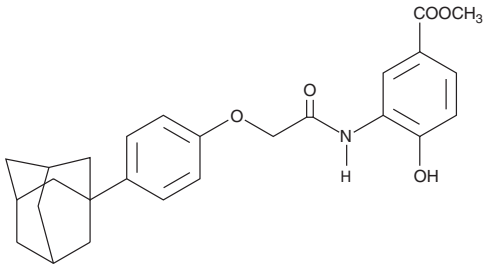
PRODUCT INFORMATION

CAY10585

Item No. 10012682

CAS Registry No.: 934593-90-5
Formal Name: 4-hydroxy-3-[[2-(4-tricyclo[3.3.1.13,7]dec-1-ylphenoxy)acetyl]amino]-benzoic acid, methyl ester
Synonym: Hypoxia-Inducible Factor-1α Inhibitor
MF: $C_{26}H_{29}NO_5$
FW: 435.5
Purity: ≥97%
UV/Vis.: λ_{max}: 234, 260 nm
Supplied as: A crystalline solid
Storage: -20°C
Stability: As supplied, 2 years from the QC date provided on the Certificate of Analysis, when stored properly



Laboratory Procedures

CAY10585 is supplied as a crystalline solid. A stock solution may be made by dissolving the CAY10585 in an organic solvent purged with an inert gas. CAY10585 is soluble in organic solvents such as DMSO and dimethyl formamide. The solubility of CAY10585 in these solvents is approximately 10 mg/ml.

If aqueous stock solutions are required for biological experiments, they can best be prepared by diluting the organic solvent into aqueous buffers or isotonic saline. Ensure that the residual amount of organic solvent is insignificant, since organic solvents may have physiological effects at low concentrations. We do not recommend storing the aqueous solution for more than one day.

Description

Hypoxia-inducible factor 1 (HIF-1) is a heterodimeric transcription factor composed of a HIF-1a subunit and HIF-1b subunit. Whereas the HIF-1b subunit is constitutively expressed, the HIF-1a subunit is regulated by cellular oxygen levels and therefore plays an important role in maintaining cellular oxygen homeostasis.[1,2] Under normoxic conditions, HIF-1a is selectively hydroxylated on proline residues 402 and 577 and targeted for destruction by the ubiquitin-proteasome system. Under hypoxic conditions, HIF-1a accumulates and dimerizes with HIF-1b to promote the transcription of a number of genes involved in angiogenesis, glycolysis, growth factor signaling, tumor invasion, and metastasis. CAY10585 is a novel small molecule inhibitor of HIF-1a accumulation and gene transcriptional activity.[3] In a gene reporter assay using human Hep3B and AGS cell lines, CAY10585 prevented HIF-1 transcriptional activity with IC_{50} values of 2.6 and 0.7 µM, respectively. It blocks HIF-1a accumulation in Hep3B cells in a concentration and time-dependent manner, with complete inhibition at a concentration of 30 µM within 12 hours. CAY10585 also significantly suppresses transcription of the HIF-1 target genes VEGF and erythropoietin at 10 µM.[3]

References

1. Wang, G.L., Jiang, B.-H., Rue, E.A., *et al.* Hypoxia-inducible factor-1 is a basic-helix-loop-helix-PAS heterodimer regulated by cellular O_2 tension. *Proc. Natl. Acad. Sci. USA* **92**, 5510-5514 (1995).
2. Safran, M. and Kaelin, W.G., Jr. HIF hydroxylation and the mammalian oxygen-sensing pathway. *J. Clin. Invest.* **111**, 779-783 (2003).
3. Lee, K., Lee, J.H., Boovanahalli, S.K., *et al.* (Aryloxyacetylamino)benzoic acid analogues: A new class of hypoxia inducible factor-1 inhibitors. *J. Med. Chem.* **50**, 1675-1684 (2007).

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