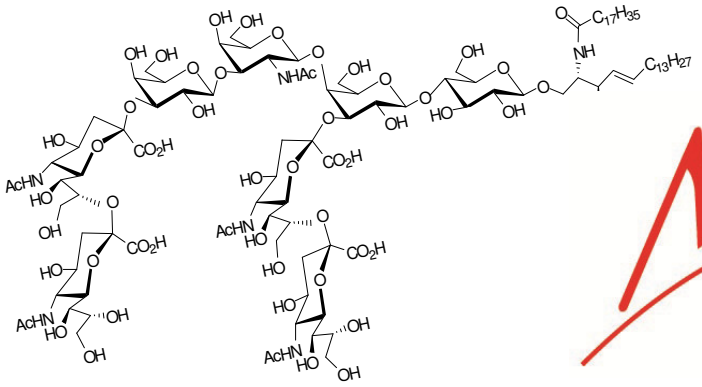

MATREYA LLC

Lipids and Biochemicals

NEWSLETTER FOR GLYCO/SPHINGOLIPID RESEARCH
JUNE 2016

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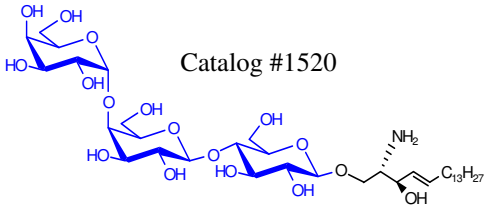
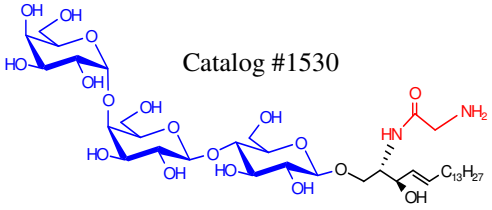
Glycinated *lyso*-CTH: A Novel *lyso*-CTH Internal Standard for Fabry Disease



Catalog #1520



Catalog #1530

Fabry disease is a lysosomal storage disorder caused by a mutated α-galactosidase gene and characterized by a deficiency in the enzyme α-galactosidase.[1] This lack of activity results in a reduced or absent ability to cleave terminal α-galactose units from glycolipids. The lysosome then begins to accumulate glycolipid intermediates, especially ceramide trihexoside (Gb_3, CTH, globotriaosylceramide) and *lyso*-ceramide trihexoside (*lyso*-Gb_3, *lyso*-CTH globotriaosylsphingosine).[3] Accumulation of these lipids leads to multiple serious systemic disorders. Gb_3 and *lyso*-Gb_3 have been shown to be excellent biomarkers for the lysosomal storage disorder Fabry disease.[2] Early detection and treatment of this disease is critical to prevent damage to multiple organs.

N-Glycinated *lyso*-ceramide trihexoside is an analogue of the important biomolecule *lyso*-Gb_3. It is ideal for use as an internal standard in the extraction and mass spectrometry (MS) analysis of the Fabry disease biomarker *lyso*-Gb_3. It's properties, such as polarity, ionization, sensitivity, and fragmentation pathway, are almost identical compared to the native specie.[1] The free amine group of glycine gives this standard very similar physical characteristics to the natural *lyso*-Gb_3 while adding an additional 57 units makes it easy to identify by MS. This is an excellent internal standard for clinical assays.

Product Name	Catalog #	Amount	Purity
Ceramide trihexoside	1067	1mg/10 mg	98+%
lyso-Ceramide trihexoside	1520	1 mg	98+%
N-Glycinated *lyso*-ceramide trihexoside	1530	1 mg	98+%

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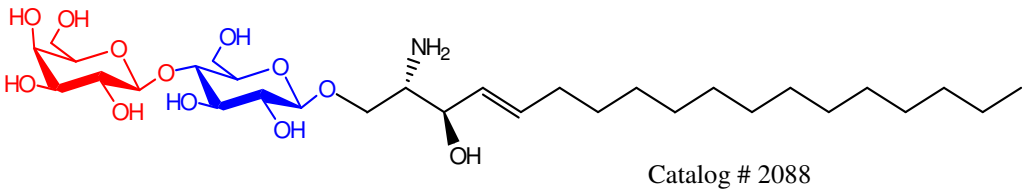
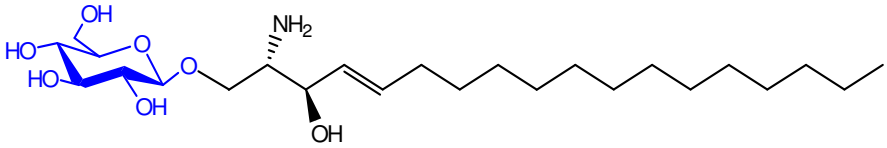
Reference:

1. R. Krüger et al. J. of Chromatography B. 883-884 (2012) 128-135
2. S. Bekri et al. Med. Chem. 4:4 (2006) 289–297
3. C. Auray-Blais et al. Clin. Chim. Acta 411:23-24 (2010) 1906-1914

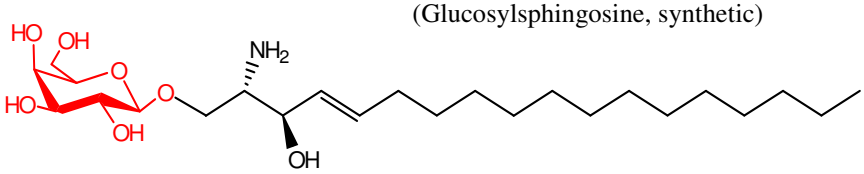
Fully Synthetic Glycosphingolipids Offer More Uniformity



Catalog # 2088
D-Lactosyl-β1-1'-D-*erythro*-sphingosine
(*lyso*-Lactosylceramide, synthetic)



Catalog # 2086
D-Glucosyl-β1-1'-D-*erythro*-sphingosine
(Glucosylsphingosine, synthetic)



Catalog # 2087
D-Galactosyl-β1-1'-D-*erythro*-sphingosine
(Psychosine, synthetic)

Synthetic Vs. Natural lyso-Glycosphingolipids

One of the major drawbacks with natural glycosphingolipid standards is that each category of lipid is comprised of a heterogeneous mixture of compounds. This can result in multiple peaks by GC, HPLC, or MS analysis. By utilizing fully synthetic glycosphingolipids, researchers can be assured that only one isomer of the lipid of interest is present. Matreya is proud to offer fully synthetic **galactosylsphingosine**, **glucosylsphingosine**, and ***lyso*-lactosylceramide** (**lactosylsphingosine**).

While natural lipids are crucial for some applications, such as to observe the effect of heterogeneous mixtures of compounds, analytical methods require uniform standards to eliminate interfering peaks in the chromatogram. Matreya's well-defined and fully synthetic glycosphingolipids are designed to give the best analytical results and simplest chromatograms possible.

Fully synthetic lipids are also often more consistent from lot to lot. Natural biomolecules can vary drastically as a result of source age, time of year, diet, and environmental conditions. These are all factors that can be extremely difficult or impossible to control. In addition, natural biochemicals are subject to less control in source handling and extraction conditions. With synthetic glycosphingolipids the starting materials and synthesis conditions are much more easily managed.

	Product Name	Catalog #	Amount	Purity
New	Psychosine, synthetic	2087	5 mg	98^{+}%
	Psychosine, bovine	1305	10 mg	98^{+}%
New	Glucosylsphingosine, synthetic	2086	5 mg	98^{+}%
	Glucosylsphingosine, bovine buttermilk	1306	5 mg	98^{+}%
	Glucosylsphingosine, plant	1310	5 mg	98^{+}%
New	*lyso*-Lactosylceramide, synthetic	2088	1 mg	98^{+}%
	lyso-Lactosylceramide, bovine buttermilk	1517	1 mg	98^{+}%

Psychosine as a Krabbe Disease Biomarker

Krabbe disease is characterized by an accumulation of cerebroside and psychosine due to a lack in activity of the lysosomal enzyme *beta*-galactosidase.[1] Therefore psychosine can be a useful biomarker for the detection of Krabbe disease. The accumulation of these lipids negatively affects the myelin of the nerve cells, causing severe nervous system deterioration. Psychosine is highly cytotoxic and may significantly contribute to the degeneration of axons, causing oligodendrocyte death, astrocyte activation and the formation of multinuclear globoid-like cells.[2] Although GM_1 gangliosidase can degrade cerebrosides it cannot degrade psychosine.[3] Bone marrow transplantation may be an effective therapeutic approach to slow down the disease in cases of early detection.

References:

1. S. Giri et al., (2006) Journal of Lipid Research, 47:1478
2. Deane J., et al., (2011) PNAS 108(37):15169-15173
3. M. van der Knaap and J. Valk (2005) "Magnetic Resonance of Myelination and Myelin Disorders" 3rd ed., Springer-Verlag Berlin Heidelberg, ISBN 978-3-540-27660-9

Glucosylsphingosine as a Gaucher Disease Biomarker

Gaucher disease is characterized by an accumulation of glucocerebroside due to a deficiency in the enzyme glucocerebrosidase and it has now been found that glucosylsphingosine also accumulates in this disease.[1] This accumulation of glucopsychosine contributes to neuronal dysfunction and destruction in patients with neuronopathic Gaucher disease[2] and it has been found to be a potent inhibitor of glucocerebrosidase. At least some instances of Gaucher disease also have a deficiency in the activity of glucosylsphingosine *beta*-glucosidase, the enzyme responsible for cleaving off the glucose of glucopsychosine and glucocerebroside. Like glucocerebroside and galactocerebroside, glucosylsphingosine can increase Ca_2^+ mobilization from intracellular stores although it uses a different mechanism.[3] Conduritol B epoxide (CBE), an inhibitor of *beta*-glucosidase, and l-phenyl-2-decanoylamino-3-morpholino-l-propanol (PDMP), an inhibitor of glucosylceramide synthase, can be used to create a model of Gaucher disease and consequently an accumulation of glucosylsphingosine.[4]

References:

1. E. Orvisky et al. Molecular genetics and metabolism 76:4 (2002) 262-270
2. R. Brady et al. Neurobiology of Disease 14:3 (2003) 595-601
3. E. Loyd-Evans et al. The Journal of Biological Chemistry 278 (2003) 23594-23599
4. D. Sillance et al. Journal of Lipid Research 43 (2002) 1837-1845

Lactosylsphingosine as a Lactosylceramidosis Biomarker

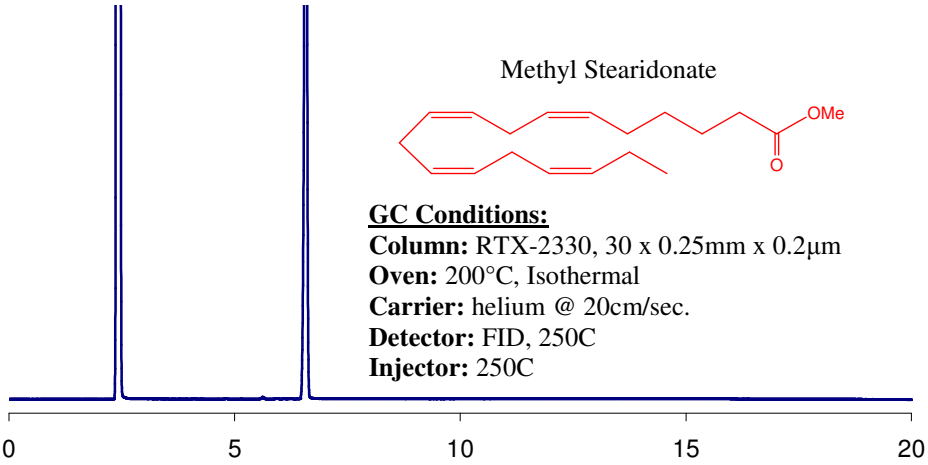
A deficiency in the enzyme responsible for hydrolyzing the galactose of lactosylceramide leads to lactosylceramidosis, which is characterized by an accumulation of lactosylceramide that causes a primary neurological disorder.[1] Lactosylceramide is also important in the activation of platelet/endothelial cell adhesion molecule-1 which causes adhesion and diapedesis of monocytes/lymphocytes.[2] In animals neutral *lyso*-glycosphingolipids occur naturally in small amounts. *lyso*-Lactosylceramide can release calcium stores from microsomes in the brain cortex and cerabellum.[3] Other *lyso*-glycosphingolipids also release calcium but in a mechanism different from *lyso*-lactosylceramide.

References:

1. Glyn Dawson Journal of Lipid Research 13 (1972) 207-219
2. NanLing Gong Proceedings of the National Academy of Sciences 101:17 (2004) 6490-6495
3. E. Loyl-Evans et al. Biochem. J. 1:375(Pt 3) (2003) 561-565

Stearidonic acid

Stearidonic acid (SDA) is a C18:4 *omega*-3 fatty acid that occurs in various edible oils and is believed to be a dietary precursor to eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).[1] SDA from plant oil is a dietary alternative to directly consuming EPA and DHA, both of which demonstrate important health benefits and are found mainly in marine oils. Stearidonic acid has been referred to as a "pro-eicosapentaenoic acid".[2]



Methyl Stearidonate

GC Conditions:
Column: RTX-2330, 30 x 0.25mm x 0.2µm
Oven: 200°C, Isothermal
Carrier: helium @ 20cm/sec.
Detector: FID, 250C
Injector: 250C

SDA itself has been found to have numerous health benefits in humans. It has been demonstrated to reduce serum triglyceride levels, decrease the production of cytokines, adhesion molecules, and C-reactive proteins, and was shown to reduce colon cancer by 46%. SDA has been demonstrated to inhibit platelet aggregation in a manner similar to EPA making it useful in the prevention and treatment of various chronic and acute diseases.[3] SDA, as well as its biological precursor *gamma*-linolenic acid, produces anti-inflammatory eicosanoids.[4] Recently it has been found that conjugated SDA can be produced by *bifidobacteria* and *propionibacteria* from SDA, suggesting an as yet unexplored pathway of SDA in mammals through intestinal microbes.[5] SDA-containing lipids are of great interest in a number of areas such as in fortified foods, dietary supplements, medicated foods, pharmaceuticals, and personal care products.

Product Name	Catalog #	Amount	Purity
Stearidonic acid (all *cis*-6,9,12,15)	1276	25 mg	99$^+$%
Methyl stearidonate (all *cis*-6,9,12,15)	1277	25 mg	99$^+$%

References:

1. W. Harris et al. Lipids 42:4 (2007) 325-333
2. W. Harris. Current Opinion in Lipidology 23:1 (2012) 30
3. J. Whelan J. Nutr. 139:1 (2009) 5-10
4. V. Kockmann et al. Lipids 24:12 (1989) 1004-1007
5. A. Hennessy et al. Lipids 47:3 (2012) 313-327

Custom Synthesis

Matreya's strength is in synthesis, extraction, and purification of natural products. We routinely produce custom preparations of high quality and purity which are not part of our standard product line. We are capable of producing large volumes of our products to meet your needs.

In order to insure a viable pipeline of new products, we strive to maintain and develop close working relationships with leading academics. We continually solicit their advice in specialty areas, particularly with regard to expanding our product line. As custom preparations often lead to important new products, we make every effort to accommodate the needs of our customers by being committed to offering a wide range of products.

Matreya's staff has many years of experience in the field of lipid chemistry. Our technology of extraction, isolation, and purification of natural products is unique, allowing us to produce high quality preparations. If your need exceeds the catalog size, please contact us. We can quote from milligram to multigram sizes on our products. Also, our staff combines the experience of synthetic chemistry with expertise in natural product chemistry. We will work with you to arrive at answers to your problems in research.

Our pride and reputation is in our customer satisfaction.