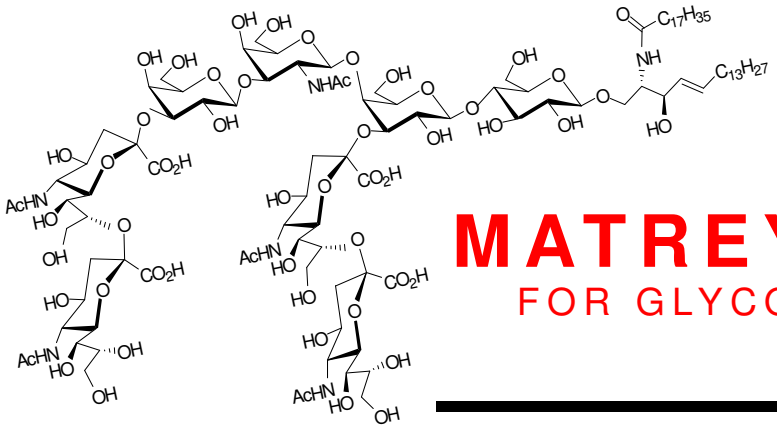
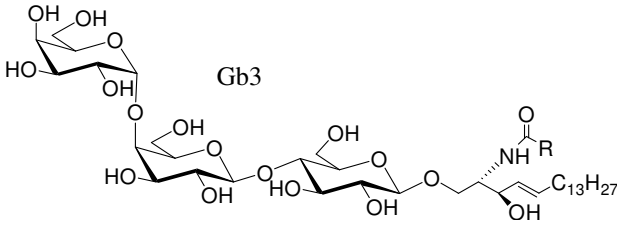


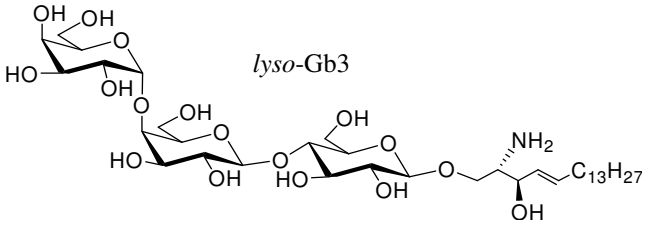
MATREYA NEWSLETTER

FOR GLYCO/SPHINGOLIPID RESEARCH

JUNE 2012

Gb3 *vs.* *lyso*-Gb3 in Fabry Disease





Fabry disease is an X-linked lysosomal storage disorder that is characterized by a deficiency in the activity of the enzyme *alpha*-galactosidase A. The direct result of this deficiency is the lysosomal accumulation of globotriaosylceramide (Gb3), a glycosphingolipid that is prominent in endothelial cells. Gb3 has long been thought to be one of the primary causes of the renal insufficiency, cardiac involvement, and CNS pathology associated with Fabry disease. Recently, Dutch researchers have found that globotriaosylsphingosine (*lyso*-Gb3) is also greatly elevated in patients with Fabry disease and may be responsible for much of the disease's pathogenesis[1].

lyso-Gb3 is a cationic amphiphile that moves easily across cell membranes. Although lysosomal storage of Gb3 is a clear prerequisite for the manifestation of Fabry disease, the presence of *lyso*-Gb3 appears to be instrumental with regard to the onset and proliferation of the disease's pathogenesis. The accumulation of *lyso*-Gb3 makes the identification and quantitation of this compound very important in the evaluation of Fabry disease. The presence of *lyso*-Gb3 in Fabry disease is similar to psychosine in Krabbe disease where high levels of this pathogenic substance is found[2].

At Matreya we have specialized in isolating pure Gb3 (ceramide trihexoside) and *lyso*-Gb3 (*lyso*-ceramide trihexoside) for the past 20 years. Matreya also has a variety of well-defined Gb3 products that are acylated with deuterated, fluorescent, and long-chain fatty acids for internal standards.

Catalog #	Product Name	Unit Size	Purity
1067;1067-10	Ceramide trihexoside (Gb3)	1 mg; 10 mg	98+%
1513	Ceramide trihexoside (contains non-hydroxy fatty acid side chains)	0.5 mg	98+%
1514	Ceramide trihexoside (contains hydroxy fatty acid side chains)	0.5 mg	98+%
1520	*lyso*-Ceramide trihexoside (*lyso*-Gb3)	1 mg	98+%
1523	N-Heptadecanoyl ceramide trihexoside (C17:0 Gb3)	0.5 mg	98+%
1524	N-Tricosanoyl ceramide trihexoside (C23:0 Gb3)	0.5 mg	98+%
1631; 1631-001	N-Dodecanoyl-NBD-ceramide trihexoside (fluorescent Gb3)	100 µg; 1 mg	98+%
1537	N-Octadecanoyl-D3-ceramide trihexoside (deuterated Gb3)	0.5 mg	98+%

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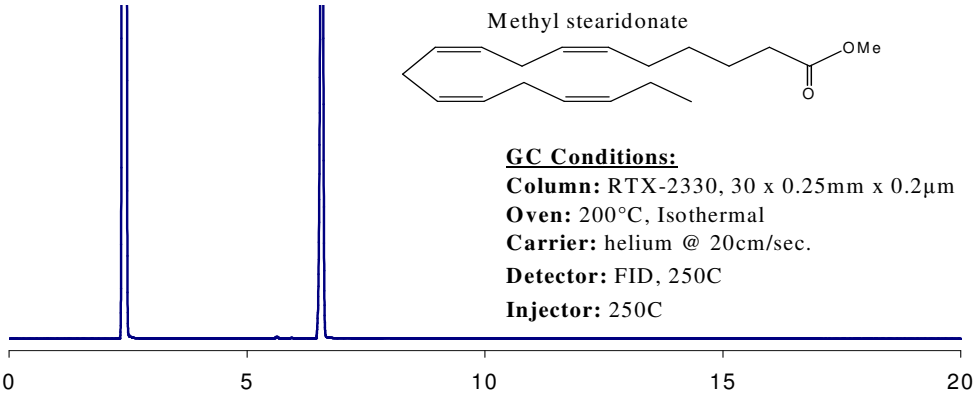
References:

1. J. Aerts et al. "Elevated globotriaosylsphingosine is a hallmark of Fabry disease" *PNAS*, Vol. 105(8) pp. 2812-2817, *2008*

2. S. Giri et al. "Krabbe disease: psychosine-mediated activation of phospholipase A2 in oligodendrocyte cell death" *JLR*, Vol. 47 (7) pp. 1478-1492, *2006*

Stearidonic Acid



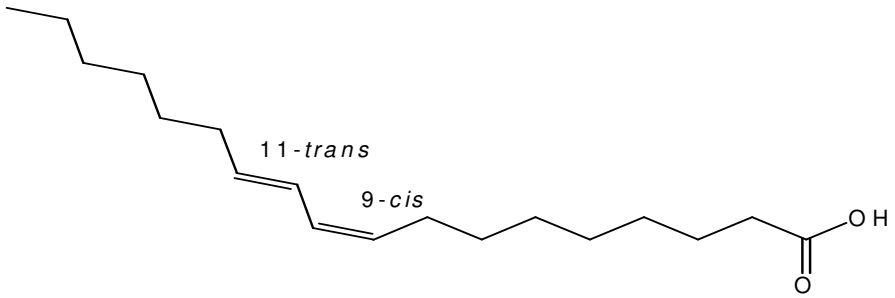
Matreya now has available high purity stearidonic acid and methyl stearidonate standards. Stearidonic acid (SDA) is a C18:4 *omega*-3 fatty acid that occurs in various edible oils and is believed to be a dietary precursor to eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)[1]. SDA from plant 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. In a recent article, Dr. W. Harris called stearidonic acid "pro-eicosapentaenoic acid"[2].

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.

	Catalog#	Product Name	Unit Size	Purity
New!	1276	Stearidonic acid	25 mg	99%
New!	1277	Methyl stearidonate	25 mg	99%

References:
1. W. Harris et al. "Stearidonic acid increases the red blood cell and heart eicosapentaenoic acid content in dogs" Lipids, Vol. 42(4) pp. 325-333, 2007
2. W. Harris, Current Opinion in Lipidology, Vol. 23(1) pp. 30, 2012
3. Whelan J. "Dietary Stearidonic Acid is a Long Chain (n-3) Polyunsaturated Fatty Acid with Potential Health Benefits" The Journal of Nutrition" doi: 10.3945/jn.108.09268, 2008
4. V. Kockmann et al. "Inhibitory effects of stearidonic acid (18:4 n-3) on platlet aggregation and arachidonate oxygenation" Lipids, Vol. 24 (12) pp. 1004-1007, 1989
5. A. Hennessy et al. "The Production of Cojugated alpha-Linolenic, gamma-Linolenic and Stearidonic Acids by Strains of bifidobacteria and propionibacteria" Lipids, Vol. 47(3) pp. 313-327, 2012

Conjugated Linoleic Acid



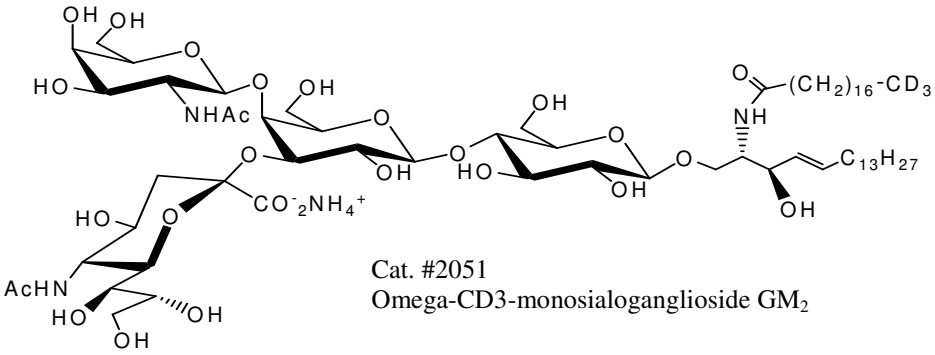
Recently Jones and coworkers reported that high doses of *trans*-10,*cis*-12 CLA increases lean body mass in hamsters but elevates levels of plasma lipids and liver enzyme biomarkers[1]. A 1:1 mixture of *cis*-9,*trans*-11 and *trans*-10,*cis*-12 CLA supplemented in oil was fed to rats with some results differing based on whether bio-formed or synthetic CLA was used[2].

Research in the CLA area is often hindered by a lack of pure standards. Matreya is proud to offer an extensive line of CLA isomers of high purity. These products are ideal for determining the specific effects of the individual CLA isomers in biological systems.

Catalog#	Product Name	Unit Size	Purity
1245; 1245-1; 1245-10	9(Z),11(E)-Octadecadienoic acid	25 mg; 1 g; 10 g	98^{+}%
1247-1; 1247-10	9(Z),11(E)-Octadecadienoic acid	1 g; 10 g	74%
1255	Methyl 9(Z),11(E)-Octadecadienoate	25 mg	98^{+}%
1258	Methyl 9(Z),11(E)-Octadecadienoate	25 mg	74%
1181	9(E),11(E)-Octadecadienoic acid	25 mg	98^{+}%
1257	Methyl 9(E),11(E)-Octadecadienoate	25 mg	98^{+}%
1248; 1248-1	9(Z),11(Z)-Octadecadienoic acid	25 mg; 1 g	96^{+}%
1256	Methyl 9(Z),11(Z)-Octadecadienoate	25 mg	96^{+}%
1249; 1249-1; 1249-10	10(E),12(Z)-Octadecadienoic acid	25 mg; 1 g; 10 g	98^{+}%
1254	Methyl 10(E),12(Z)-Octadecadienoate	25 mg	98^{+}%
1259	11(Z),13(E)-Octadecadienoic acid	25 mg	77%

References:
1. P. Jones et al. “High Dose *trans*-10,*cis*-12 CLA Increases Lean Body Mass in Hamsters, but Elevates Levels of Plasma Lipids and Liver Enzyme Biomarkers” *Lipids*, Vol. 47 pp. 39-46, *2012*
2. J. Prates et al. “Dietary CLA Combined with Palm Oil or Ovine Fat Differentially Influences Fatty Acid Deposition in Tissues of Obese Zucker Rats” *Lipids*, Vol. 47 pp. 47-58, *2012*

Deuterated Gangliosides



Cat. #2051
Omega-CD3-monosialoganglioside GM_2

Matreya is pleased to introduce a series of high purity **deuterated** gangliosides that are ideal as mass spectrometry standards. We now offer monosialogangliosides GM_1, GM_2 and GM_3 as labeled compounds. These deuterated ganglioside is ideal for the identification of gangliosides in samples and biological systems using mass spectrometry.[1] Gangliosides are acidic glycosphingolipids that form lipid rafts in the outer leaflet of the cell plasma membrane, especially in neuronal cells in the central nervous system. They participate in cellular proliferation, differentiation, adhesion, signal transduction, cell-to-cell interactions, tumorigenesis, and metastasis.[2]

GM_1 stimulates neuronal sprouting and enhances the action of nerve growth factor (NGF) by directly and tightly associating with Trk, the high-affinity tyrosine kinase-type receptor for NGF. It is the specific cell surface receptor for cholera toxin.

GM_2 regulates the function of ciliary neurotrophic factor receptors. The accumulation of GM_2 (due to a deficiency in β-hexosaminidase) has characterized Tay-Sachs disease (due to a mutation in the gene *HEXA*) and Sandhoff disease (due to a mutation in the gene *HEXB*). A mutation in the *GM2A* gene results in GM2 activator deficiency that also leads to accumulation of GM_2.[3]

GM_3 is the main ganglioside of human fibroblasts and can regulate fibroblast and epidermal growth factors[4] and is also able to regulate the adhesion and migration of several carcinoma cell lines. GM_3 was also shown to inhibit tumor cell invasion. GM_3 can induce human promyelocytic leukemia HL-60 cells to differentiate to monocyte/macrophage lineage instead of granulocytes.[5]

	Catalog #	Product Name	Unit Size	Purity
	2050	N-omega-CD_3-Octadecanoyl monosialoganglioside GM_1 (NH_4^+ salt)	0.5 mg	98+%
New!	2051	N-omega-CD_3-Octadecanoyl monosialoganglioside GM_2 (NH_4^+ salt)	250 µg	98+%
New!	2052	N-omega-CD_3-Octadecanoyl monosialoganglioside GM_3 (NH_4^+ salt)	250 µg	98+%

References:
1. J. Gu, C. Tifft and S. Soldin **"**Simultaneous quantification of G_{M1} and G_{M2} gangliosides by isotope dilution tandem mass spectrometry" *Clinical Biochemistry*, Vol. 41(6) pp. 413-417, *2008*
2. S. Birkle, G. Zeng, L. Gao, R.K. Yu, and J. Aubry "Role of tumor-associated gangliosides in cancer progression" *Biochimie*, Vol. 85 pp. 455–463, *2003*
3. R. Gravel et al., *The Metabolic and Molecular Bases of Inherited Disease* (C. R. Scriver, W. S. Sly, B. Childs, A. L. Beaudet, D. Valle, K. W. Kinzler, and B. Vogelstein, eds) pp. *3827*–3876, McGraw-Hill Inc., New York, *2001*
4. E. G. Bremer, J. Schlessinger, and S. Hakomori "Ganglioside-mediated modulation of cell growth. Specific effects of GM3 on tyrosine phosphorylation of the epidermal growth factor receptor" *J. Biol. Chem.*, Vol. 261 pp. 2434–2440, *1986*
5. T. Chung, H. Choi, Y. Lee, and C. Kim "Molecular mechanism for transcriptional activation of ganglioside GM3 synthase and its function in differentiation of HL-60 cells" *Glycobiology,* Vol. 15:3, pp. 233-244, *2004*