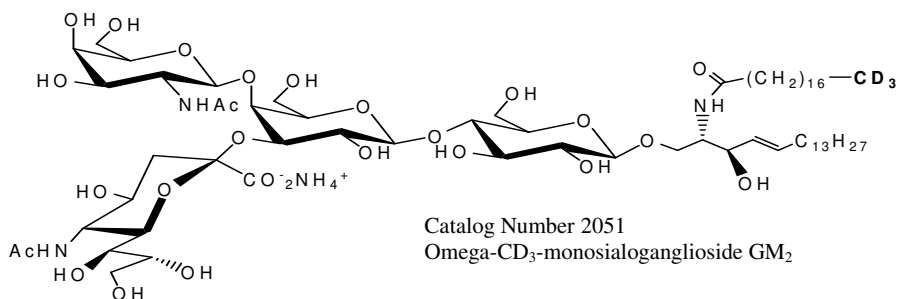


MATREYA NEWSLETTER

FOR GLYCO/SPHINGOLIPID RESEARCH

APRIL 2011

Deuterated Gangliosides



Matreya is pleased to introduce a series of high purity **deuterated** gangliosides that are ideal as mass spectrometry standards. We now offer monosialogangliosides GM₁, GM₂ and GM₃ as labeled compounds. These deuterated gangliosides are 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

GM₁ 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.

GM₂ regulates the function of ciliary neurotrophic factor receptors. The accumulation of GM₂ (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 GM₂.³

GM₃ is the main ganglioside of human fibroblasts and can regulate fibroblast and epidermal growth factors⁴ and is also able to regulate the adhesion and migration of several carcinoma cell lines. GM₃ was also shown to inhibit tumor cell invasion. GM₃ can induce human promyelocytic leukemia HL-60 cells to differentiate to monocyte/macrophage lineage instead of granulocytes.⁵

| Catalog Number | Product Name | Unit | Purity |
|------------------|--|-------|-------------------|
| 2050 | N-omega-CD ₃ -Octadecanoyl monosialoganglioside GM ₁ (NH ₄ ⁺ salt) | 0.5mg | 98 ⁺ % |
| New! 2051 | N-omega-CD ₃ -Octadecanoyl monosialoganglioside GM ₂ (NH ₄ ⁺ salt) | 250μg | 98 ⁺ % |
| New! 2052 | N-omega-CD ₃ -Octadecanoyl monosialoganglioside GM ₃ (NH ₄ ⁺ salt) | 250μg | 98 ⁺ % |

References:

1. Gu, C. Tiff and S. Soldin "Simultaneous quantification of GM₁ and GM₂ 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

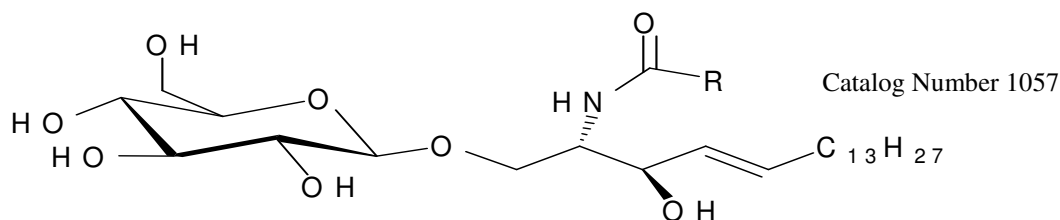
5. T. Chung, H. Choi, Y. Lee, and C. Kim "Molecular mechanism for transcriptional activation of ganglioside GM3 synthase and its function in differentiation of HL-60 cells" *Glycobiology*, Vol. 15:3, pp. 233-244, 2004

INSIDE THIS ISSUE

- Deuterated Gangliosides
- Glucocerebrosides (Gaucher's spleen)
- Antibodies Against Gangliosides
- Long-Chain Fatty Acids
- AOCs Reference Standards

- 1
- 2
- 2
- 3
- 4

Glucocerebrosides (Gaucher's spleen)



This cerebroside product is a glycosphingolipid containing a glucose attached to a ceramide (glucocerebroside) acylated with hydroxy and non-hydroxy fatty acids. It is a major constituent of skin lipids where it has an important role in lamellar body formation and in maintaining the water permeability barrier. Glucocerebroside is very important due to its function as the biosynthetic precursor for lactosylceramide and from which most of the **neutral oligoglycolipids** and **gangliosides**¹ are derived. Glucocerebroside is the only **glycosphingolipid** that is found in plants, fungi, and animals and is one of the most abundant glycosphingolipid in plants. Due to the relatively high melting point of cerebroside (much greater than physiological body temperature) they have a para-crystalline structure. Glucocerebroside tends to be concentrated in the outer leaflet of the plasma membrane in lipid rafts. It has been reported that glucocerebroside is essential for the activity of tyrosinase (a key enzyme in melanin biosynthesis), to elicit defense responses in plants, and to help the plasma membrane in plants to withstand stresses brought about by cold and drought. In **Gaucher's** disease glucocerebroside accumulates in the spleen, liver, lungs, bone marrow, and brain due to a deficiency of the enzyme glucocerebrosidase.^{2,3} This accumulation of glucocerebroside has been associated with chemotherapy resistance. Glucocerebroside has been shown to be able to modulate membrane traffic along the endocytic pathway.⁴

| | <u>Catalog Number</u> | <u>Product Name</u> | <u>Unit</u> | <u>Purity</u> |
|-------------|-----------------------|--------------------------------------|-------------|---------------|
| New! | 1057; 1057-25 | Glucocerebrosides (Gaucher's spleen) | 5 mg; 25 mg | 98+% |

References:

1. D. Sillence et al. "Assay for the transbilayer distribution of glycolipids: selective oxidation of glucosylceramide to glucuronylceramide by TEMPO nitroxyl radicals" *Journal of Lipid Research*, Vol. 41(8) pp. 1252-1260, 2000
2. C. Walden et al. "Accumulation of Glucosylceramide in Murine Testis, Caused by Inhibition of β -Glucosidase 2: IMPLICATIONS FOR SPERMATOGENESIS" *The Journal of Biological Chemistry*, Vol. 282 pp. 32655-32664, 2007
3. R. Brady "Gaucher's disease: past, present and future" *Baillieres Clin Haematol*, Vol. 10:4 pp. 621-634, 1997
4. D. Sillence et al. "Glucosylceramide modulates membrane traffic along the endocytic pathway" *Journal of Lipid Research*, Vol. 43(11) pp. 1837-1845, 2002

Antibodies Against Gangliosides

Matreya is pleased to introduce anti-ganglioside GD₂ and anti-ganglioside GD_{1b} as two new antibodies against gangliosides with very high specificity. Matreya also has many other antibodies against gangliosides which are very useful in the identification of gangliosides and in immunotargeting cells expressing those gangliosides.

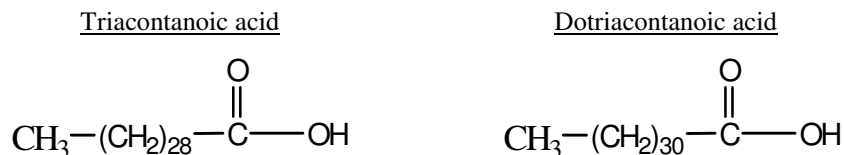
Several gangliosides have been found to have an elevated expression in tumor cells. Many therapeutic treatments of tumor cells are being investigated using ganglioside antibodies to target cells that express these elevated levels of gangliosides. GD₂ has been found to have an increased surface membrane expression on malignant melanoma and cancer cells. Therapies targeting this carbohydrate antigen have led to the production of antibodies against GD₂. Because gangliosides are very important in neuronal cells, autoantibodies against gangliosides or other glycosphingolipids can lead to many autoimmune neuropathies such as demyelinating polyneuropathy, Guillain-Barré syndrome, motor neuron disease¹ and sensorymotor neuropathy. For example, IgM anti-GM₁ occurs frequently in the serum of patients with multifocal motor neuropathy.²

| | <u>Catalog Number</u> | <u>Product Name</u> | <u>Unit</u> |
|-------------|-----------------------|--|-------------|
| New! | 1963 | Anti-ganglioside GD ₂ (polyclonal) | 50 μ l |
| New! | 1964 | Anti-ganglioside GD _{1b} (polyclonal) | 50 μ l |

References:

1. H. Yoshino, et al. "Isolated bovine spinal motoneurons have specific ganglioside antigens recognized by sera from patients with motor neuron disease and motor neuropathy." *Journal of Neurochemistry*, Vol. 59(5):1684, 1992
2. A. Pestronk, MD and R. Choksi, MS "Multifocal motor neuropathy: Serum IgM anti-GM1 ganglioside antibodies in most patients detected using covalent linkage of GM1 to ELISA plates" *Neurology*, Vol. 49:1289, 1997

Long-Chain Fatty Acids



Long-chain fatty acids (LCFA) consisting of 26 carbons or more comprise a small but very important group of biological lipids that are found in both plants and animals. There is relatively little known about LCFA, especially those with more than 30 carbons, and the need for high purity standards to explore their mechanisms and processes is greatly needed. LCFA are found in small amounts in most animal tissues and are especially abundant in the brain, skin, testis, and some glands, such as the meibomian gland.

The recognition of LCFA in human diseases has recently sparked a renewed interest in the investigation of these crucial compounds. LCFA are implicated in several diseases and standards for the determination of the lipids associated with these diseases are needed. One of these human diseases, X-linked adrenoleukodystrophy, causes an increase in plasma of LCFA due to a genetic defect that affects the peroxisomal assembly and contributes to severe pathological changes such as inflammatory responses; This disease can also lead to neurological changes and severe demyelination. Another disease that results in unusually high levels of LCFA is Zwellerger syndrome which is characterized by a reduced number of and morphologically-abnormal peroxisomes.¹

The major site of LCFA synthesis beyond C₁₈ occurs on the membranes of the endoplasmic reticulum. The microsomal fatty acid elongase (FAE) enzyme is involved in the biosynthesis of LCFA and the *Fatty Acid Elongation1 (FAE1)* gene encodes a condensing enzyme activity which is one of the four activities of the FAE enzyme and is responsible for controlling the biosynthesis and the chain length of LCFA.² LCFA are then involved in the synthesis of polyunsaturated fatty acids, waxes, esters, amides and other biological compounds.

In plants LCFA are converted to long chain hydrocarbons which are used to make waxes that are essential to their survival.³ LCFA acylated to sphingolipids are critical in many biological functions⁴ and substantial amounts are found to be amide-linked to the long-chain sphingoid base sphinganine, forming a ceramide, which constitutes the lipid backbone of sphingomyelin and other sphingolipids. LCFA can often be found in esterified linkages with cholesterol, gangliosides, galactocerebrosides, sphingomyelin, and phosphatidylcholine. In myelin LCFA are important in increasing the structural stability. Omega-hydroxy-LCFA-ceramides are vital to skin barrier functions and a deficiency of these lipids can cause death from water loss through the skin. Polyunsaturated LCFA are also found in the brain and the retina where they have vital functions. Lipids are very important in signaling and the influence of LCFA in signaling needs to be further explored.⁵

Studies that explore the roles of LCFA acylated to phospholipids, sphingolipids and glycerolipids or esterified to triglycerides, sterols, and other compounds show great promise in revealing much about the various biological functions of these lipids. If you require LCFA acylated or esterified to a specific backbone the team at Matreya will be happy to synthesize them for you.

| Catalog Number | Product Name | Unit | Purity |
|------------------|---|---------|--------|
| 1038 | Methyl tetracosanoate | 100mg | 98+% |
| 1252 | Methyl hexacosanoate | 25mg | 98+% |
| New! 1271 | Methyl octacosanoate | 50mg | 98+% |
| New! 1273 | Methyl triacontanoate | 50mg | 98+% |
| New! 1275 | Methyl dotriacontanoate | 50mg | 98+% |
| New! 2011 | Long Chain Fatty Acid Methyl Ester Mix (C24:0, C26:0, C28:0, C30:0, C32:0 methyl esters) | 25mg/ml | 98+% |

References:

1. R. Wanders et al. "Direct demonstration that the deficient oxidation of very long chain fatty acids in X-linked adrenoleukodystrophy is due to an impaired ability of peroxisomes to activate very long chain fatty acids" *Neurology*, Vol. 51(2) pp. 334-334-a, 1998
2. A. Millar, L. Kunst "Very-long-chain fatty acid biosynthesis is controlled through the expression and specificity of the condensing enzyme" *The Plant Journal*, Vol. 12(1) pp. 121-131, 1997
3. A. Millar et al. "CUT1, an Arabidopsis Gene Required for Cuticular Wax Biosynthesis and Pollen Fertility, Encodes a Very-Long-Chain Fatty Acid Condensing Enzyme" *Plant Cell*, Vol. 11 pp. 825-838, 1999
4. P. Tvrđika et al. "Role of a New Mammalian Gene Family in the Biosynthesis of Very Long Chain Fatty Acids and Sphingolipids" *Journal of Cell Biology*, Vol. 149(3) pp. 707, 2000
5. A. Poulos "Very long chain fatty acids in higher animals—A review" *Lipids* Vol. 30(1) pp. 1-14, 1995

AOCS Reference Standards for Edible Oils

Matreya offers many lipid mixtures that are ideal as GC standards. These mixtures are carefully and accurately prepared using great precautions. The individual components are carefully analyzed before being combined with the mixture and are stored under inert gas at -20°C. Each component is carefully measured using calibrated instruments. After the mixture is prepared it is re-analyzed to ensure that it meets all quality standards. After passing rigorous inspection the mixture is carefully packaged under inert gas and stored at -20°C.

By studying problems with the quantitative analysis of animal and vegetable oils and fats, the American Oil Chemists' Society has found certain mixtures to be useful as reference standards. The composition of each mixture (see the table below for weight composition) is similar to the fatty acid distribution of certain oils. All mixtures are in methyl ester form and are ready for GC analysis. If you need a mixture that is not listed we will be happy to prepare one that will meet your specifications.

Each methyl ester mixture is carefully prepared by weight and the composition verified by gas chromatography. The weight percentage of each component is indicated in the Table.

| Mix No. Catalog No. | RM-1 1084 | RM-2 1085 | RM-3 1086 | Rapeseed 1083 | RM-4 1087 | RM-5 1088 | RM-6 1089 |
|---|---|--|-------------------------------|------------------|-------------------------------|---|--|
| C8:0 Caprylate | | | | | | 7.0 | |
| C10:0 Caprate | | | | | | 5.0 | |
| C12:0 Laurate | | | | | | 48.0 | |
| C14:0 Myristate | | | 1.0 | 1.0 | | 15.0 | 2.0 |
| C16:0 Palmitate | 6.0 | 7.0 | 4.0 | 4.0 | 11.0 | 7.0 | 30.0 |
| C16:1 Palmitoleate | | | | | | | 3.0 |
| C18:0 Stearate | 3.0 | 5.0 | 3.0 | 3.0 | 3.0 | 3.0 | 14.0 |
| C18:1 Oleate | 35.0 | 18.0 | 45.0 | 60.0 | 80.0 | 12.0 | 41.0 |
| C18:2 Linoleate | 50.0 | 36.0 | 15.0 | 12.0 | 6.0 | 3.0 | 7.0 |
| C18:3 Linolenate | 3.0 | 34.0 | 3.0 | 5.0 | | | 3.0 |
| C20:0 Arachidate | 3.0 | | 3.0 | 3.0 | | | |
| C20:1 Eicosenoate | | | | 1.0 | | | |
| C22:0 Behenate | | | 3.0 | 3.0 | | | |
| C22:1 Erucate | | | 20.0 | 5.0 | | | |
| C24:0 Lignocerate | | | 3.0 | 3.0 | | | |
| *These are the oils that the mixtures are suitable for. | Corn Cottonseed Soybean Safflower Sesame Poppy seed Walnut Kapok Rice | Linseed Perilla Hempseed Rubberseed | Peanut Rapeseed Mustard | Rapeseed | Olive Teaseed Neatsfoot | Coconut Palm Babassu Ouri-ouri | Lard Beef tallow Mutton tallow Palm |