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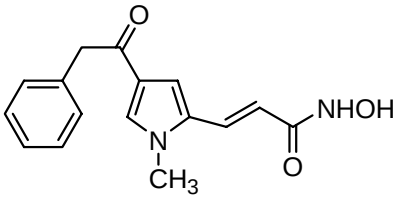
ProductInformation

APHA Compound 8

Product Number **A 2478**
Store at 2-8 °C

Chemical Name: 3-(1-Methyl-4-phenylacetyl-1*H*-2-pyrrolyl)-*N*-hydroxypropenamide



Product Description
Molecular Formula: $C_{16}H_{16}N_2O_3$
Molecular Weight: 284.3

Mammalian Histone Deacetylase (HDAC) belongs to a large family of enzymes that antagonizes the activities of Histone Acetyltransferases (HATs) thereby determining the acetylation state of histone/nonhistone nucleosomal proteins and hence control chromatin structure, transcriptional activities, and gene expression.[1] Hyperacetylation disrupts charge interaction between histones and the phosphate backbone of DNA leading to an open chromatin structure assessible to transcription factors, RNA polymerase and regulatory complexes with the consequence of transcription activation. Conversely, histone deacetylation is generally associated with compact chromatin conformation and the silencing of pre-programmed set of genes, leading to cell and tumor growth. HDAC inhibitors have been shown to be useful therapeutically in blocking angiogenesis, cell cycle, and promote apoptosis and differentiation.[2] There are three classes of HDACs and 11 known members in human. HDACs form complexes with regulatory proteins in a combinatorial manner. HDAC inhibitors of different structural classes are needed to target specific HDAC:protein complexes for greater specificity and efficacy in modulating cellular function and physiology.

APHAs (3-(4-aroyl-1*H*-2-pyrrolyl)-*N*-hydroxypropenamides) are a new class of synthetic HDAC (histone deacetylase) inhibitors. APHA Compound 8, a potent novel hydroxamate HDAC inhibitor, is in the same structural class as SAHA, an investigational drug standard currently in clinical trial. The IC_{50} for mouse HDAC1 using [H^3]acetate-prelabeled chicken reticulocyte histones as substrate was 0.5 μM.[3] In a separate study, significant inhibition was found in the proliferation of MEL cells at 24 μM and differentiation, assayed as the accumulation of hemoglobin, at 5 μM.[4]

APHA Compound 8 is a new and valuable addition to the expanding toolbox for studying the epigenetic code of histone acetylation in gene transcription control.

Storage/Stability
Store at 2-8 °C

References

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2. Marks, P., et al., Histone deacetylases and cancer: causes and therapies. Nat. Rev. Cancer, **1**, 194-202 (2001).
3. Mai, A., et al., 3-(4-Aroyl-1-methyl-1*H*-2-pyrrolyl)-*N*-hydroxy-2-alkylamides as a new class of synthetic histone deacetylase inhibitors. 1. Design, synthesis, biological evaluation, and binding mode studies performed through three different docking procedures. J. Med. Chem., **46**, 512-524 (2003).

4. Mai, A., et al., Binding mode analysis of 3-(4-Benzoyl-1-methyl-1*H*-2-pyrrolyl)-*N*-hydroxy-2-propenamide: A new synthetic histone deacetylase inhibitor inducing histone hyperacetylation, growth inhibition, and terminal cell differentiation. J. Med. Chem., **45**, 1778-1784 (2002).

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