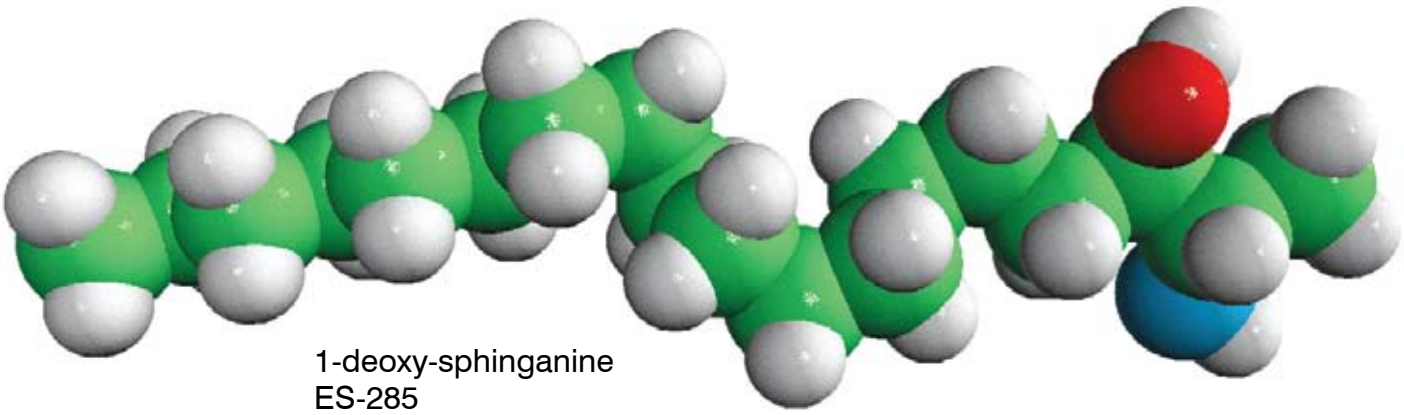
A New Sphingolipid 1-deoxy-sphinganine Only from Avanti®



1-deoxy-sphinganine
ES-285
Spisulosine
Avanti Number 860493

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Investigational anticancer drug reported to inhibit proliferation of numerous cancer cell lines

"Sphingosin" was first described by J. L. W. Thudichum in 1884 and structurally characterized as 2S,3R,4E-2-aminooctadec-4-ene-1,3-diol in 1947 by Herb Carter, who also proposed the designation of "lipides derived from sphingosine as sphingolipides." This category of amino alcohols is now known to encompass hundreds of compounds that are referred to as sphingoid bases and sphingoid base-like compounds, which vary in chain length, number, position, and stereochemistry of double bonds, hydroxyl groups, and other functionalities. Some have especially intriguing features, such as the tail-to-tail combination of two sphingoid bases in the alpha,omega-sphingoids produced by sponges. Most of these compounds participate in cell structure and regulation, and some (such as the fumonisins) disrupt normal sphingolipid metabolism and cause plant and animal disease. Many of the naturally occurring and synthetic sphingoid bases are cytotoxic for cancer cells and pathogenic microorganisms or have other potentially useful bioactivities; hence, they offer promise as pharmaceutical leads. This thematic review gives an overview of the biodiversity of the backbones of sphingolipids and the broader field of naturally occurring and synthetic sphingoid base-like compounds.

Pruett, S.T., A. Bushnev, K. Hagedorn, M. Adiga, C.A. Haynes, M.C. Sullards, D.C. Liotta, and A.H. Merrill Jr. (2008). Thematic Review Series: Sphingolipids. Biodiversity of sphingoid bases ("sphingosines") and related amino alcohols. *J Lipid Res* 49:1621-39.

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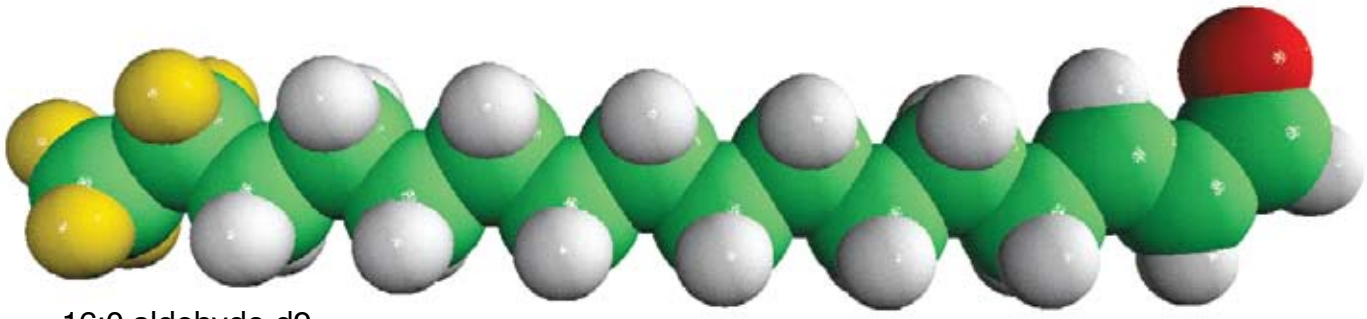
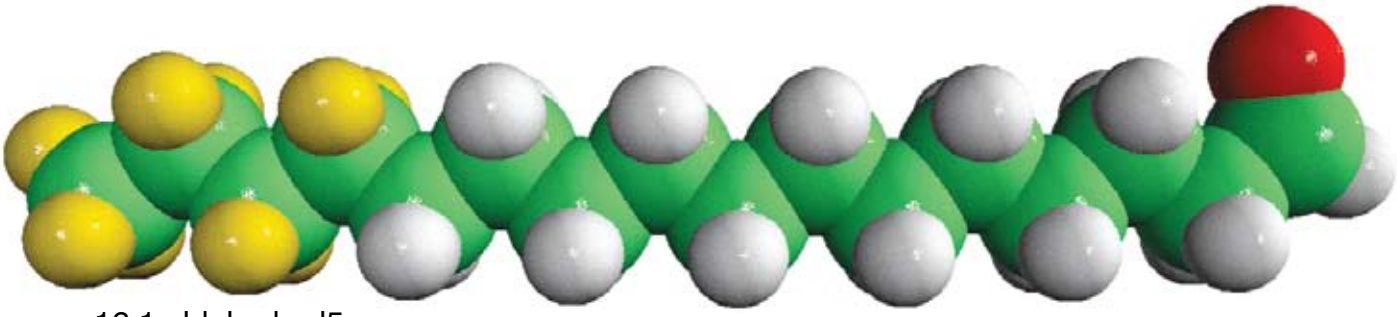
New Standards for S1P Lyase



16:0 aldehyde-d9
Avanti Number 857460



16:1 aldehyde-d5
Avanti Number 857461

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Sphingosine-1-phosphate lyase (SPL) catalyzes the cleavage of sphingosine-1-phosphate (S1P) into ethanolamine phosphate and a long-chain aldehyde. Avanti now offers a deuterium-labeled long-chain aldehyde for use as an internal standard in the quantitation of cell-derived reaction products.

Sphingosine-1-phosphate lyase is a widely expressed enzyme that catalyzes the essentially irreversible cleavage of the signaling molecule sphingosine 1-phosphate. To investigate whether sphingosine-1-phosphate lyase influences mammalian cell fate decisions, a recombinant human sphingosine-1-phosphate lyase fused to green fluorescent protein was expressed in HEK293 cells. The recombinant enzyme was active, localized to the endoplasmic reticulum, and reduced baseline sphingosine and sphingosine-1-phosphate levels. Stable overexpression led to diminished viability under stress, which was attributed to an increase in apoptosis and was reversible in a dose-dependent manner by exogenous sphingosine-1-phosphate. In contrast to sphingosine-1-phosphate, the products of the lyase reaction had no effect on apoptosis. Lyase enzymatic activity was required to potentiate apoptosis, because cells expressing a catalytically inactive enzyme behaved like controls. Stress increased the amounts of long- and very long-chain ceramides in HEK293 cells, and this was enhanced in cells overexpressing wild type but not catalytically inactive lyase. The ceramide increases appeared to be required for apoptosis, because inhibition of ceramide synthase with fumonisin B1 decreased apoptosis in lyase-overexpressing cells. Thus, sphingosine-1-phosphate lyase overexpression in HEK293 cells decreases sphingosine and sphingosine 1-phosphate amounts but elevates stress-induced ceramide generation and apoptosis. This identifies sphingosine-1-phosphate lyase as a dual modulator of sphingosine 1-phosphate and ceramide metabolism as well as a regulator of cell fate decisions and, hence, a potential target for diseases with an imbalance in these biomodulators, such as cancer.

Reiss, U., B. Oskouian, J. Zhou, V. Gupta, P. Sooriyakumaran, S. Kelly, E. Wang, A.H. Merrill Jr, and J.D. Saba. (2004). Sphingosine-phosphate lyase enhances stress-induced ceramide generation and apoptosis. *J Biol Chem* 279:1281-90.

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New Products

As always the Avanti scientists have been hard at work developing many exciting new lipids.

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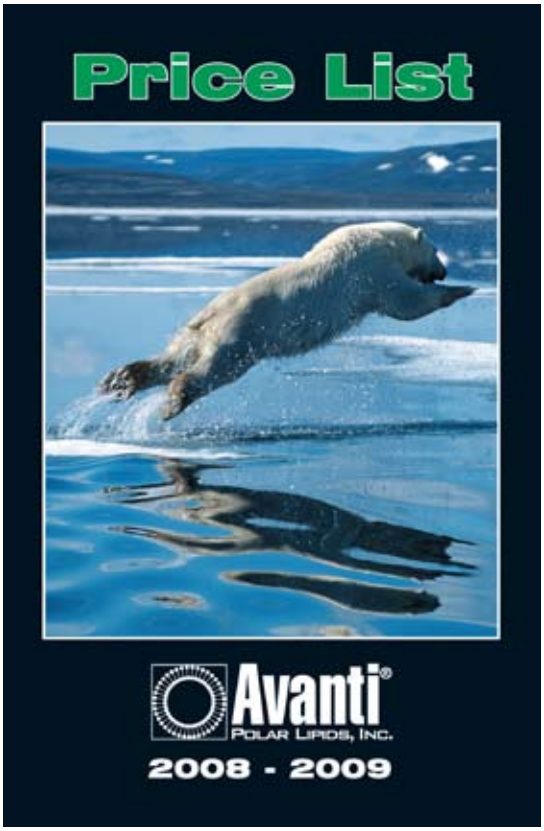

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- CPhI Worldwide
Avanti will be Exhibiting
September 30 - October 2,
Frankfurt a.M., Germany

- NIH Research Festival
Avanti will be Exhibiting
October 14 - 17
Bethesda, MD

- Sphingolipid Club 7th Annual Meeting
November 14 - 16
Leiden, The Netherlands

- AAPS Annual Meeting and Exposition
Avanti will be Exhibiting
November 16 - 20th
Atlanta, GA