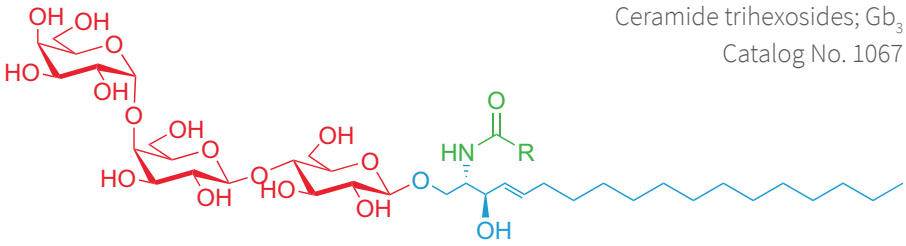
GLYCOLIPID & SPHINGOLIPID RESEARCH DECEMBER 2019
NEWSLETTER

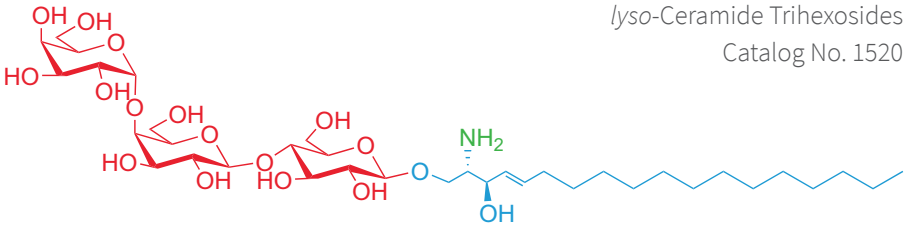
MATREYA LLC
Lipids and Biochemicals
A Cayman Chemical Company

Gb_3 and *lyso*-Gb_3 and Fabry Disease

Fabry disease is a multisystemic, X-linked disorder with variable prevalence ranging from 1:3,000 to 1:117,000 in newborn males. It is caused by deficiency in α-galactosidase, which leads to the storage of sphingolipids such as globotriaosylceramide (Gb_3), *lyso*-Gb_3, and galabiosylceramide (Ga_2) in organs, tissues, and biological fluids.



Ceramide trihexosides; Gb_3
Catalog No. 1067



lyso-Ceramide Trihexosides
Catalog No. 1520

Enzyme replacement therapy (ERT) for the disease has been available since 2001. Several studies support the clinical benefit of ERT towards quality of life, disease progression, and stabilization of end organ structure and function.[1]

Thurberg *et al.* evaluated 48 Fabry patients on ERT and found good correlation of urinary Gb_3 excretion normalized to creatine.[2] However, other studies indicated incomplete relationships between plasma and urinary Gb_3 levels and disease manifestations. Recently, Aerts *et al.* postulated that Gb_3 metabolites could play a role in Fabry pathogenesis.[3] They reported the presence of elevated *lyso*-Gb_3 in the plasma of Fabry patients, and that plasma *lyso*-Gb_3 levels were reduced after ERT.

Circulating *lyso*-Gb_3 levels are an important indicator of Fabry disease and correlate significantly with cerebrovascular white matter lesions in males and the left ventricle mass in females. Urinary *lyso*-Gb_3 levels correlate with mutation types, gender, and ERT status.

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Available Ceramide Trihexosides

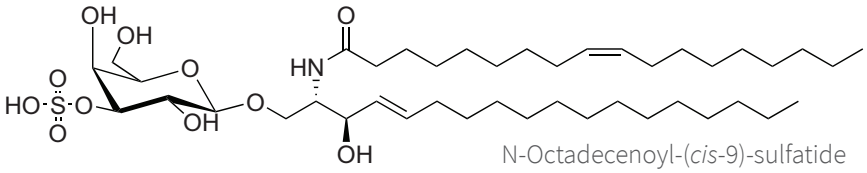
Catalog No.	Product Name	Size	Purity
1067	Ceramide trihexoside (Globotriaosylceramide, Gb_3)	1 mg	98+%
1520	*lyso*-Ceramide trihexoside (*lyso*-Globotriaosylsphingosine, *lyso*-CTH)	1 mg	98+%
1530	N-Glycinated *lyso*-ceramide trihexoside	1 mg	98+%
1523	N-Heptadecanoyl-ceramide trihexoside	500 µg	98+%
1528	N-Hexadecanoyl-ceramide trihexoside	500 µg	98+%
1529	N-Octadecanoyl-ceramide trihexoside	500 µg	98+%
1524	N-Tricosanoyl-ceramide trihexoside	500 µg	98+%
1537	N-*omega*-CD_3-Octadecanoyl-ceramide trihexoside	500 µg	98+%
1513	Ceramide trihexosides (top spot)	500 µg	98+%
1514	Ceramide trihexosides (bottom spot)	500 µg	98+%
1631	N-Dodecanoyl-NBD-ceramide trihexoside	100 µg	98+%

View Matreya's full list of ceramide trihexosides at www.matreya.com

References

1. Lavoie, P., Boutin, M., and Auray-Blais, C. Multiplex analysis of novel urinary lyso-Gb_3-related biomarkers for Fabry disease by tandem mass spectrometry. *Anal. Chem.* **85(3)**, 1743-1752 (2013).
2. Thurberg, B.L., Rennke, H., Colvin, R.B., *et al.* Globotriaosylceramide accumulation in the Fabry kidney is cleared from multiple cell types after enzyme replacement therapy. *Kidney Int.* **62(6)**, 1933-1946 (2002).
3. Aerts, J.M., Groener, J.E., Kuiper, S., *et al.* Elevated globotriaosylsphingosine is a hallmark of Fabry disease. *Proc. Natl. Acad. Sci. USA* **105(8)**, 2812-2817 (2008).

The Biological Role of Sulfatides



N-Octadecenoyl-(*cis*-9)-sulfatide
Catalog No. 1933

Sulfatides are 3'-sulfated galactosylceramides that are found primarily on oligodendrocytes, renal tubular cells, and some tumor cells. They are prominently involved in nerve conduction and cell adhesion, although many other cellular functions have been observed. Sulfatides can induce intracellular signaling in neutrophils through an L-selectin-dependent pathway and provide a binding site for human immunodeficiency virus *Helicobacter pylori* and malaria sporozoites. In the brain and spinal cord, sulfatides have different molecular species of varying fatty acyl chains containing saturated, unsaturated, and 2-hydroxy fatty acids, the composition of which are vital for influencing their function. Over the last several decades, sulfatides have been linked to many physiological processes and recently there has been a renewed interest in their role in diseases.

Demyelinating Diseases

Both sulfatide and its metabolic precursor galactosylcermide are present in high concentrations in multilamellar layers of the myelin surrounding the axons of neuronal cells where they are involved in nerve conduction. The production of anti-sulfatide antibodies in the cerebrospinal fluid, leading to a deficiency in sulfatides, may be a cause of degeneration of the myelin sheath, leading to multiple sclerosis and other demyelinating diseases.[1]

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Platelet Aggregation

Sulfatides interact with several cell adhesion molecules such as laminin, thrombospondin, von Willebrand factor, and selectin.[2] They have recently been identified as a major ligand for P-selectin in platelet adhesion aggregation, which is necessary for the formation of stable platelet aggregates. Platelets expressing sulfatides were found to adhere to P-selectin, while platelets expressing P-selectin adhered to sulfatides. When sulfatide presence was masked by forming sulfatide micelles or introducing sulfatide-binding recombinant malaria circumsporozoite protein, the adhesion was inhibited. The role of sulfatide/P-selectin interaction may play a significant role in hemostasis and thrombosis.[3]

Leukotriene Synthesis

In adherent human polymorphonuclear leukocytes, sulfatides have been found to suppress leukotriene synthesis by directly inhibiting 5-lipoxygenase and impeding its translocation to the nuclear envelope. The mechanism for this inhibition may be due to sulfatide causing a redistribution of cholesterol, increasing its abundance at the uropod region.[4]

Ovarian Tumors

Cancerous cells are known to present unusually high levels of glycosphingolipids. Sulfatides have now been identified as being present in elevated levels in ovarian tissues of patients with advanced ovarian tumors. The elevated levels of sulfatide in these cells may play a role in the pathogenesis of ovarian cancer. These elevated sulfatide levels can be used as a biomarker to predict the presence of advanced-stage ovarian cancer even when the patient otherwise appears to be in the early stage of the disease.[5]

Available Sulfatides

Catalog No.	Product Name	Size	Purity
1049	Sulfatides (bovine)	50 mg	98+%
1904	*lyso*-Sulfatide (NH_4^+salt)	1 mg	98+%
2076	N-Acetyl-sulfatide (C2:0)	1 mg	98+%
1938	N-Dodecanoyl-sulfatide (C12:0)	1 mg	98+%
1875	N-Hexadecanoyl-sulfatide (C16:0)	1 mg	98+%
1934	N-Heptadecanoyl-sulfatide (C17:0)	1 mg	98+%
1932	N-Octadecanoyl-sulfatide (C18:0)	1 mg	98+%
1933	N-Octadecenoyl-(*cis*-9)-sulfatide (C18:1)	1 mg	98+%
1935	N-Nonadecanoyl-sulfatide (C19:0)	1 mg	98+%
1888	N-Tetracosanoyl-sulfatide (C24:0)	1 mg	98+%
1931	N-Tetracosenoyl-(*cis*-15)-sulfatide (C24:1)	1 mg	98+%
1632	N-Dodecanoyl-NBD-sulfatide (C12:0 NBD)	100 µg	98+%
2207	N-Hexanoyl-biotin-sulfatide (C6:0 biotin)	1 mg	98+%
2092	N-Glycinated *lyso*-sulfatide	1 mg	98+%

View Matreya's full list of sulfatides at www.matreya.com

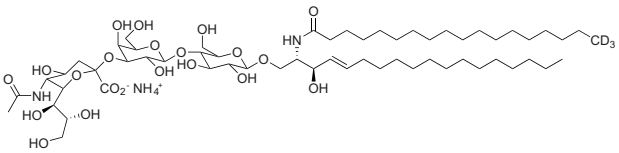
References

1. Halder, R.C., Jahng, A., Maricic, I., *et al.* Mini review: Immune response to myelin-derived sulfatide and CNS-demyelination. *Neurochem. Res.* **32(2)**, 257-262 (2007).
2. Borthakur, G., Cruz, M.A., Dong, J.F., *et al.* Sulfatides inhibit platelet adhesion to von Willebrand factor in flowing blood. *J. Thromb. Haemost.* **1(6)**, 1288-1295 (2003).
3. Merten, M. and Thiagarajan, P. Role for sulfatides in platelet aggregation. *Circulation* **104(24)**, 2955-2960 (2001).
4. Grishina, Z.V., Pushkareva, M.A., Pletjushkina, O.Y., *et al.* Sulfatides inhibit leukotriene synthesis in human polymorphonuclear granulocytes by a mechanism involving lipid rearrangement in intracellular membranes. *Int. J. Biochem. Cell Biol.* **40(1)**, 110-124 (2008).
5. Makhlouf, A.M., Fathalla, M.M., Zakhary, M.A., *et al.* Sulfatides in ovarian tumors: Clinicopathological correlates. *Int. J. Gynecol. Cancer* **14(1)**, 89-93 (2004).

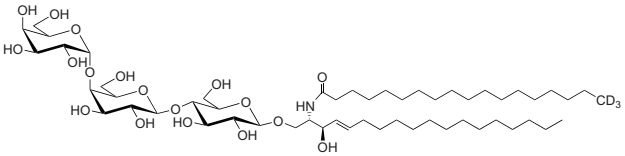
Stable Isotope-Labeled Glycosphingolipids

Matreya offers a variety of high-purity, deuterium-labeled glycosphingolipids. These compounds are made by several steps and rigorous purifications. Deuterated standards are ideal for use in mass spectrometry and can be used as biomarkers.

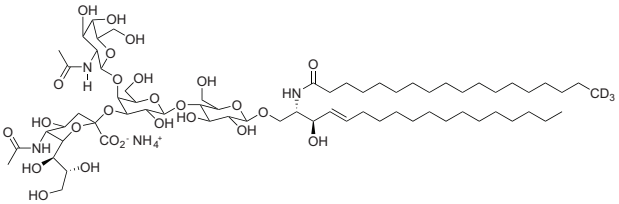
Don't see the compound you need? Let Matreya's experts provide a competitive quote by sending your specifications to rdcustomsynthesis@matreya.com.



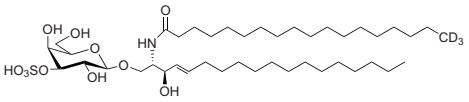
N-*omega*-CD_3-Octadecanoyl monosialoganglioside GM_3 (NH_4^+ salt)
Catalog No. 2052



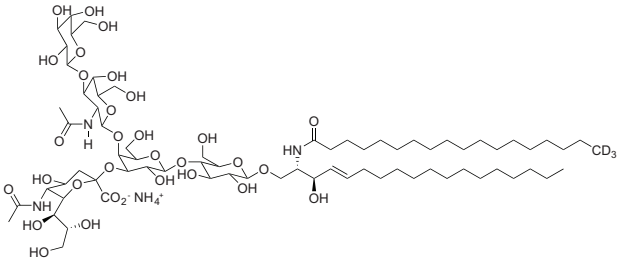
N-*omega*-CD_3-Octadecanoyl-ceramide trihexoside
Catalog No. 1537



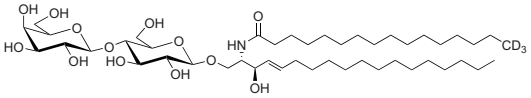
N-*omega*-CD_3-Octadecanoyl monosialoganglioside GM_2 (NH_4^+ salt)
Catalog No. 2051



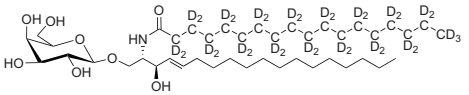
N-*omega*-CD_3-Octadecanoyl-sulfatide
Catalog No. 1536



N-*omega*-CD_3-Octadecanoyl monosialoganglioside GM_1 (NH_4^+ salt)
Catalog No. 2050



N-*omega*-CD_3-Hexadecanoyl-lactosylceramide
Catalog No. 1534



N-Octadecanoyl-D_{35}-psychosine (perdeuterated, C18:0 fatty acid)
Catalog No. 1914

Catalog No.	Product Name	Size	Purity
1914	N-Octadecanoyl-D_{35}-psychosine (perdeuterated, C18:0 fatty acid)	5 mg	98+%
1533	N-*omega*-CD_3-Hexadecanoyl-glucopsychosine	1 mg	98+%
1534	N-*omega*-CD_3-Hexadecanoyl-lactosylceramide	1 mg	98+%
1536	N-*omega*-CD_3-Octadecanoyl-sulfatide	1 mg	98+%
1537	N-*omega*-CD_3-Octadecanoyl-ceramide trihexoside	500 µg	98+%
2050	N-*omega*-CD_3-Octadecanoyl monosialoganglioside GM_1 (NH_4^+ salt)	500 µg	98+%
2051	N-*omega*-CD_3-Octadecanoyl monosialoganglioside GM_2 (NH_4^+ salt)	250 µg	98+%
2052	N-*omega*-CD_3-Octadecanoyl monosialoganglioside GM_3 (NH_4^+ salt)	250 µg	98+%

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