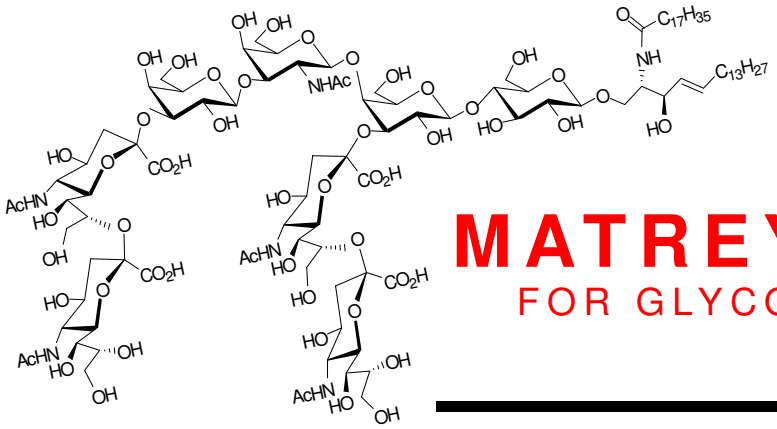
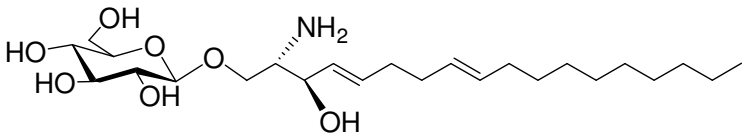


MATREYA NEWSLETTER

FOR GLYCO/SPHINGOLIPID RESEARCH

NOVEMBER 2012

Biomarkers for Gaucher, Krabbe, and Fabry Disease



Glucopsychosine, Catalog number 1310

Lysosomal storage diseases are a heterogeneous group of disorders caused by lysosomal enzyme dysfunction[(1)]. In these lipid storage disorders it is very important to diagnose and treat patients as early as possible. One very effective method of diagnosis is the use of biomarkers.

Gaucher disease is a lysosomal storage disorder that has recently warranted much research due to the debilitating effects of excess lipid storage in Gaucher cells. A lack of activity in the lysosomal enzyme glucocerebrosidase causes accumulation of glucosylceramide and other glycosphingolipids. Recently Dutch scientists concluded that plasma glucosylsphingosine can function as a biomarker for type I Gaucher disease but cautioned, "that further investigations are warranted regarding its relationship with clinical manifestations of Gaucher disease" [(2)].

Krabbe disease is characterized by an accumulation of galactosylceramide due to a lack in the activity of the enzyme *beta*-galactosidase. The accumulation of this lipid negatively affects the myelin of the nerve cells, causing severe nervous system deterioration. Psychosine (galactosylsphingosine, the deacylated form of galactosylceramide) is also accumulated in this disorder and may significantly contribute to the degeneration of axons[(3)]. Bone marrow transplantation may be an effective therapeutic approach to slow down the disease in cases of early detection.

Fabry disease is characterized by an accumulation of globotriaosylceramide (CTH) due to a lack in the activity of the enzyme *alpha*-galactosidase A and is a length-dependent peripheral neuropathy. Fabry disease has recently become of great interest due to its implication in cardiac and cerebrovascular disease as well as in initial ischemic stroke[(4)].

Enzyme replacement therapy (ERT)[(5)] is a strategy used for treating a number of lysosomal storage diseases. By replacing the inactive enzymes of these diseases with active enzymes the accumulated lipids, which are toxic in high concentrations, are able to be degraded. One of the first clinical applications of ERT was in the treatment of Gaucher disease. Some of the available drugs for ERT in Gaucher disease are: Imiglucerase (Cerezyme, Genzyme), Velaglucerase alfa (VPRIV, Shire plc), Taliglucerase alfa (Protalix/Pfizer), and N-butyl-deoxynojirimycin (Zavesca, Actelion).
Matreya's high purity glycosphingolipids and lyso-glycosphingolipids are ideal biomarker standards for lysosomal storage diseases.

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Gaucher Disease Biomarkers	***Cat #***
Glucocerebroside (Gauchers spleen)	1057
Glucocerebrosides (bovine buttermilk)	1521
Glucocerebrosides (plant)	1522
Glucopsychosine (bovine buttermilk)	1306
Glucopsychosine (plant)	1310
N-Docosanoyl-glucopsychosine	1531
N-Palmitoyl-D_3-glucopsychosine	1533
N-Hexanoyl-NBD-glucopsychosine	1622

Biomarkers for Gaucher, Krabbe, and Fabry Disease Continued

Krabbe Disease Biomarkers	***Cat #***
Cerebrosides (bovine)	1050
Psychosine	1305
N-Acetyl-psychosine	1325
N-Octanoyl-psychosine	1334
N-Heptadecanoyl-psychosine	1335
N-Stearoyl-D_{35}-psychosine	1914
N-Hexanoyl-NBD-psychosine	1621
N-Dodecanoyl-NBD-psychosine	1633

Fabry Disease Biomarkers	***Cat #***
Ceramide trihexoside (CTH) (porcine)	1067
lyso-Ceramide trihexoside (*lyso*-CTH)	1520
N-Heptadecanoyl-ceramide trihexoside	1523
N-Tricosanoyl-ceramide trihexoside	1524
N-Octadecanoyl-D_3-ceramide trihexoside	1537
N-Dodecanoyl-NBD-ceramide trihexoside	1631

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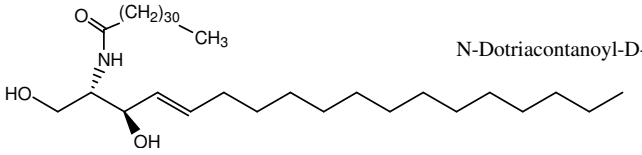
1. Manger B., Z Rheumatol, 69(6): 527-38 (2010)
2. Dekker N., van Dussen L., Hollak C., Overkleeft H., Scheij S., Ghauharali K., van Breemen M., Ferraz M., Groener J., Maas M., Wijburg F., Speijer D., Tylki-Szymanska A., Mistry P., Boot R., and Aerts J., Blood, 118(16): e118-e1127 (2011)
3. Deane J., Graham S., Kim N., Stein P., McNair R., Cachon-Gonzalez M., Cox T., Read R., PNAS 108(37): 15169-15173 (2011)
4. Wozniak M., Kittner S., Tuhrim S., Cole J., Stern B., Dobbins M., Grace M. Nazarenko I., Dobrovolny R., McDade E., Desnick R., Stroke 41(1): 78-81 (2010)
5. Brady R., Baillieres Clin Haematol. 10(4): 621-34 (1997)

Ceramides



N-Dotriacontanoyl-D-*erythro*-sphingosine, Catalog number 2048

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.

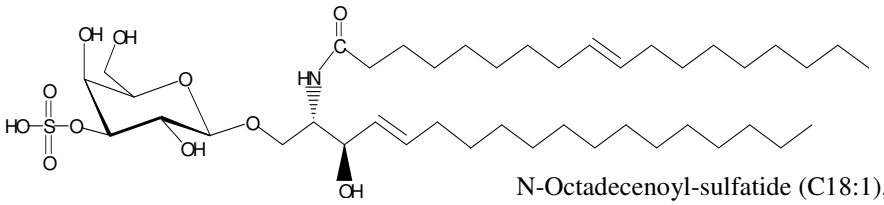
Ceramides	***Cat #***	
N-Triacontanoyl-D-*erythro*-sphingosine	2049	**New!**
N-Dotriacontanoyl-D-*erythro*-sphingosine	2048	**New**
N-Hexadecanoyl-D-*erythro*-dihydrosphingosine	2078	**New!**
N-Hexanoyl-NBD-D-*erythro*-sphingosine	1841	
N-Dodecanoyl-NBD-D-*erythro*-sphingosine	1618	
N-Hexanoyl-NBD-L-*threo*-sphingosine	1857	
N-Dodecanoyl-NBD-L-*threo*-sphingosine	1620	

Ceramides	***Cat #***
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:
1. Hauser J., Buehrer B., and Bell R., Journal of Biological Chemistry, 269: 6803 (1994)
2. Radin N., Biochemical Journal, 371: 243-256, (2003)
3. Sawada M., et al., Cell Death Differ. 11(9): 997-1008 (2004)

The Biological Role of Sulfatides



N-Octadecenoyl-sulfatide (C18:1), Catalog number 1933

Sulfatides are 3'-sulfated galactosylceramides that are found primarily on oligodendrocytes, renal tubular cells, and some tumor cells. The most prominent role of sulfatides is in their involvement in nerve conduction and cell adhesion, although many other cellular functions have been observed. Sulfatides are able to induce intracellular signaling in neutrophils through a L-selectin dependent pathway and provide a binding site for human immunodeficiency virus, *helicobacter pylori* and malaria sporozites. In the brain and spinal cord sulfatides have different molecular species of varying fatty acyl chains containing saturated, unsaturated, and 2-hydroxy fatty acids, the composition of which are vital in influencing their function. Over the last several decades sulfatides have been linked to many physiological processes and recently there has been a renewed interest in their role in diseases.

Demyelintating Diseases:

Both sulfatide and its metabolic precursor galactosylcermide are present in high concentrations in multilamellar layers of the myelin surrounding the axons of neuronal cells where they are involved in nerve conduction. A production of anti-sulfatide antibodies in the cerebrospinal fluid, leading to a deficiency in sulfatides, may be a cause of degeneration of the myelin sheath, leading to multiple sclerosis and other demyelinating diseases[(1)].

Platelet Aggregation:

Sulfatides interact with several cell adhesion molecules such as laminin, thrombospondin, von Willibrand factor, and selectin[(2)]. They have recently been identified as a major ligand for P-selectin in platelet adhesion aggregation, which is necessary for the formation of stable platelet aggregates. Platelets expressing sulfatides were found to adhere to P-selectin while platelets expressing P-selectin adhered to sulfatides. When sulfatide presence was masked by forming sulfatide micelles or introducing sulfatide-binding recombinant malaria circumsporozoite protein the adhesion was inhibited. The role of sulfatide/P-selectin interaction may play a significant role in hemostasis and thrombosis[(3)].

Leukotriene Synthesis:

In adherent human polymorphonuclear leukocytes sulfatides have been found to suppress leukotriene synthesis by directly inhibiting 5-lipoxygenase and impeding its translocation to the nuclear envelope. The mechanism for this inhibition may be due to sulfatide causing a redistribution of cholesterol, increasing its abundance at the uropod region[(4)].

Ovarian Tumors:

Cancerous cells are known to present unusually high levels of specific molecules, especially glycosphingolipids. Sulfatides have now been identified as being present in elevated levels in benign and malignant tumors and especially in patients having advanced ovarian tumors. The elevated levels of sulfatide in these cells may play a role in the pathogenesis of ovarian cancer. These elevated sulfatide levels can be used as a biomarker to predict the presence of advanced stage ovarian cancer even when the patient otherwise appears to be in the early stage of the disease[(5)].

Sulfatides	***Cat #***	***Sulfatides***	***Cat #***
Sulfatides (bovine)	1049	N-Octadecenoyl-sulfatide (C18:1)	1933
lyso-sulfatide	1904	N-Tetracosanoyl-sulfatide (C24:0)	1888
N-Acetyl-sulfatide (C2:0)	2076	N-Tetracosenoyl-sulfatide (C24:1)	1931
N-Hexadecanoyl-sulfatide (C16:0)	1875	N-Octadecanoyl-D_3-sulfatide (C18:0 D_3)	1536
N-Octadecanoyl-sulfatide (C18:0)	1932	N-Dodecanoyl-NBD-sulfatide (C12:0 NBD)	1632

References:
1. Halder C., Jahng A., Maricic I., and Kumar V., Neurochemical Research, 32(2): 257-262 (2007)
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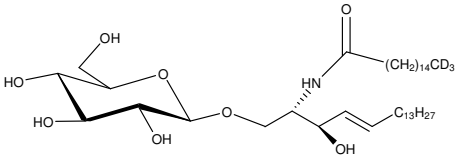
5. Makhlouf A., Fathalla M., Zakhary M. and Makarem M., Int J. Gynecol Cancer 14(1): 89-93 (2004)

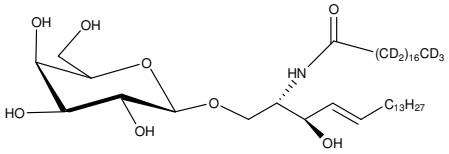
Deuterated Lipids

Matreya offers a variety of high purity deuterated labeled glycosphingolipids. These compounds are made by several steps and rigorous purifications. These are ideal as mass spectrometric standards and can be used as biomarkers.

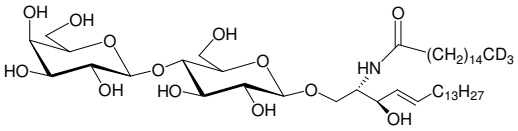
If you need any other deuterium labeled compounds please do not hesitate to contact us.



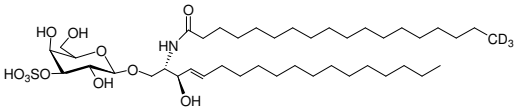
N-Octadecanoyl-D_{35}-galactopsychosine



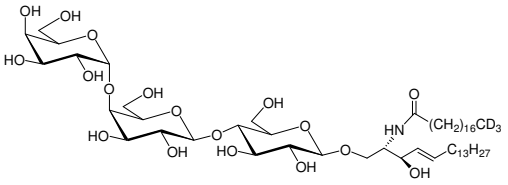
N-Hexadecanoyl-D_3-glucopsychosine



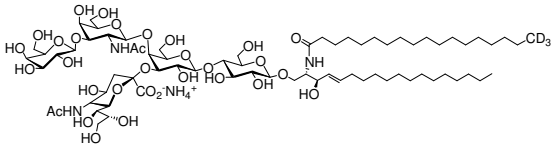
N-Hexadecanoyl-D_3-lactosylceramide



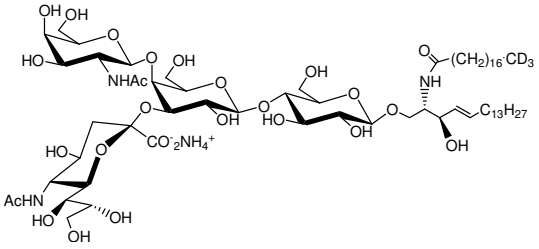
N-Octadecanoyl-D_3-sulfatide



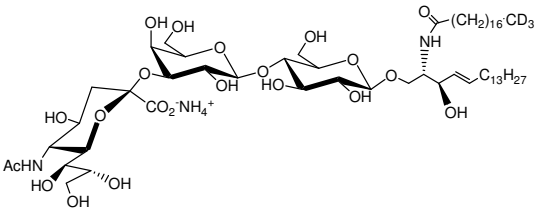
N-Octadecanoyl-D_3-ceramide trihexoside



N-Octadecanoyl-D_3-monosialoganglioside GM_1



N-Octadecanoyl-D_3-monosialoganglioside GM_2



N-Octadecanoyl-D_3-monosialoganglioside GM_3

Deuterated Lipids	***Cat #***
N-Octadecanoyl-D_{35}-galactopsychosine	1914
N-Hexadecanoyl-D_3-glucopsychosine	1533
N-Hexadecanoyl-D_3-lactosylceramide	1534
N-Octadecanoyl-D_3-sulfatide	1536
N-Octadecanoyl-D_3-ceramide trihexoside	1537
N-Octadecanoyl-D_3-monosialoganglioside GM_1	2050
N-Octadecanoyl-D_3-monosialoganglioside GM_2	2051
N-Octadecanoyl-D_3-monosialoganglioside GM_3	2052