

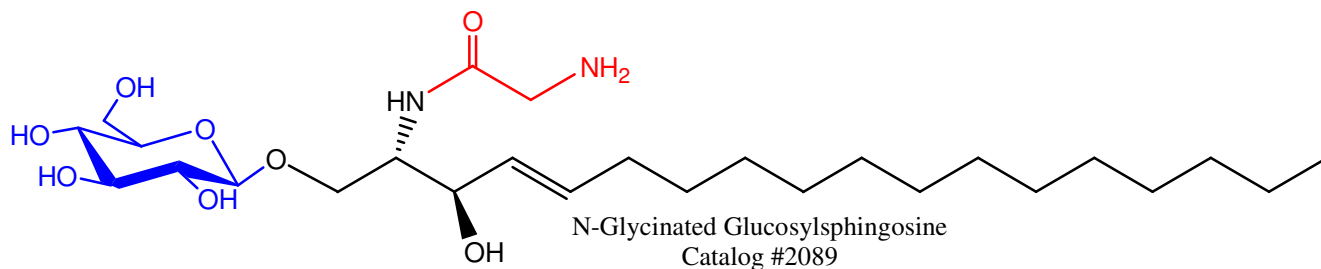
NEWSLETTER FOR GLYCO/SPHINGOLIPID RESEARCH DECEMBER 2016

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Glycinated *lyso*-Glycosphingolipids as New Mass Spectrometry Internal Standards



lyso-Glycosphingolipids are important biomolecules in both healthy and diseased physiological processes. Suitable standards are needed for identifying and quantitating these key biological components in order to understand their functions and to diagnosis and monitor associated diseases. Often glycosphingolipids are labeled with a stable isotope on the fatty acid of the ceramide, however *lyso*-sphingolipids lack the fatty acid component and therefore do not have this option. Synthetically attaching a label to either the sphingosine or oligosaccharide involves a difficult synthesis. As an alternative approach R. Krüger et al.⁽¹⁾ demonstrated that a glycine molecule attached to the amine of sphingosine would give an easily identifiable compound that shares almost identical physical properties with the native unlabeled *lyso*-glycosphingolipid. Matreya now offers 3 glycinated *lyso*-glycosphingolipids as mass spectrometry internal standards: N-glycinated glucosylsphingosine, N-glycinated lactosylsphingosine, and N-glycinated *lyso*-ceramide trihexoside.

A. Rolfs et al.⁽²⁾ recently demonstrated that glucosylsphingosine can be used as a promising, reliable, and specific biomarker for Gaucher disease (GD). They evaluated the sensitivity and specificity of glucosylsphingosine with regard to healthy controls vs. GD carriers and other lysosomal storage disease control groups. Only GD patients displayed elevated levels of glucosylsphingosine higher than the pathological cut-off, verifying the specificity of glucosylsphingosine as a biomarker for this disease. Glucosylsphingosine was monitored during enzyme replacement therapy and demon-

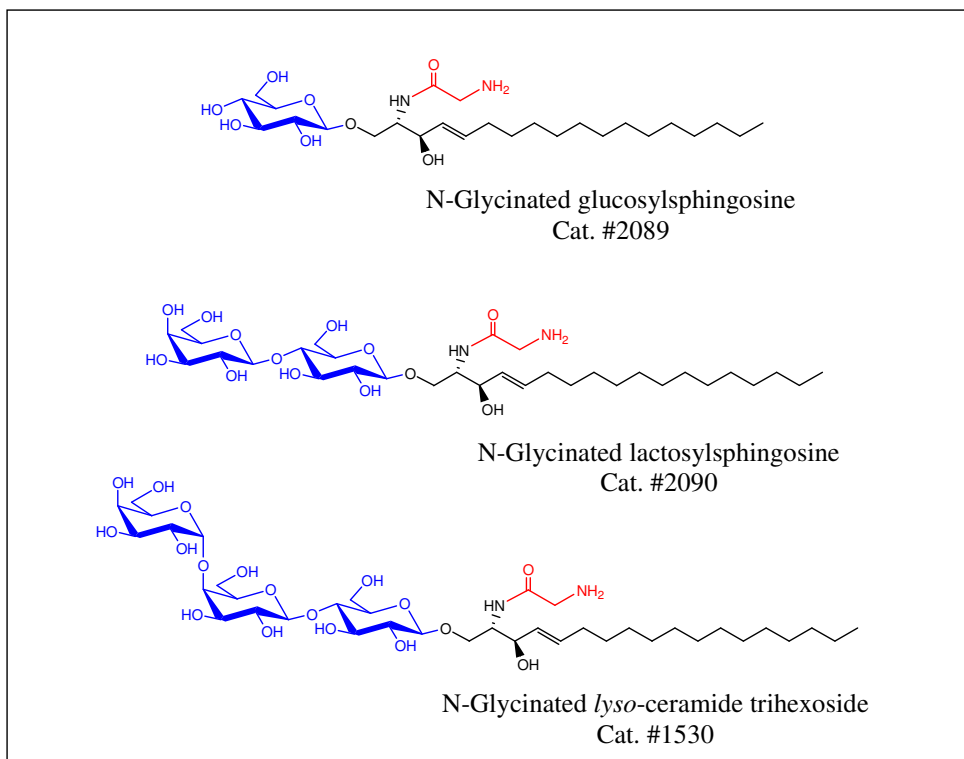
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strated a decrease in this sphingolipid biomarker over time.

Lactosylceramide is the precursor of many other glycosphingolipids and also functions as a second messenger and protein receptor, making it a very important biochemical. Many cellular processes are dependent on lactosylceramide since it is the substrate for neutral oligoglycosylceramides and gangliosides, all of which have their own vital functions. Lactosylceramide also helps to stabilize the lipid membrane, activate receptor molecules, and act as a receptor for certain bacteria and toxins. In animals, where it is found mostly in epithelial and neuronal cells, it is expressed on neutrophils and macrophages, where it binds to toxins and bacteria which are then engulfed and eliminated. Niemann-Pick Type C, a neurovisceral lysosomal cholesterol trafficking and lipid storage disorder, leads to an accumulation of multiple lipids, including excess unesterified cholesterol, GM2 and GM3 gangliosides, lactosylceramide, lactosylsphingosine, and glucosylceramide.⁽³⁾

lyso-Ceramide trihexoside (globotriaosylsphingosine or *lyso*-Gb₃) and its acylated form ceramide trihexoside (globotriaosylceramide or Gb₃) are important biomarkers for the lysosomal storage disorder Fabry disease (FD). FD is characterized by a deficiency of the enzyme α -galactosidase A, resulting in an accumulation of globotriaosylceramide, globotriaosylsphingosine, galabiosylceramide (Ga₂), and blood group B glycolipids. It is an X-linked chromosomal disorder and early diagnosis is critical as progression will lead to multiorgan dysfunction and early death.⁽⁴⁾ Glycinated *lyso*-ceramide trihexoside (cat. #1530) was explored as an internal standard and the physical and chemical properties were found to be almost identical to that of natural globotriaosylsphingosine in terms of extraction, stability, and sensitivity, making it an excellent internal standard for clinical work.⁽¹⁾

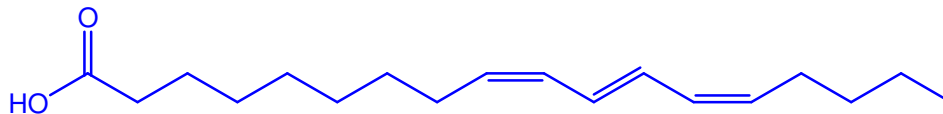


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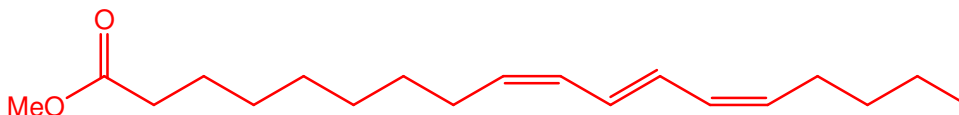
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Catalog #	Amount	Purity	Product Name
2089	1 mg	98 ⁺ %	N-Glycinated glucosylsphingosine
2086	5 mg	98 ⁺ %	Glucosylsphingosine, synthetic
1306	5 mg	98 ⁺ %	Glucosylsphingosine, bovine buttermilk
1310	5 mg	98 ⁺ %	Glucosylsphingosine, plant
2090	1 mg	98 ⁺ %	N-Glycinated lactosylsphingosine
2088	1 mg	98 ⁺ %	<i>lyso</i> -Lactosylceramide, synthetic
1517	1 mg	98 ⁺ %	<i>lyso</i> -Lactosylceramide, bovine buttermilk
1530	1 mg	98 ⁺ %	N-Glycinated <i>lyso</i> -ceramide trihexoside
1520	1 mg	98 ⁺ %	<i>lyso</i> -Ceramide trihexoside, porcine RBC

Potent Physiological Effects of Punicic Acid and Other Conjugated Linolenic Acids



Punicic acid
Cat. #1239



Methyl punicate
Cat. #1240

Conjugated linolenic acids (CLnAs) contain 3 double bonds (which can be any combination of *cis* or *trans*) having 9,11,13- and 8,10,12-octadecatrienoic acid positional isomers. Research indicates that CLnAs possess strong antidiabetic, anti-obesity, antiproliferative, and anticarcinogenic activities as well as a significant effect on lipid metabolism⁽¹⁾ making them important biological lipids. These physiological actions make CLnAs potential candidates as therapeutic and diabetic agents, although more research is needed to verify previous findings.⁽²⁾

Punicic acid is a CLnA that is found in high amounts in several natural oils, including pomegranate and snake guard seed oils. Some studies suggest that punicic acid and other CLnAs can reduce adipose tissue in mouse models, making it potentially useful as a weight-controlling lipid.⁽³⁾ CLnAs, including punicic, jacaric, and α -eleostearic acids, have been shown to suppress tumor cell growth through lipoperoxidation and apoptotic pathways.^(4,5) It has been found that punicic acid and jacaric acid, exert a potent anti-inflammatory effect through the inhibition of TNF α -induced priming of ROS production and inhibition of cyclooxygenase 1 (COX-1).^(6,7) Punicic acid also modulates mucosal immune responses and ameliorates gut inflammation through PPAR γ and δ -dependent mechanisms.⁽⁸⁾ In addition, pomegranate oil has been demonstrated to inhibit estrogen receptors α and β , with both punicic acid and α -eleostearic acid being identified as active inhibitors.⁽⁹⁾

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Catalog #	Amount	Purity	Product Name
1239	25 mg	97+%	Punicic acid
1240	25 mg	97+%	Methyl punicate

The Role of Sulfatides in Disease

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. By understanding the correlation between sulfatides, normal physiological functions, and specific diseases, new diagnostic and therapeutic methods can be evaluated.

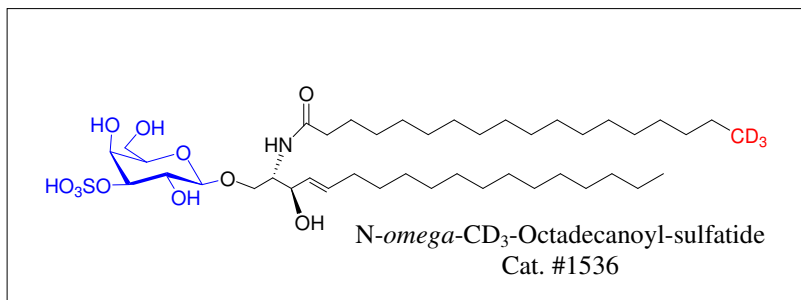
Sulfatides derived from the brain and spinal cord have varying fatty acyl chains containing saturated, unsaturated, and 2-hydroxy acyl chains, the composition of which are vital in influencing function.

Sulfatides have been found to have many critical physiological roles, both inter- and intracellularly and are involved in numerous diseases, especially demyelinating diseases. Various infections, including influenza virus A and tuberculosis, have been demonstrated to be influenced by the actions of sulfatides⁽¹⁾. Recently 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 is its involvement in hemostasis and thrombosis by forming stable platelet aggregates^(2,3). 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⁽⁴⁾.

One of the most important areas of sulfatide research today is the study of its involvement in diseases and disorders. Sulfatide levels have been found to be elevated in ovarian cancer with the most prevalent sulfatide species detected via MALDI-TIMS being d18:1/C16:0, d18:1/C24:1 and d18:1/C24:0⁽⁵⁾. This elevation in sulfatides can be exploited as an ovarian cancer biomarker and as a possible therapeutic approach.

Due to its presence in the myelin sheath of nerves, it is not surprising that sulfatide metabolism has been implemented in many neural degenerative diseases. Sulfatide content precipitously drops in Alzheimers Disease and CNS sulfatide content has been found to be modulated by apolipoprotein E⁽⁶⁾. In multiple sclerosis the identity of the target antigen has long been unidentified but it was found that levels of anti-sulfatide antibodies were significantly higher in multiple sclerosis patients than in controls⁽⁷⁾. Sulfatide has also been demonstrated to be able to activate inflammatory responses as an endogenous stimulator in brain-resident immune cells⁽⁸⁾. Sulfatide derived from myelin binds promiscuously to several human CD1 molecules and to murine CD1d and is 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⁽⁹⁾. It therefore may be able to reverse autoimmune demyelinating diseases in humans⁽¹⁰⁾.

In hepatic ischemic reperfusion injury subsets of NKT cells have opposing roles⁽¹¹⁾. 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.



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Cat. #	Amount	Purity	Product Name
1049	50 mg	98 ⁺ %	Natural Sulfatides
1904	1 mg	98 ⁺ %	<i>lyso</i> -Sulfatide
2076	1 mg	98 ⁺ %	N-C2:0-sulfatide
1938	1 mg	98 ⁺ %	N-C12:0-sulfatide
1875	1 mg	98 ⁺ %	N-C16:0-sulfatide
1934	1 mg	98 ⁺ %	N-C17:0-sulfatide
1932	1 mg	98 ⁺ %	N-C18:0-sulfatide
1933	1 mg	98 ⁺ %	N-C18:1(<i>cis</i> -9)-sulfatide
1935	1 mg	98 ⁺ %	N-C19:0-sulfatide
1888	1 mg	98 ⁺ %	N-C24:0-sulfatide
1931	1 mg	98 ⁺ %	N-C24:1(<i>cis</i> -15)-sulfatide
1536	1 mg	98 ⁺ %	N-C18:0-D3-sulfatide
1632	100 µg	98 ⁺ %	N-C12:0-NBD-sulfatide