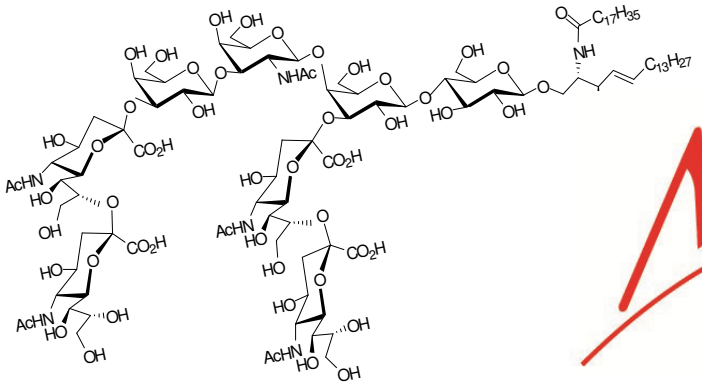

MATREYA LLC

Lipids and Biochemicals

NEWSLETTER FOR GLYCO/SPHINGOLIPID RESEARCH
AUGUST 2016

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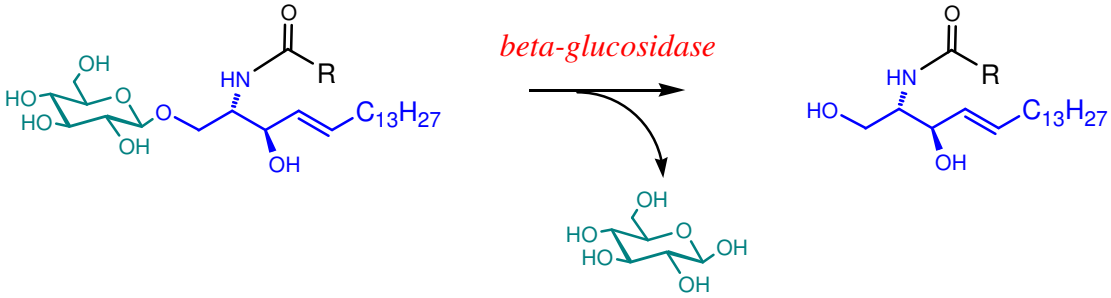
N-Glycinated Glucosylsphingosine: An Exciting New Internal Standard for Gaucher Disease Diagnosis



Lysosomal storage diseases (LSDs) are a heterogeneous group of disorders caused by lysosomal enzyme dysfunction[1]. Gaucher disease (GD) is the most common of these lysosomal storage disorders and 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 β-glucosidase, or occasionally in its activator protein saposin C, causes an accumulation of glucosylceramide, glucosylsphingosine and other glycosphingolipids in macrophage cells, especially in the liver, spleen, lung, and bone marrow. These lipid heavy cells are commonly known as "Gaucher cells" and can result in hepatosplenomegaly, cytopenia, skeletal disfunctions, lung disorders, and neuronal degradation. In lipid storage disorders such as GD, it is very important to diagnose and treat patients as early as possible. One very effective method of diagnosis is the use of biomarkers.

Chitotriosidase is the most well-established biomarker for GD. However, it is not specific for GD and may give a false negative in a significant percentage of GD patients due to mutation. Chitotriosidase also reflects the changes in the course of the disease belatedly. Furthermore, a significant percentage of the population, 6%, are deficient in the chitotriosidase gene.[2] Due to these limitations a more specific biomarker is needed for GD.

A. Rolfs et al.[3] recently demonstrated that glucosylsphingosine can be used as a promising, reliable, and specific biomarker for GD. They evaluated the sensitivity and specificity of glucosylsphingosine with regard to healthy controls vs. Gaucher desease carriers and other LSD control groups. Only GD patients displayed elevated levels of glucosylsphingosine higher than the pathological

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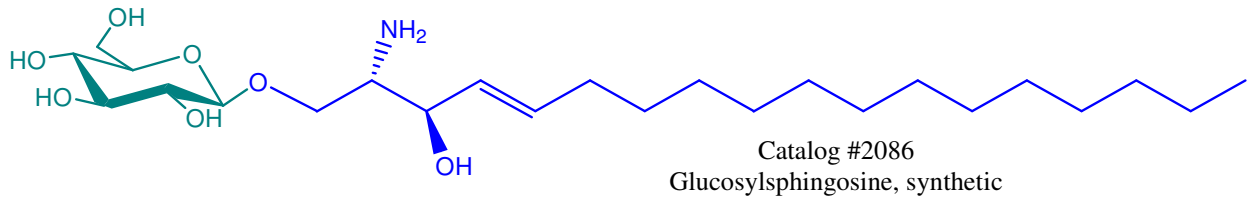
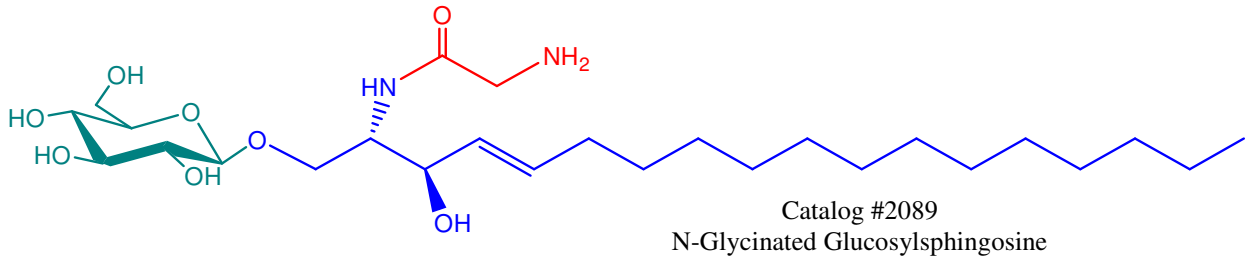


Catalog #2086
Glucosylsphingosine, synthetic
Mass: 461.3353



Catalog #2089
N-Glycinated Glucosylsphingosine
Mass: 518.3567

cut-off, verifying the specificity of glucosylsphingosine as a biomarker for GD. Glucosylsphingosine was monitored during enzyme replacement therapy and demonstrated a decrease in glucosylsphingosine over time.

Taking advantage of this glucosylsphingosine biomarker, M. Fuller et al.[4] have developed a quick and reproducible-method for the determination of abnormally high glucosylsphingosine levels from 0.01 mL of plasma. The plasma is spiked with N-palmitoyl-d3-lactosylceramide as an internal standard, extracted with choroform/methanol, and centrifuged to remove the insoluble protein precipitates. The sample is then ready to be analyzed by LC/ESI-MS/MS. Recovery of the glucosylsphingosine was found to be >90% as calculated from the quality control samples and the calibration curve was linear over the entire relevant range. The assay was described as "accurate, reproducible, robust, and easy to perform in routine laboratory settings". This method found that glucosylsphingosine was elevated in all GD patients compared to unaffected controls and patients with other metabolic disorders. These results have validated the effectiveness of glucosylsphingosine in diagnosing Gaucher disease and in monitoring the results of enzyme replacement therapy.

Matreya is pleased to now offer **N-glycinated glucosylsphingosine** as a new, highly specific, glucosylsphingosine **internal standard**. N-Glycinated glucosylsphingosine contains a glycine molecule attached to the amine of glucosylsphingosine. Glycinated sphingolipids have been found to be ideal for use as internal standards in the extraction and mass spectrometry analysis of natural samples.[5] The free amine group gives this product very similar physical characteristics to the natural sphingolipid while the glycine adds an additional 57 units to the molecule, making it easy to detect by MS methods.

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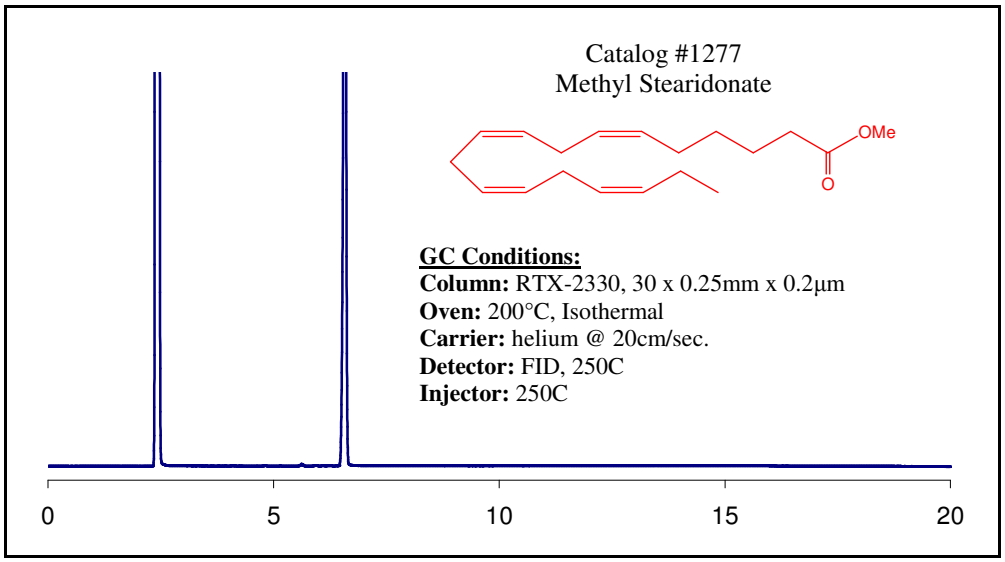
	Product Name	Catalog #	Amount	Purity
	Glucocerebroside, Gaucher's Spleen	1057	5 mg	98+%
	Glucosylsphingosine, synthetic	2086	5 mg	98+%
	Glucosylsphingosine, bovine buttermilk	1306	5 mg	98+%
	Glucosylsphingosine, plant	1310	5 mg	98+%
New!	N-Glycinated glucosylsphingosine	2089	1 mg	98+%
	N-Hexanoyl-biotin-glucosylceramide	2085	5 mg	98+%
	N-Hexadecanoyl-D_3-lactosylceramide, deuterated	1534	1 mg	98+%

Please visit www.matreya.com for a full list of glucosylceramides and derivatives

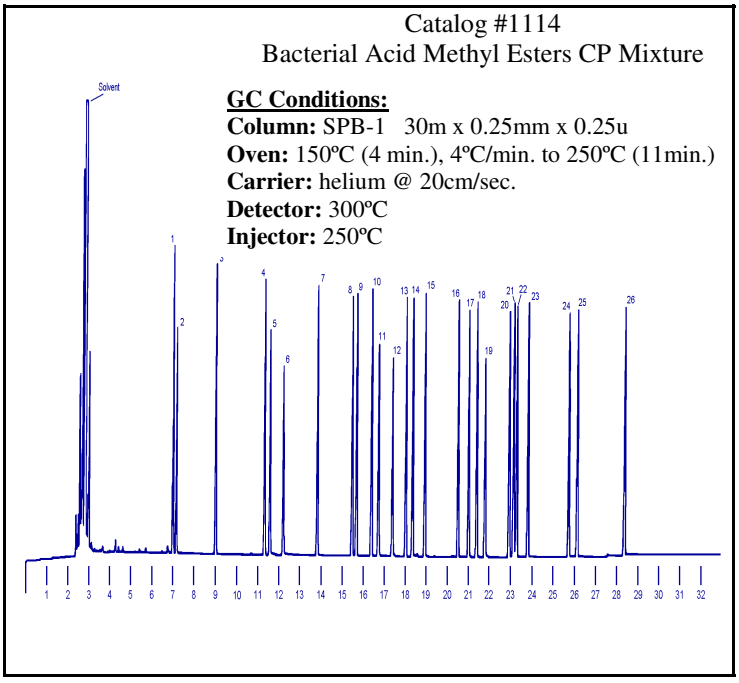
Fatty Acid and Methyl Ester Standards from Matreya

Matreya offers an extensive list of highly purified straight chain, branched chain, polyunsaturated, hydroxy, and cyclopropane fatty acids and fatty acid methyl esters (FAMEs) for your research needs. Our team at Matreya brings many years of experience in organic synthetic chemistry allowing us to custom synthesize or extract from natural sources various fatty acids to help you meet your specific goals.

Matreya is the best choice for your fatty acid and fatty acid methyl ester mixtures due to our continuing excellence in:



- QUALITY. Purity of the compounds used are 99+%
- METHODOLOGY. Product preparation is followed with the utmost caution to preserve the quality of the materials.
- EXPERIENCE. Matreya's staff understands the selection and usefulness of the individual components in your research and analysis.
- GUIDANCE. Matreya's decades of experience in fatty acid preparation and analysis will help to answer your technical questions as we guide you in using our products.



In addition to individual fatty acids and methyl esters, Matreya offers a wide selection of FAME mixtures. By studying 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 many of these mixtures is similar to the fatty acid distribution of certain oils. All mixtures are in methyl ester form and are ready for GC analysis. Each methyl ester mixture is carefully prepared by weight and the composition is verified by gas chromatography.

Knowledge of the fatty acid content of bacteria can be of great benefit in understanding microbials and can be of great nutritional importance in animals. Understanding the role of enzymes and regulatory pathways in human pathogens is important in drug development. Microbial fatty acid profiles are unique from one species to another and can therefore be used in the determination of bacterial identity.

If you do not see a mixture listed that meets your specific need please contact the staff at Matreya. We are always happy to make custom mixtures according to your individual requirements.

Please visit www.matreya.com for a complete list of standards.

Phospholipid Research Tools

Phospholipids are well known for their role as the main component of membranes where they form the lipid bilayer due to their amphipathic character. However, phospholipids are also important as cellular messengers, enzyme activators, and more[1]. Hundreds of different phospholipid molecular species are present in cells, each having variations in their phospholipid headgroup or acyl tails that give them unique properties. Matreya offers an extensive list of highly purified natural and synthetic phospholipids to meet your research needs. Please visit **www.matreya.com** to see our full list.

Phosphatidylcholine is a major component of biological membranes, especially in the outer leaflet, often comprising almost 50% of the total phospholipids in mammals[2]. It plays an important role in membrane-mediated cell signaling by generating arachidonic aid, diacylglycerols, and phosphatidic acid[3].

Phosphatidylethanolamine is frequently the main lipid component of microbial membranes and the second most abundant phospholipid in mammals, comprising as much as 45% of brain lipids. One of its primary roles in bacterial membranes is to dilute the high negative charge density of the anionic phospholipids. In animals it is involved in the secretion of very-low-density lipoproteins and aids in membrane fusion and fission[4].

Phosphatidylinositol is a source for lipids involved in the signal transduction of many hormones, neurotransmitters and growth factors. The activation of phosphoinositide 3-kinase results in the formation of three novel phosphatidyl lipids phosphorylated at the D3 position of the inositol ring: PI-3-P, PI-3,4-P2, and PI-3,4,5-P3. These D3 lipids have functions as second messengers[5].

Phosphatidylserine is a negatively charged glycerophospholipid that is widespread but quantitatively minor in mammalian cells. It is externalized by cells for various cellular functions such as cell fusion, blood clotting, and regulation of cell signaling and it acts as an important part of the lipid-calcium-phosphate complex needed for mineral formation[6].

Phosphatidic acid is not generally a major component in cells but is used extensively as an intermediate in the biosynthesis of other glycerophospholipids and as a signaling molecule. It
acts as the precursor to a number of phospholipids and triacylglycerols, is integral in forming the shape of cellular membranes[7], has functions in cellular signaling[8], and has a role in vesicle fission and fusion.

Phosphorylglycerols are found in relatively large amounts in pulmonary surfactants, the lipoprotein complex that is formed by type II alveolar cells in the lung. The enzyme cardiolipin synthase attaches two phosphorylglycerols together to form cardiolipid which is a major component of the mitochondrial inner membrane[9].

- **Sphingomyelin** is found in mammalian cell membranes, especially in the membranes of the myelin sheath and is the most abundant sphingolipid in mammals. An improper ratio of sphingomyelin to ceramide has been shown to be a factor in Niemann-Pick disease[10] and neonatal respiratory distress syndrome[11]. It is also an important amphiphilic component when plasma lipoprotein pools expand in response to large lipid loads or metabolic abnormalities[12].

Sphingosylphosphorylethanolamine is analogous to sphingomyelin, containing an ethanolamine rather than a choline headgroup, and is thought to have similar structural functions. It has been found in marine invertebrates, anaerobic bacteroides, insects, and in the eukaryotic microorganism Oomycete but not in plants or mammals. It is thought that it may be produced when there is a lack of choline to make sphingomyelin[13].

Sphingosylphosphorylcholine has been identified in normal blood plasma, ascites and various other tissues. It is a bioactive lipid that acts as an intracellular and extracellular signalling molecule in numerous biological processes and activates various signaling cascades.

Sphingosine-1-phosphate has important signaling functions both intra- and inter- cellularly and is present at low concentrations in cells. It can promote cellular division, regulate calcium mobilization and cell growth, and can either inhibit or promote apoptosis depending on the circumstances[14]. Unlike most other sphingolipids it does not form lipid rafts in membranes but exerts its extra-cellular effects by acting as a ligand for specific receptors. These ligand-receptor interactions are important for the growth of new blood vessels, vascular maturation, cardiac development and immunity, the inflammatory process, and for directed cell movement[15]. Sphingosine-1-phosphate is involved in regulating the proliferation, survival, differentiation and migration of many types of stem cells, especially in the development of the vascular and nervous systems.

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