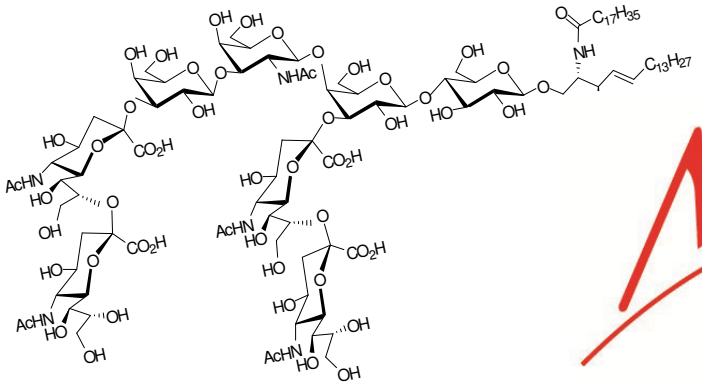


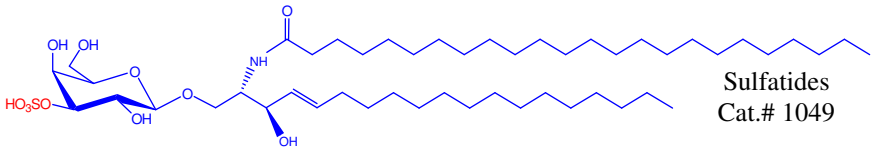
MATREYA LLC

Lipids and Biochemicals

NEWSLETTER FOR GLYCO/SPHINGOLIPID RESEARCH

FEBRUARY 2018

The Role of Sulfatides in Disease



Sulfatides
Cat.# 1049

Sulfatides are 3-sulfated galactosylceramides that are found primarily in the central nervous system and are myelin specific sphingolipids. Over the last several decades, sulfatides have been linked to many physiological functions and recently there has been a renewed interest in their role in diseases. Sulfatides are highly multifunctional glycolipids involved in the nervous system, diabetes, immune system, hemostasis/thrombosis, and bacterial and viral infection. By understanding the correlation between sulfatide's normal physiological functions and specific roles in disease, new diagnostic and therapeutic methods can be evaluated.

Sulfatides derived from the brain and spinal cord can have saturated, unsaturated, and 2-hydroxy fatty acyl chains, the composition of which are vital to influencing its function. They have demonstrated many critical physiological processes, both inter- and intracellularly, and are involved in numerous diseases such as demyelinating diseases. Various infections, including influenza virus A and tuberculosis, have been shown to be influenced by the actions of sulfatides.[1] Recent studies have implicated sulfatides in numerous inflammatory responses and there has been significant interest in its biological role towards CD1-restricted T cells. An important physiological role of sulfatides are their involvement in hemostasis and thrombosis by forming stable platelet aggregates.[2,3]

In ovarian cancer, sulfatide levels have been found to be elevated, with the most prevalent species detected via MALDI-TIMS being d18:1/C16:0, d18:1/C24:1 and d18:1/C24:0.[4] This elevation in sulfatide levels can be exploited as an ovarian cancer biomarker and as a possible therapeutic approach. In hepatic ischemic reprofusion injury, subsets of NKT cells have opposing roles.[5] Type I NKT cells promote injury while sulfatide-reactive type II NKT cells protect against injury. CD1d activation of NKT cells is conserved from mice to humans, so strategies to modify these processes might be developed to treat patients with hepatic reperfusion injury.

Abnormal sulfatide metabolism, such as in Metachromatic leukodystrophy, can induce cell apoptosis due to endosome-mediated ceramide generation and the accumulation of cytotoxic levels of sulfatides in lysosomes.[6] Metachromatic leukodystrophy is an autosomal-recessive lysosomal storage disease caused by mutations in the arylsulfatase A (ARSA) gene leading to ARSA deficiency and causing sulfatide accumulation. Main symptoms of the disease are progressive demyelination, neurological dysfunction, and reduced life expectancy.[7]

Due to its prevalence in the myelin sheath of nerves, it is not surprising that sulfatide metabolism has been implicated in many neural degenerative diseases such as Alzheimer's disease and multiple sclerosis. Sulfatide content is found to precipitously drop in Alzheimer's disease, with its concentration in the central nervous system being modulated by apolipoprotein E.[8] Multiple sclerosis is a chronic inflammatory disease of the central nervous system where the myelin sheath around nerve fibers becomes the target of an autoimmune attack leading to demyelination, axonal loss, and subsequent progressive neurologic functional deficits. The identity of the target antigen of multiple sclerosis has long been unidentified but it was recently demonstrated that levels of anti-sulfatide antibodies were significantly higher in multiple sclerosis patients than in controls.[9] Sulfatides are also able to activate inflammatory responses as an endogenous stimulator in brain-resident immune cells.[10]

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These sulfatides bind to several human CD1 molecules as well as to murine CD1d and are recognized by type II NKT cells. Among the sulfatides, *cis*-tetracosenoyl sulfatide is immunodominant and can either prevent or reverse antigen-induced experimental autoimmune encephalomyelitis in $CD1d^{+/+}$mice.[11] It therefore may also be able to reverse autoimmune demyelinating diseases in humans.[12] It has been demonstrated that the glycosphingolipid antigen sulfatide presented on the major histocompatibility complex (MHC) class I-like CD1d and CD1c molecules was recognized by Vδ1 lymphocyte cells. The myelin sheath, the target of the autoimmune attack in multiple sclerosis, is a rich source of sulfatides, suggesting that CD1c/d-restricted T cells could be activated by myelin-derived sulfatide and, thereby, could be implicated in the onset of the disease.[13] A depletion of different sulfatide species from the earliest stages of multiple sclerosis in both white and gray matter areas of the frontal cortex could be considered as a marker of the disease, but may also indicate neurochemical modifications related to its pathogenesis.[14] Sulfatides are highly dynamic glycosphingolipids with far reaching biological processes. A greater understanding of these functions in living systems will lead to the elucidation of associated diseases and the development of therapeutic treatments to various sulfatide associated diseases.

References:

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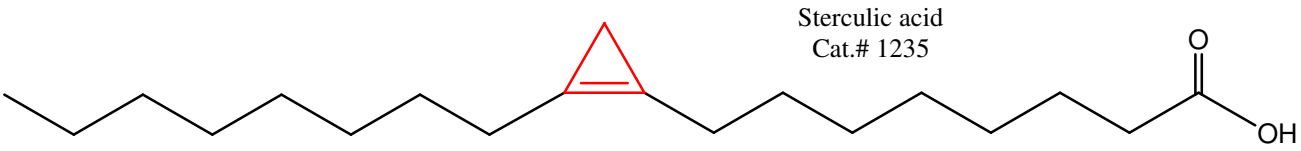
Cat.#	Amount	Purity	Product Name
1049	50 mg	98^{+}%	Natural Sulfatides
1904	1 mg	98^{+}%	*lyso*-Sulfatide
2076	1 mg	98^{+}%	N-Acetyl-sulfatide (N-C2:0-sulfatide)
1938	1 mg	98^{+}%	N-Dodecanoyl-sulfatide (N-C12:0-sulfatide)
1875	1 mg	98^{+}%	N-Hexadecanoyl-sulfatide (N-C16:0-sulfatide)
1934	1 mg	98^{+}%	N-Heptadecanoyl-sulfatide (N-C17:0-sulfatide)
1932	1 mg	98^{+}%	N-Octadecanoyl-sulfatide (N-C18:0-sulfatide)
1933	1 mg	98^{+}%	N-Oleoyl-sulfatide (N-C18:1(*cis*-9)-sulfatide)

Cat.#	Amount	Purity	Product Name
1935	1 mg	98^{+}%	N-Nonadecanoyl-sulfatide (N-C19:0-sulfatide)
1888	1 mg	98^{+}%	N-Tetracosanoyl-sulfatide (N-C24:0-sulfatide)
1931	1 mg	98^{+}%	N-Tetracosenoyl-(*cis*-15)-sulfatide (N-C24:1(*cis*-15)-sulfatide)
1536	1 mg	98^{+}%	N-omega-CD3-Octadecanoyl-sulfatide (N-C18:0-D3-sulfatide)
1632	100 µg	98^{+}%	N-Dodecanoyl-NBD-sulfatide (N-C12:0-NBD-sulfatide)
2207	1 mg	98^{+}%	N-Hexanoyl-biotin-sulfatide
2092	1 mg	98^{+}%	N-Glycinated *lyso*-sulfatide

Sterculic Acid and its Methyl Ester Inhibit *Toxoplasma Gondii*



Sterculic acid is a monounsaturated fatty acid containing a cyclopropene ring, which gives it specific and unusual physiological properties. The major sources of sterculic acid are the seed oils of various plants, including *sterculia foetida*, cotton, and *Bombax munguba*. Cyclopropenoid fatty acids have been reported to have several deleterious effects on mammals, such as carcinogenicity and acute and chronic toxicity.[1,2] Because of the harmful effects of cyclopropenoids, cottonseed oil (a major world-wide edible oil which contains around 1% of these fatty acids) is required to be heat treated and hydrogenated before consumption. *Sterculia foetida* seeds have been used in traditional Chinese medicine as an anti-parasitic drug and recent research has found that sterculic acid and its methyl ester analog have a significant inhibitory effect towards the wide-spread parasite *Toxoplasma gondii*.[3] Oil from *Sterculia foetida* has also been shown to have significant insecticide and possible anti-fungal properties, making it a potentially useful alternative to more environmentally toxic synthetic compounds.[4,5] Cyclopropenoids, such as sterculic acid, inhibit the enzyme Δ9-desaturase, preventing the conversion of stearic acid to oleic acid and potentially causing significant health problems for organisms which consume them.

Stearoyl-coenzyme A desaturase (Δ9-desaturase) is an endoplasmic reticulum enzyme found in a wide number of organisms that catalyzes the insertion of a double bond into the *cis*-Δ9 position of various fatty acyl-CoAs. The most common substrates are palmitic acid (C16:0) and stearic acid (C18:0) which are converted to palmitoleic acid (C16:1) and oleic acid (C18:1), respectively. In mammalian organisms, Δ9-desaturase has been found to have a role in modulating metabolic and signaling processes involved in cellular proliferation, survival, and malignant tumor generation.

The presence of Δ9-desaturases in several parasitic organisms has been identified and the desaturation of palmitic acid and stearic acid noted. Since Δ9-desaturase is likely to be an essential enzyme for these parasites, it is probable that the anti-parasitic properties of sterculic acid and its methyl ester arise from their inhibition of this enzyme. Pan Hao et al.[3] have recently demonstrated that sterculic acid and methyl sterculate are effective in inhibiting *T. gondii* growth in vitro, suggesting that these compounds target Δ9-desaturase in the parasite and could therefore be effective agents for the treatment of toxoplasmosis.

References:

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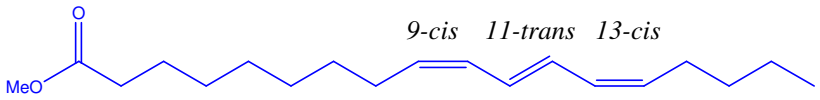
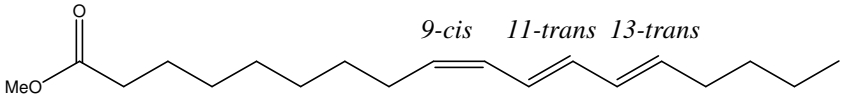
Product Name	Catalog #	Amount	Purity
Sterculic acid (9,10-Methylene-octadec-9Z-enoic acid)	1235	25 mg	98+%
Methyl sterculate (Methyl 9,10-Methylene-octadec-9Z-enoate)	1236	25 mg	98+%
Methyl malvalate (Methyl 8,9-Methylene-heptadec-8Z-enoate)	1238	5 mg	95+%
Dihydrosterculic acid (*cis*-9,10-Methyleneoctadecanoic acid)	1822	25 mg	98+%
Methyl dihydrosterculate (Methyl *cis*-9,10-methyleneoctadecanoate)	1823	25 mg	98+%

Potent Physiological Functions of Conjugated Linolenic Acids

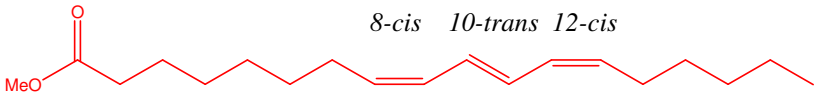
Methyl punicate
Cat. 1240



Methyl *alpha*-eleostearate
Cat. 1233



Methyl jacarate
Cat. 1234



Conjugated linolenic acids (CLnAs) are plant derived lipids that posses strong antidiabetic, antiobesity, antiproliferative, and anticarcinogenic activities as well as a significant affect on lipid metabolism, making them important biochemicals.(1) CLnAs contain 3 or 4 double bonds (which can be any combination of *cis* or *trans*) having 9,11,13- and 8,10,12-octadecatrienoic acid positional isomers. The potent physiological roles of CLnAs make them potential candidates as therapeutic and diabetic agents.(2) Matreya has recently introduced three high purity CLnAs as their methyl ester: methyl punicate, methyl *alpha*-eleostearate, and methyl jacarate.

CLnAs are found in high amounts in several natural oils, including pomegranate, tung, and mimosofilia oils. Some studies suggest that punicic and *alpha*-eleostearic acids can reduce adipose tissue in mouse models, making it potentially useful as a weight-controlling lipid.(3,4) CLnAs, including punicic, jacaric, and *alpha*-eleostearic acids, have been shown to suppress tumor cell growth through lipoperoxidation and apoptotic pathways and exhibit potent anti-inflammatory effects.(5,6,7,8) Punicic acid also modulates mucosal immune responses and ameliorates gut inflammation through PPAR γ and δ-dependent mechanisms.(9) In addition, punicic acid and *alpha*-eleostearic acid from pomegranate oil have been shown to inhibit estrogen receptors α and β.(10)

References:

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Product Name	Catalog #	Amount	Purity
Methyl punicate (Methyl 9(Z),11(E),13(Z)-Octadecatrienoate)	1240	25 mg	97+%
Methyl *alpha*-eleostearate (Methyl 9(Z),11(E),13(E)-Octadecatrienoate)	1233	25 mg	98+%
Methyl jacarate (Methyl 8(Z),10(E),12(Z)-Octadecatrienoate)	1234	25 mg	96+%