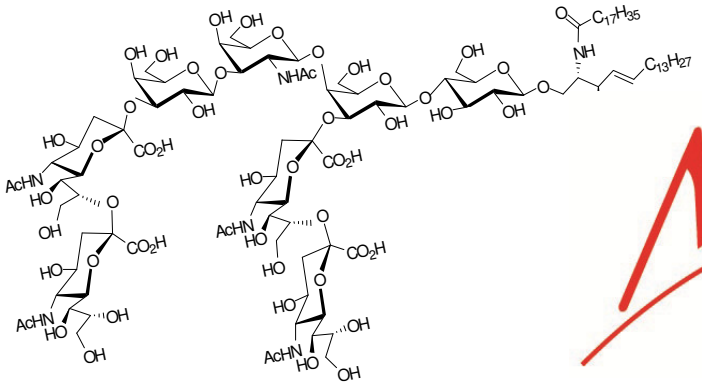


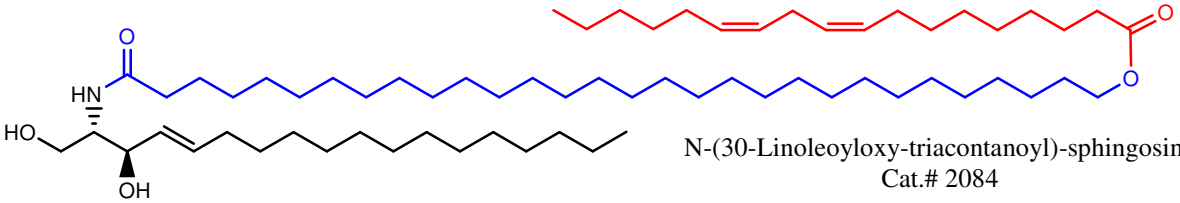
MATREYA LLC

Lipids and Biochemicals

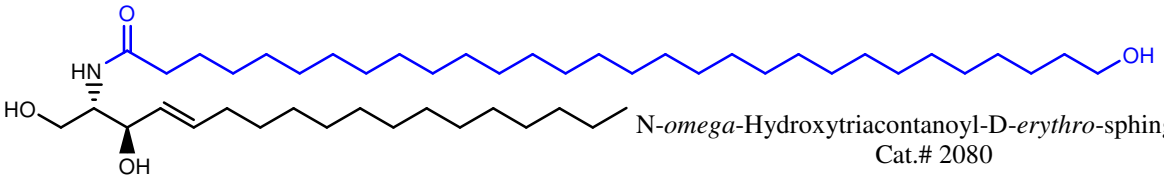
NEWSLETTER FOR GLYCO/SPHINGOLIPID RESEARCH

OCTOBER 2017

The Essential Role of Esterified *omega*-Hydroxy Ceramides as Skin Lipids



N-(30-Linoleoyloxy-triacontanoyl)-sphingosine
Cat.# 2084



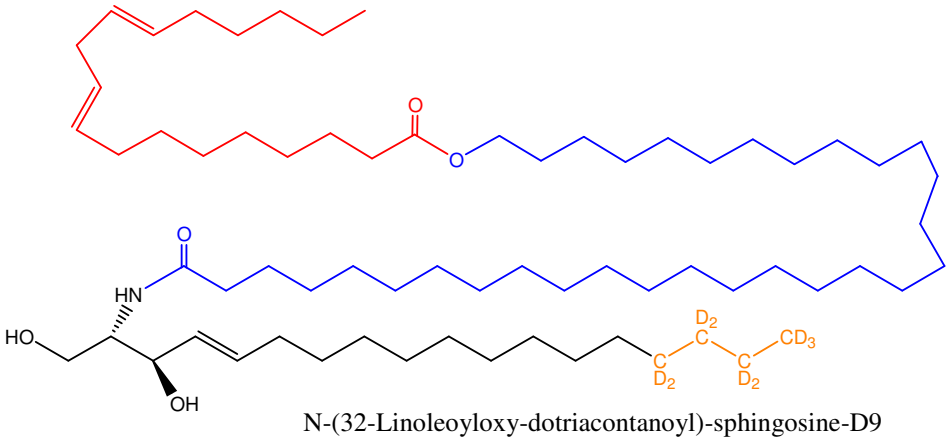
N-*omega*-Hydroxytriacontanoyl-D-*erythro*-sphingosine
Cat.# 2080

Ceramides in human cells have important and divergent functions that make their study both challenging and important. The roles of these ubiquitous lipids include signal transduction and cell regulation relevant to apoptosis, cell growth arrest, differentiation, senescence, and immune responses. Many of the functions of individual ceramides are dependent on the specific structure of each ceramide specie. Relative to other tissues, human *stratum corneum* contains a number of very complex ceramide species that play important physicochemical roles in determining the cutaneous barrier's water-retaining functions.

The *stratum corneum* is the outermost cellular layer of the epidermis and functions as the permeability barrier in mammals. Of all the species of ceramides, the *stratum corneum* contains 12 extractable ceramide sub-groups including sphingosine, 6-hydroxysphingosine, dihydrosphingosine, and phytosphingosine bases. Mammalian skin contains significant amounts of sphingolipids (as much as 50% of the total lipids), particularly very long chain linoleoyl esterified ceramide and glucosylceramide (also called O-acylceramide and O-acylglucosylceramide, respectively). These lipids, which are mostly found in the extracellular domains, are vital to the water permeability barrier's ability to prevent lethal loss of water and pathogen invasion. The esterified *omega*-hydroxy-ceramides are formed from glucosylceramide and sphingomyelin in special lamellar bodies in epidermal cells from which they are excreted into the *stratum corneum*. These skin-specific ceramides can be covalently bound to proteins of the cornified envelope where they form a hydrophobic layer.

INSIDE THIS ISSUE

A deficiency of linoleoyl *omega*-esterified ceramides is strongly correlated with skin diseases such as ichthyosis, psoriasis, and atopic dermatitis.[1,2,3] Mutations in the enzyme patatin-like phospholipase domain-containing 1 (PNPLA1), which plays a crucial role in the biosynthesis of esterified *omega*-hydroxy-ceramides by esterifying the *omega*-fatty acids with linoleic acid, have been shown to cause autosomal recessive congenital ichthyosis.[4] A lack of activity in the enzyme serine palmitoyltransferase prevents the *de novo* synthesis of ceramides and has been strongly linked to the development of psoriasis.[5] In atopic



N-(32-Linoleoyloxy-dotriacontanoyl)-sphingosine-D9
Cat.# 2208

dermatitis, a deficiency of activity of the ELOVL (elongase of long-chain fatty acids) enzymes results in a reduction in very long-chain fatty acids and a subsequent shortage of esterified long-chain ceramides.[5]

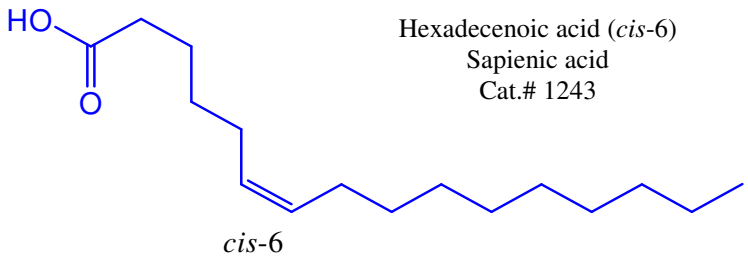
Due to the complex nature of the human *stratum corneum*, which contains dozens of ceramide species, analysis can be highly challenging. Shotgun lipidomics is a recent liquid chromatography-mass spectrometry technique that provides data on large amounts of analytes in a single experimental run. This approach allows for the rapid, high throughput analysis of difficult samples. By taking advantage of specific esterified *omega*-hydroxy-ceramide internal standards, whole classes of skin lipids have been identified and quantified.[6]

References:

1. B. Breiden and K. Sandhoff., The role of sphingolipid metabolism in cutaneous permeability barrier formation. Biochimica et Biophysica Acta (2014) 1841, 441-452
2. R. Sandhoff., Very long chain sphingolipids: Tissue expression, function and synthesis. FEBS Letters (2010) 584, 1907-1913
3. Y. Masukawa et al., Characterization of overall ceramide species in human *stratum corneum*. Journal of Lipid Research (2008) 49:7, 1466-1476
4. S. Grond et al., PNPLA1 Deficiency in Mice and Humans Leads to a Defect in the Synthesis of Omega-O-Acylceramides. Invest Dermatol. (2017) 137:2, 394-402
5. S. Borodzicz et al., The role of epidermal sphingolipids in dermatologic diseases. Lipids in Health and Disease (2016) 15:13, 1-9
6. T. Sadowski et al., Large-scale human skin lipidomics by quantitative, high-throughput shotgun mass spectrometry. Sci Rep. (2017) 7:7, 43761, 1-11

Skin Sphingolipids	Catalog #	Amount	Purity
D-*erythro*-sphingosine, D_9	2079	1 mg	98+%
N-*omega*-CD_3-Octadecanoyl-D-*erythro*-sphingosine	2201	1 mg	98+%
N-*omega*-CD_3-Octadecanoyl-D-*erythro*-dihydrosphingosine	2202	1 mg	98+%
N-1-^{13}C-Hexadecanoyl-D-*erythro*-sphingosylphosphorylcholine	2200	1 mg	98+%
N-Octadecanoyl-D_3-D-*erythro*-sphingosine-1-phosphate, deuterated	2206	1 mg	98+%
N-*omega*-Hydroxytriacontanoyl-D-*erythro*-sphingosine	2080	5 mg	98+%
N-(30-Linoleoyloxy-triacontanoyl)-sphingosine	2084	1 mg	98+%
N-(32-Linoleoyloxy-dotriacontanoyl)-sphingosine-D9	2208	1 mg	98+%

The Role of Sapienic Acid in Antimicrobial Skin Barrier Defense



Hexadecenoic acid (*cis*-6)
Sapienic acid
Cat.# 1243

Hexadecenoic acid (*cis*-6) is an unusual unsaturated fatty acid that is found in the human body, some marine organisms, and in some seed oils. In humans, hexadecenoic acid (*cis*-6) is the major constituent of human sebaceous lipids, from which it derives its common name sapienic acid. In the skin, it is involved in self-sterilization and atopic dermatitis amelioration.[1] Among all hair-bearing animals, humans are the only ones to produce this fatty acid and it is not found in any organ other than the skin.[2]

Sapienic acid is formed from palmitic acid by the action of the enzyme *delta*-desaturase (or fatty acid desaturase-2).[3] It can then be converted to sebaleic acid (C18:2 *cis*-5,*cis*-8), another fatty acid unique to sebum, by the extension of two carbons and the addition of a double bond.[4] While it has been found that hexadecenoic acid (*cis*-6) has powerful antibacterial properties, the mechanisms have not been fully explored.

As a skin lipid, a primary purpose of sapienic acid is to act as an antimicrobial lipid for the skin barrier. Unsaturated long-chain fatty acids, including sapienic and linoleic acids, cause membrane depolarization in certain bacteria leading to large transcriptional changes, especially in those pathways associated with cellular energetics. From the transcriptomic response, it is inferred that the membrane depolarization leads to disruption of the electron transport chain.[5]

Sapienic acid seems to be linked to the prevention of various illnesses. For example, *Staphylococcus aureus* is a bacteria that is strongly linked with dermatological conditions such as atopic dermatitis. It has been identified that individuals with large *S. aureus* colonization have low levels of sapienic acid, thus strongly indicating it as a host factor that can contribute to the prevention of some long-term skin diseases.[5] In this, and other cases, the contribution of other lipids and the specific mechanisms involved have not been fully elucidated.

References:

1. D. Downing et al., Essential fatty acids and acne. Journal of the American Academy of Dermatology (1986) 14:2, 221-225
2. N. Nicolaides, Skin Lipids: Their Biochemical Uniqueness. Science (1974) 186:4 19-26
3. L. Ge et al., Identification of the *delta*-6 Desaturase of Human Sebaceous Glands: Expression and Enzyme Activity. Journal of Investigative Dermatology (2003) 120, 707-714
4. M. Ottaviani, E. Camera, and M. Picardo, Lipid Mediators in Acne. Mediators of Inflammation (2010) 2010, 1-6
5. J. Moran et al., Comparative Transcriptomics Reveals Discrete Survival Responses of *S. aureus* and *S. epidermidis* to Sapienic Acid. Frontiers in Microbiology (2017) 8:33 1-12

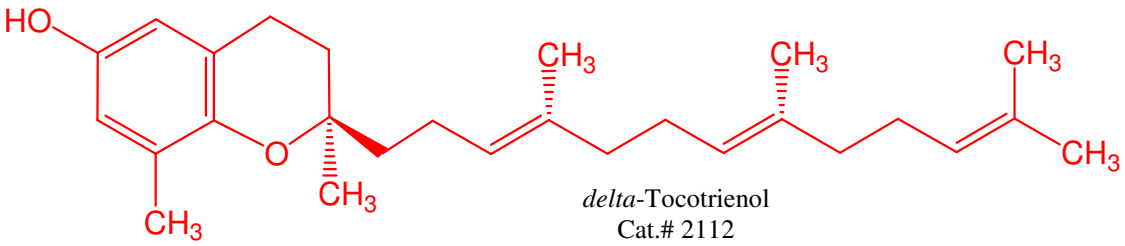
Name	Catalog #	Amount	Purity
Hexadecenoic acid (*cis*-6) (Sapienic acid)	1243	25 mg	99%

δ-Tocotrienol suppresses tumorigenesis by inducing apoptosis and blocking the COX-2/PGE_2 pathway that stimulates tumor–stromal interactions in colon cancer

An abstract from a 2017 issue of the Journal of Functional Foods

Anticancer effects of δ-tocotrienol have been reported for several types of cancer, but have not been fully elucidated in colorectal cancer. We investigated the anti-proliferative effect of tocotrienols *in vitro*, in colon epithelial cells and stromal cells, and *in vivo*, in an induced colorectal cancer mouse model. Of the four isoforms tested, δ-tocotrienol exerted the most potent anti-proliferative effect on colon adenocarcinoma cells. δ-Tocotrienol reduced the nitrite and prostaglandin E_2 (PGE_2) concentrations in mouse embryonic fibroblasts (MEFs) pretreated with δ-tocotrienol and stimulated with lipopolysaccharide (LPS) and interferon γ. Furthermore, supernatants of LPS-stimulated MEFs promoted adenocarcinoma cell proliferation, while δ-tocotrienol treatment suppressed this effect. Additionally, a δ-tocotrienol-enriched diet significantly suppressed tumor formation in azoxymethane and dextran sulfate sodium-treated mice. Taken together, these data suggest that a δ-tocotrienol-enriched diet prevents colorectal cancer. At the molecular level, tocotrienols exert a direct anti-proliferative effect on colon adenocarcinoma cells, and an indirect, stromal cell-mediated, anti-proliferative effect.

S. Wada et. al., δ-Tocotrienol suppresses tumorigenesis by inducing apoptosis and blocking the COX-2/PGE_2 pathway that stimulates tumor–stromal interactions in colon cancer. J. Functional Foods (2017) 35, 428-435



delta-Tocotrienol
Cat.# 2112

Tocotrienols	Catalog #	Amount	Purity (GC/TLC)
alpha-Tocotrienol	2109	25 mg	98^+%/98^+%
beta-Tocotrienol	2110	25 mg	98^+%/98^+%
gamma-Tocotrienol	2111	25 mg	98^+%/98^+%
delta-Tocotrienol	2112	25 mg	98^+%/98^+%
Tocopherols			
rac-alpha-Tocopherol	1072	1 ml, 50 mg/ml	98^+%/95^+%
rac-beta-Tocopherol	1071	1 ml, 50 mg/ml	98^+%/95^+%
rac-gamma-Tocopherol	1073	1 ml, 50 mg/ml	98^+%/95^+%
(+)-*delta*-Tocopherol	1790	1 ml, 50 mg/ml	98^+%/95^+%
Internal Standards			
rac-5,7-Dimethyltocol	1074	1 ml, 50 mg/ml	98^+%/95^+%
Tocol	1797	1 ml, 50 mg/ml	98^+%/95^+%