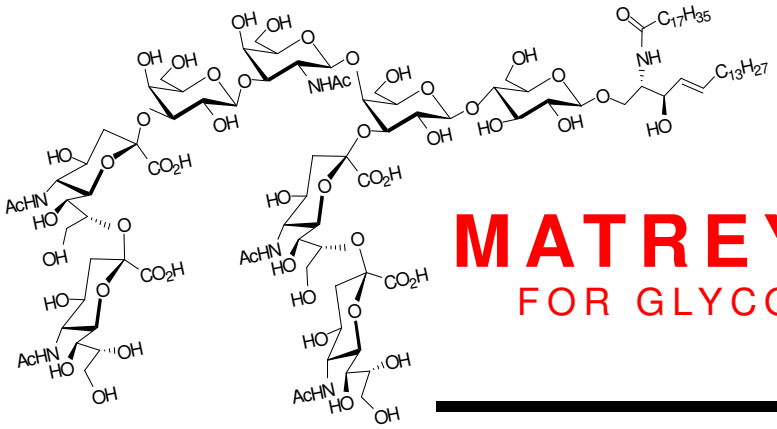


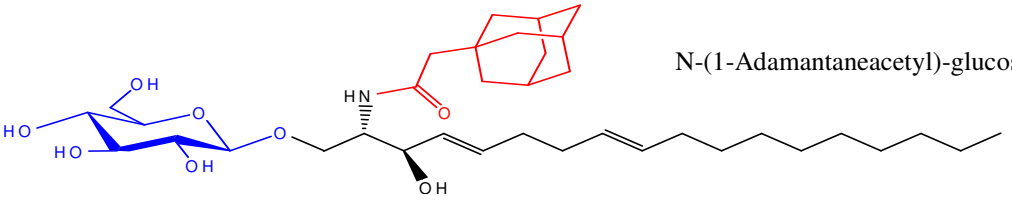
MATREYA NEWSLETTER

FOR GLYCO/SPHINGOLIPID RESEARCH

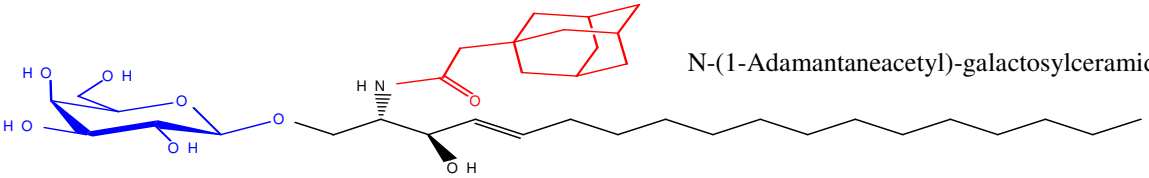
APRIL 2013

New Tools to Study Fabrys and Gauchers Syndrome

Glucosylceramides and galactosylceramides play very important roles in glycosphingolipid (GSL) metabolism. Dr. Lingwood's laboratory in Canada modified these two lipids, acylating an adamantaneacetyl group to the amine of the ceramide, creating the following compounds:



N-(1-Adamantaneacetyl)-glucosylceramide (Catalog# 1945)



N-(1-Adamantaneacetyl)-galactosylceramide (Catalog# 1946)

These two amphipathic monohexosyl ceramide analogues serve as inhibitors and alternate substrates to redirect cellular GSL metabolism, and provide new approaches to reduce GSL accumulation in lysosomal storage disease (LSD) patients.

N-(1-Adamantaneacetyl)-glucosylceramide (adaGlcCer, Catalog# 1945), at low doses and at pH 7, has been found to inhibit glucocerebrosidase, thereby increasing cellular GSLs and making it a useful tool in the study of Gauchers disease. However, at 40μM adaGlcCer (which was converted to adaLacCer) inhibited lactosylceramide synthase, decreasing lactosylceramide levels as well as more complex GSL levels, and making it the first cellular lactosylceramide synthase inhibitor.

N-(1-Adamantaneacetyl)-galactosylceramide (adaGalCer, Catalog # 1946) stimulates glucocerebrosidase at pH 5 (but not at pH 7), reducing glucosylceramide levels in cells. At 40 μM adaGalCer reduces globotriaosylceramide (Gb_3) and globoside (Gb_4) synthesis in Fabrys LSD cells by acting as a substrate for Gb_3 synthase. Gb_3 synthase converts adaGalCer to a novel $adaGb_2$ which is readily lost from cells, making it a "safety valve" to offset Gb_3 accumulation in Fabrys disease. AdaGalCer has also been found to inhibit cell sulfatide synthesis.

LacCer + Gb_3 synthase → Gb_3 (elevated levels in Fabrys disease)

AdaGalCer + Gb_3 synthase → $AdaGb_2$ (readily eliminated)

Matreya is offering these novel glycolipid inhibitors under an exclusive license from The Hospital for Sick Children, Toronto, Ontario. We at Matreya believe that the addition of these two new inhibitors will aid in the understanding of glycosphingolipid metabolism and complement our glucosylceramide synthase inhibitor D-*threo*-PDMP (Catalog # 1756).

Reference:

M. Kamani, M. Mylvaganam, R. Tian, B. Rigat, B. Binnington, and C. Lingwood, J. Biol. Chem. 2011, 286:21413-21426

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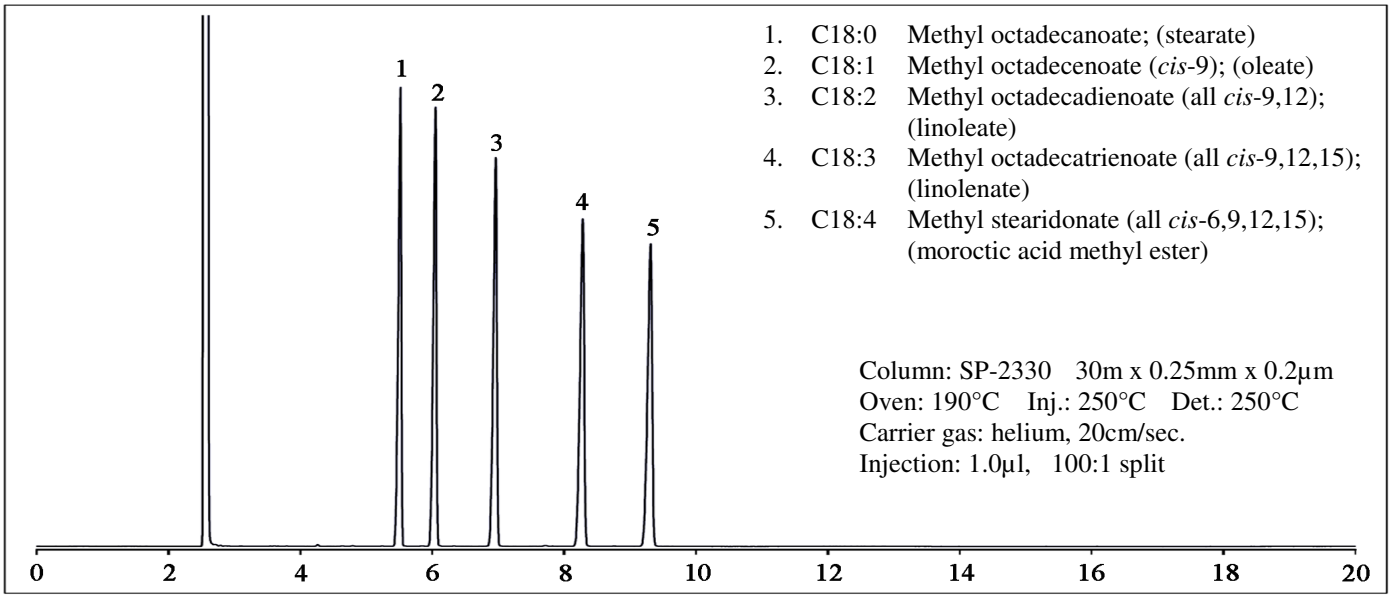
Matreya FAMES

Matreya FAMEs (Fatty Acid Methyl Esters) are used to calibrate and identify fatty acids in research samples. Recently there has been a lot of activity in the research area of polyunsaturated fatty acids such as 18:3, 18:4, 20:5, and 22:6.

Matreya is pleased to introduce two FAME standard mixtures containing equal amounts of 18:0, 18:1, 18:2, 18:3, and 18:4 in the 18 carbon series and 20:0, 20:1, 20:2, 20:3, 20:4, 20:5, and 22:6 in the 20 carbon series.

These quantitative mixtures are ideal for component identification, instrument calibration, and column performance studies.

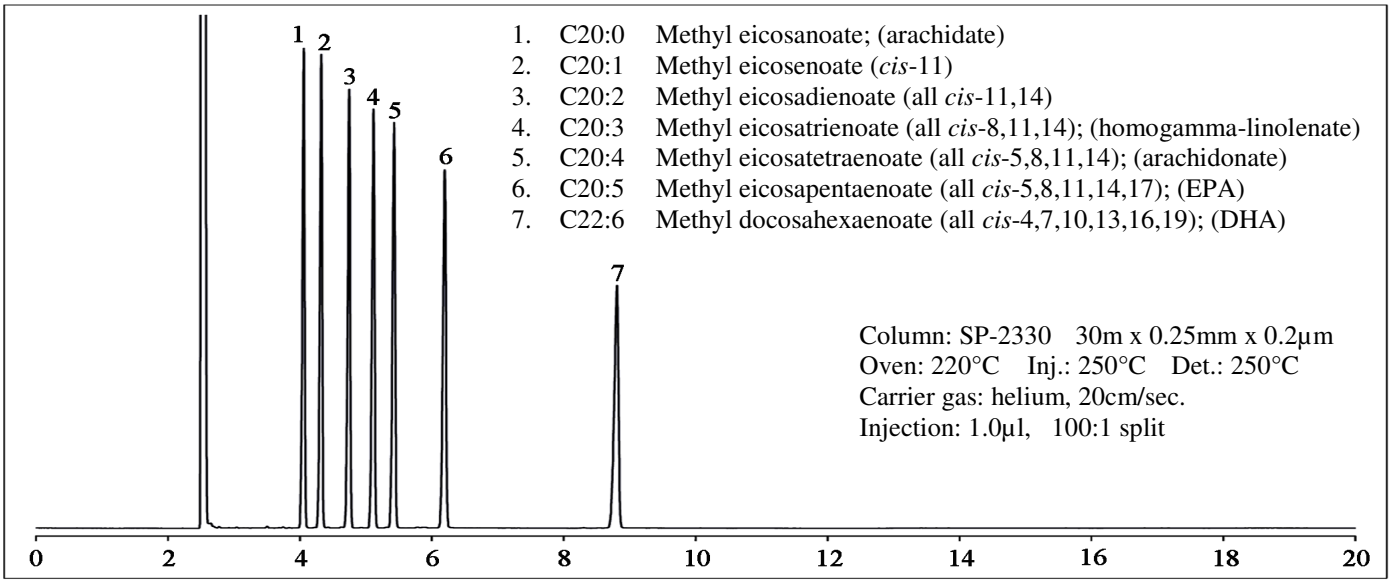
Catalog# 2012



1. C18:0 Methyl octadecanoate; (stearate)
2. C18:1 Methyl octadecenoate (*cis*-9); (oleate)
3. C18:2 Methyl octadecadienoate (all *cis*-9,12); (linoleate)
4. C18:3 Methyl octadecatrienoate (all *cis*-9,12,15); (linolenate)
5. C18:4 Methyl stearidonate (all *cis*-6,9,12,15); (moroctic acid methyl ester)

Column: SP-2330 30m x 0.25mm x 0.2µm
Oven: 190°C Inj.: 250°C Det.: 250°C
Carrier gas: helium, 20cm/sec.
Injection: 1.0µl, 100:1 split

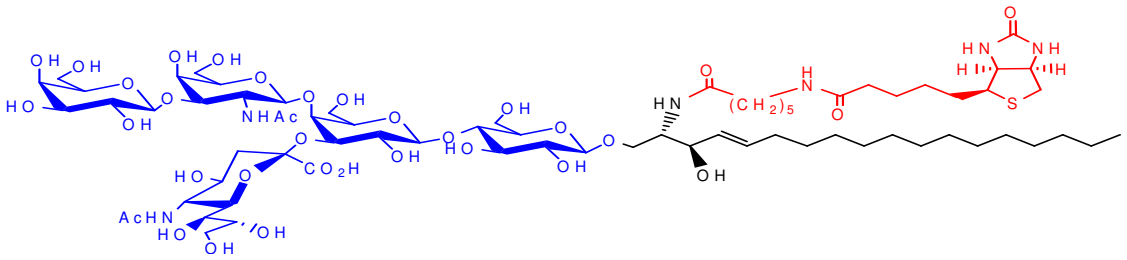
Catalog# 2013



1. C20:0 Methyl eicosanoate; (arachidate)
2. C20:1 Methyl eicosenoate (*cis*-11)
3. C20:2 Methyl eicosadienoate (all *cis*-11,14)
4. C20:3 Methyl eicosatrienoate (all *cis*-8,11,14); (homogamma-linolenate)
5. C20:4 Methyl eicosatetraenoate (all *cis*-5,8,11,14); (arachidonate)
6. C20:5 Methyl eicosapentaenoate (all *cis*-5,8,11,14,17); (EPA)
7. C22:6 Methyl docosahexaenoate (all *cis*-4,7,10,13,16,19); (DHA)

Column: SP-2330 30m x 0.25mm x 0.2µm
Oven: 220°C Inj.: 250°C Det.: 250°C
Carrier gas: helium, 20cm/sec.
Injection: 1.0µl, 100:1 split

N-Hexanoyl-biotin-monosialoganglioside GM_1



Matreya is pleased to introduce a monosialoganglioside GM_1 acylated with biotin. This ganglioside GM_1 analogue contains a biotin unit attached to the amine of the sphingosine moiety via a hexanoic acid linker and is ideal for use in ganglioside studies. The biotin structure allows for attachment of the ganglioside to streptavidin and avidin substrates making it extremely useful for binding to substrates and for toxin detection.[1]

Gangliosides are acidic glycosphingolipids containing one or more sialic acids that generally form lipid rafts in the outer leaflet of the cell plasma membrane, especially in neuronal cells in the central nervous system.[2,3] They participate in many cellular activities including proliferation, differentiation, adhesion, signal transduction, cell-to-cell interactions, tumorigenesis, and metastasis.[4] The accumulation of gangliosides has been linked to several diseases including Tay-Sachs and Sandhoff disease while an autoimmune response against gangliosides can lead to Guillain-Barre syndrome. Gangliosides act as receptors for various toxins and bacteria, accumulate in various tumors, and aid in many neuronal functions. They are therefore very important in therapeutic processes and have warranted much research. 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. GM_1 has also been identified as the specific cell surface receptor for cholera toxin making it an important target for therapeutic interventions.[5]

N-Hexanoyl-biotin-monosialoganglioside GM_1 Cat. #2053

References:

1. A. Pukin et al. Chemoenzymatic synthesis of biotin-appended analogues of gangliosides GM2, GM1, GD1a and GalNAc-GD1a for solid-phase applications and improved ELISA tests. *Org. Biomol. Chem.*, 9(16):5809-5815, *2011*
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3. T. Kolter, R. Proia, K. Sandhoff, Combinatorial Ganglioside Biosynthesis. *J. Biol. Chem.*, July Vol. 277, No. 29, pp. 25859-25862, *2002*
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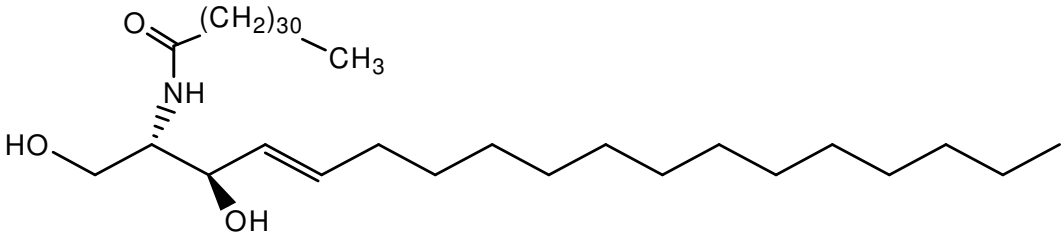
Ceramides



The ubiquitous sphingolipid ceramide has long been recognized for its many critical functions and diverse roles in the cell. Ceramide is vital as an intermediate in sphingolipid metabolism where it functions as a precursor in the synthesis of sphingomyelin, glycosphingolipids, and free sphingosine and as a signaling molecule that acts as an intracellular second messenger for various exogenous stimuli. Ceramide exerts numerous biological effects including induction of cell maturation, cell cycle arrest, terminal cell differentiation, cell senescence, and cell death[2]. It has been identified as a promoter of the mitogenesis that is produced by exogenous sphingoid bases[1]. The cytokine tumor necrosis factor alpha (TNF alpha) stimulates ceramide formation by promoting the conversion of sphingomyelin to ceramide[3].

Matreya offers a full line of ceramides for your research in cellular development, mitogenesis, and second messenger function. Matreya is pleased to now introduce synthetic very long chain ceramides that are acylated with C30 and C32 fatty acids along with new dihydroceramides. Also available are fluorescent labeled ceramides of all four sphingosine stereoisomers.

Ceramides	**Cat #**	
N-Hexadecanoyl-D-*erythro*-dihydrosphingosine	2078	**New!**
N-Dodecanoyl-D-*erythro*-sphingosine	1936	**New!**
N-Hexadecanoyl-D-*erythro*-C16-sphingosine	2077	**New!**
N-Triacontanoyl-D-*erythro*-sphingosine	2049	**New!**
N-Dotriacontanoyl-D-*erythro*-sphingosine	2048	**New!**
N-Hexanoyl-NBD-D-*erythro*-sphingosine	1841	
N-Dodecanoyl-NBD-D-*erythro*-sphingosine	1618	
N-Hexanoyl-NBD-L-*threo*-sphingosine	1857	
N-Dodecanoyl-NBD-L-*threo*-sphingosine	1620	
N-Hexanoyl-NBD-L-*threo*-dihydrosphingosine	1624	
N-Dodecanoyl-NBD-L-threo-dihydrosphingosine	1623	
N-Hexanoyl-NBD-D-*erythro*-dihydrosphingosine	1626	
N-Dodecanoyl-NBD-D-*erythro*-dihydrosphingosine	1625	
N-Hexanoyl-NBD-D-*erythro*-phytosphingosine	1628	
N-Dodecanoyl-NBD-D-*erythro*-phytosphingosine	1627	

Please see our catalog or visit us online for our full line of ceramide products.

References:

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