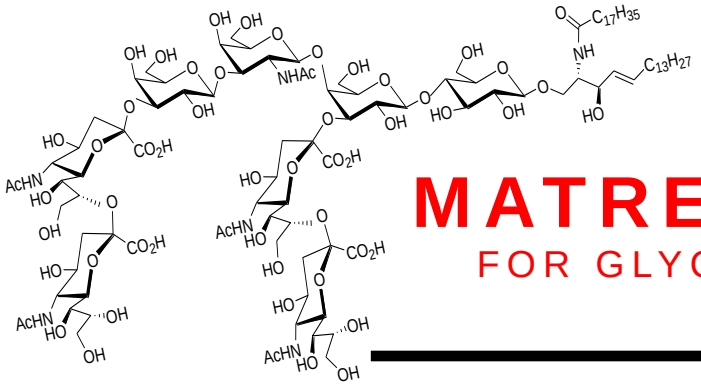


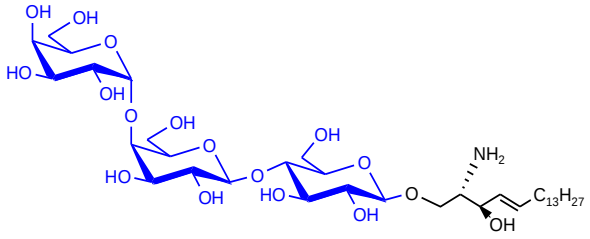
# MATREYA NEWSLETTER

FOR GLYCO/SPHINGOLIPID RESEARCH

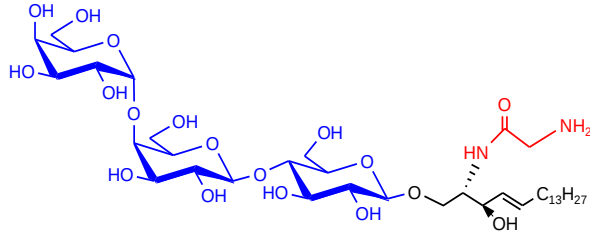
JUNE 2015

Matreya appreciates your support over the past 25 YEARS. Due to your loyalty, Matreya has become a big success in the scientific community. We send a heartfelt THANK YOU to all of you, our customers, who have given us the chance to meet your needs over the years. We at Matreya enjoy working with you to help meet your research needs, supplying you with both standards and technical assistance to make your projects excel. We are looking forward to the next 25 years of being your preferred supplier. By working together, maybe we will find a cure for cancer, lysosomal storage disorders, and other diseases.


## Glycinated *lyso*-CTH: A Better Biomarker for Fabry's Disease



Catalog #1520



Catalog #1530

Globotriaosylceramide (CTH, $Gb_3$) and globotriaosylsphingosine (*lyso*-CTH, *lyso*-$Gb_3$) are very important biomarkers in Fabry's disease. Fabry's disease is a lysosomal storage disorder characterized by a deficiency in the activity of the enzyme α-galactosidase, causing an accumulation of $Gb_3$ and lyso-$Gb_3$. $Gb_3$ has been used to monitor enzyme replacement therapy but diagnostic sensitivity is limited. *lyso*-$Gb_3$ was introduced as a better biomarker with increased sensitivity.

Karl Lackner and his coworkers glycinated *lyso*-$Gb_3$ and it functioned as a better biomarker with good sensitivity. The physical and chemical properties of glycinated *lyso*-$Gb_3$ are almost identical to that of natural *lyso*-$Gb_3$ in terms of extraction, stability, and sensitivity. It is an excellent internal standard for clinical work.

Reference:

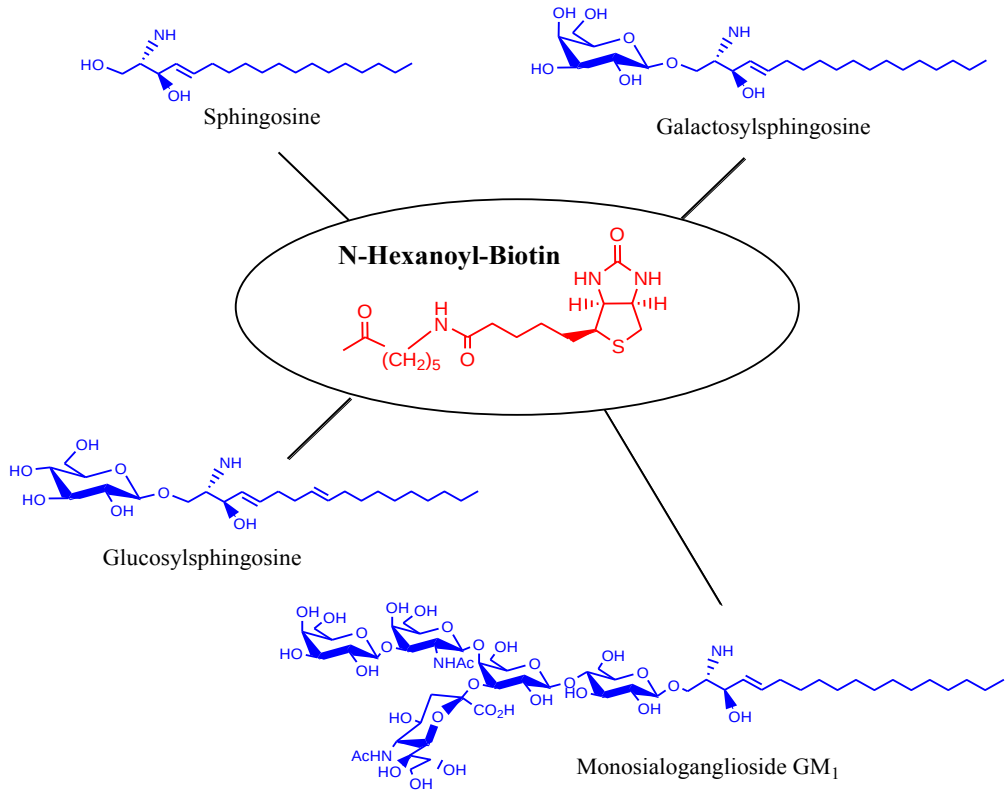
K. J. Lackner et al., J. of Chromatography B 1:883-884 (2012) 128-35

| ***Product Name*** | ***Catalog #*** | ***Amount*** | ***Purity*** |
|---|---|---|---|
| Ceramide trihexoside ($Gb_3$) | 1067 | 1 mg, 10 mg | $98^+$% |
| *lyso*-Ceramide trihexoside (*lyso*-$Gb_3$) | 1520 | 1 mg | $98^+$% |
| N-Glycinated *lyso*-ceramide trihexoside | 1530 | 1 mg | $98^+$% |

### INSIDE THIS ISSUE


- Glycinated *lyso*-CTH 1
- Biotinylated Sphingolipids 2
- Adamantane Labeled Sphingolipids 3
- Tocotrienols: The New Neuroprotective Vitamin E 4

# Biotinylated Sphingolipids




Matreya's new line of biotinylated sphingolipids are ideal for use in sphingolipid research, taking advantage of the strong and specific interaction of biotin with streptavidin/avidin. These sphingolipid analogs contain a biotin label attached to the amine of the sphingosine moiety via a hexanoic acid linker which maintains the sphingolipid's natural properties. The biotin label allows for easy attachment of the sphingolipid to streptavidin/avidin proteins making them extremely useful for binding to substrates and for toxin detection. Matreya's biotinylated products combine the natural ceramide backbone, for a more natural protein interaction, with a biotin label for very specific streptavidin/avidin binding.

Mukhopadhyay and coworkers identified the inhibitor 2 of protein phosphatase 2A (I2PP2A) as a ceramide binding protein using biotin-labeled ceramide. They found that I2PP2A-ceramide binding decreased the association between PP2A and the inhibitor, preventing the inhibition of PP2A activity *in vitro*. They also found that the direct interaction of I2PP2A with ceramide plays important biological roles *via* the regulation of PP2A activity and signaling, which in turn controls ceramide-mediated degradation of c-Myc and antiproliferation.[1]

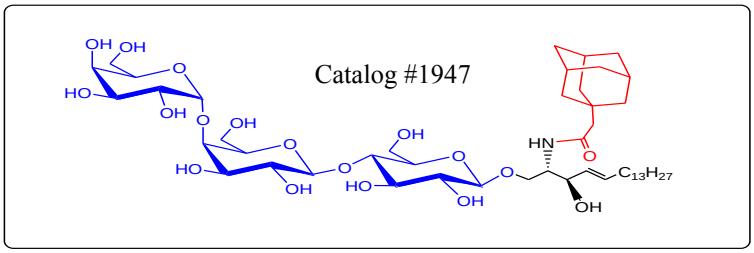
Pukin and coworkers used biotin labeled ganglioside analogs for *Escherichia coli* enterotoxin detection on streptavidin-coated ELISA plates.[2] Enterotoxigenic *Escherichia coli* is a pathogenic form of bacteria that is a serious threat to health and food safety around the world and the detection of enterotoxins is of critical importance in preventing food born diseases.

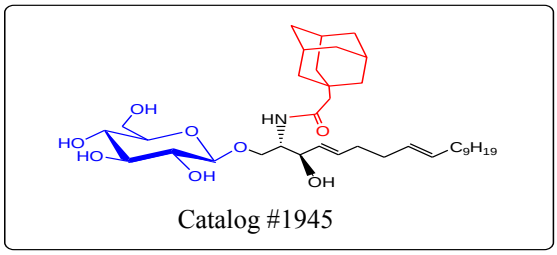
References:

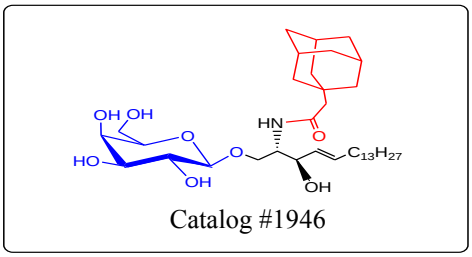
1. A. Mukhopadhyay et al. FASEB 23:3 (2009) 751-763
2. A. Pukin et al. Org. Biomol. Chem. 9:16 (2011) 5809-5815

| ***Product Name*** | ***Catalog #*** | ***Amount*** | ***Purity*** |
|---|---|---|---|
| N-Hexanoyl-biotin-D-*erythro*-sphingosine | 2081 | 5 mg | 98+% |
| N-Hexanoyl-biotin-galactosylceramide | 2203 | 5 mg | 98+% |
| N-Hexanoyl-biotin-glucosylceramide | 2085 | 5 mg | 98+% |
| N-Hexanoyl-biotin-monosialoganglioside $GM_1$ | 2053 | 500 µg | 98+% |

# Adamantane Labeled Sphingolipids




Glycosphingolipids play an important role in various disorders such as Fabry's and Gaucher's diseases. C. Lingwood and coworkers have modified several glycosphingolipids, acylating them with an adamantaneacetyl group on the amine of the ceramide. By replacing the natural fatty acyl group of the ceramide with a rigid, three dimensional hydrocarbon frame, a novel class of glycosphingolipid is produced which demonstrates similar toxin interactions to natural glycosphingolipids but increased water solubility.

Unlike the water-soluble ceramide-free globotriaosylceramide ($Gb_3$) oligosaccharide, N-(1-adamantaneacetyl)-ceramide trihexoside ($adaGb_3$) retains high affinity for verotoxin binding in aqueous solutions and also shares some properties of $Gb_3$-cholesterol complexes in solution which may relate to its several bioactivities.[1,2] $AdaGb_3$ has also been shown to functionally mimic $Gb_3$ microdomains, providing a new class of molecular tools for studying the role of glycolipids and lipid rafts in such areas as HIV-1 fusion and other biological processes. $AdaGb_3$ may be able to disrupt HIV gp120-glycolipid interactions, thereby obviating the problem of resistance mutants selected by current antiretroviral treatments and opening a new route for controlling HIV-1 replication in infected individuals.[3] $AdaGb_3$ has recently been proposed as a regulator for multidrug resistance in cancer cells by taking advantage of the interaction between $Gb_3$ and the glycoprotein MDR1, thus modulating the function of MDR1 across the intestinal endothelium.[4]

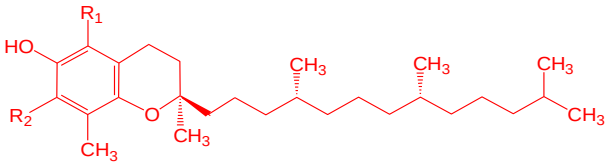
N-(1-Adamantaneacetyl)-glucosylceramide (adaGlcCer), at low doses and at pH 7, has been found to inhibit glucocerebrosidase, thereby increasing cellular glycosphingolipids and making it a useful tool in the study of Gaucher's disease. However, at 40µM adaGlcCer (which was converted to adaLacCer) inhibited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

N-(1-Adamantaneacetyl)-galactosylceramide (adaGalCer) 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 Fabry's disease 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 Fabry's disease. AdaGalCer has also been found to inhibit cell sulfatide synthesis.[1]

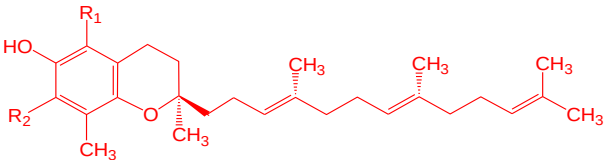
References:
1. C. Lingwood et al., Journal of Biological Chemistry, 286:24 (2011) 21413-21426
2. M. Mylvaganam and C. Lingwood, Biochemical and Biophysical Research Communications 257:2 (1999) 391-394
3. J. Fantini et al., Journal of Lipid Research 43 (2002) 1670-1679
4. C. Lingwood et al., Journal of Biological Chemistry 283 (2008) 4501-4511

| ***Product Name*** | ***Catalog #*** | ***Amount*** | ***Purity*** |
|---|---|---|---|
| N-(1-Adamantaneacetyl)-glucosylceramide | 1945 | 5mg | $98^{+}$% |
| N-(1-Adamantaneacetyl)-galactosylceramide | 1946 | 5mg | $98^{+}$% |
| N-(1-Adamantaneacetyl)-ceramide trihexoside | 1947 | 1mg | $98^{+}$% |

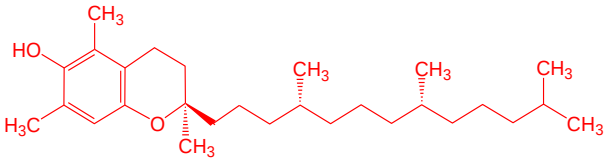
# Tocotrienols:
# The New Neuroprotective Vitamin E



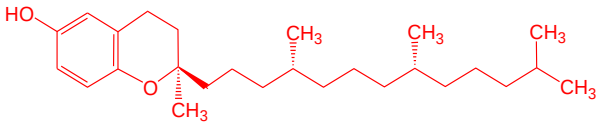

| | $R_1$ | $R_2$ | Cat.# |
|---|---|---|---|
| α-Tocopherol | $CH_3$ | $CH_3$ | 1072 |
| β-Tocopherol | $CH_3$ | H | 1071 |
| γ-Tocopherol | H | $CH_3$ | 1073 |
| δ-Tocopherol | H | H | 1790 |




| | $R_1$ | $R_2$ | Cat.# |
|---|---|---|---|
| α-Tocotrienol | $CH_3$ | $CH_3$ | 2109 |
| β-Tocotrienol | $CH_3$ | H | 2110 |
| γ-Tocotrienol | H | $CH_3$ | 2111 |
| δ-Tocotrienol | H | H | 2112 |




Catalog # 1074




Catalog # 1797

Vitamin E consists of eight major isomers: *alpha*-, *beta*-, *gamma*-, and *delta*-tocopherols and *alpha*-, *beta*-, *gamma*-, and *delta*-tocotrienols. The difference between tocopherols and tocotrienols is found in the three double bonds of the tocotrienol's isoprenoid tail. Vitamin E has a vital role in maintaining neuronal function and structure and acts as a powerful antioxidant. Orally supplemented tocopherols are known to reach the brain and now tocotrienols have been demonstrated to reach the brain as well. Almost all vitamin E supplements consist of only *alpha*-tocopherol. However, *alpha*-tocotrienol has been demonstrated to be much more potent than *alpha*-tocopherol in protecting HT4 and primary neuronal cells against toxicity induced by glutamate as well as by a number of other toxins.[1] Tocotrienol supplemented rats show more protection against stroke-induced injury compared to matched controls. Such protection is associated with lower c-Src activation and 12-Lox phosphorylation at the stroke site.[2]

Matreya offers the complete line of very high purity vitamin E isomers as well as several excellent internal standards (Cat# 1074 and Cat# 1797). Relatively little research has been done on tocotrienols as compared to tocopherols. A major reason for this has been the lack of purified tocotrienols for research. With Matreya's comprehensive line of vitamin E, all eight forms of this critical nutrient can be studied and compared.

References:
1. C. Sen et al., Ann N Y Acad Sci. 1031 (2004) 127-42
2. S. Khanna et al., Stroke 36:10 (2005) 2258–2264

| ***Product Name*** | ***Catalog #*** | ***Amount*** | ***Purity*** |
|---|---|---|---|
| *alpha*-Tocotrienol | 2109 | 25 mg | 98$^+$% TLC/98$^+$% GC |
| *beta*-Tocotrienol | 2110 | 25 mg | 98$^+$% TLC/98$^+$% GC |
| *gamma*-Tocotrienol | 2111 | 25 mg | 98$^+$% TLC/98$^+$% GC |
| *delta*-Tocotrienol | 2112 | 25 mg | 98$^+$% TLC/98$^+$% GC |
| *rac-alpha*-Tocopherol | 1072 | 50 mg | 95$^+$% TLC/98$^+$% GC |
| *rac-beta*-Tocopherol | 1071 | 50 mg | 95$^+$% TLC/98$^+$% GC |
| *rac-gamma*-Tocopherol | 1073 | 50 mg | 95$^+$% TLC/98$^+$% GC |
| *delta*-Tocopherol | 1790 | 50 mg | 95$^+$% TLC/98$^+$% GC |
| *rac*-5,7-Dimethyltocol | 1074 | 50 mg | 95$^+$% TLC/98$^+$% GC |
| Tocol | 1797 | 50 mg | 95$^+$% TLC/98$^+$% GC |