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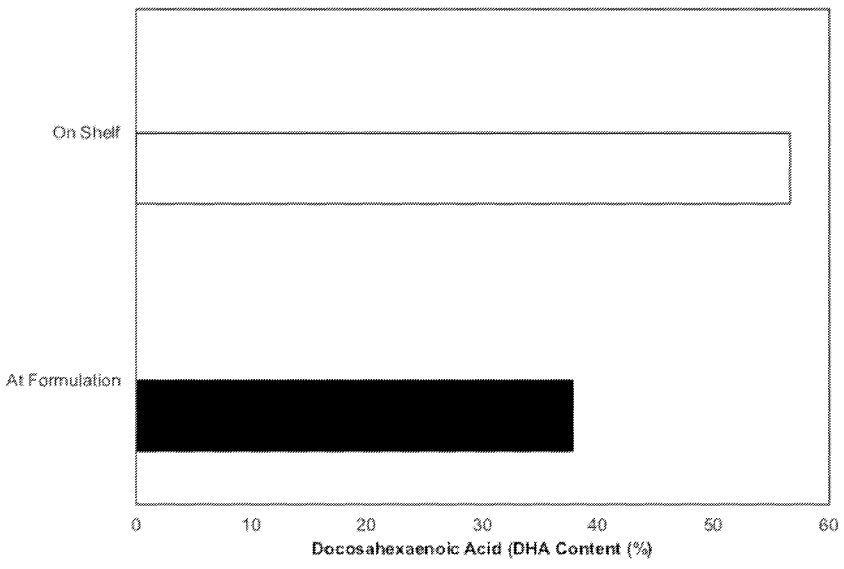
(54) Title: STABLE FATTY ACID COMPOSITIONS

Figure 1, Change in DHA content



(57) Abstract: A composition comprising a medium chain fatty acid (MCFA), at least one polyunsaturated fatty acid (PUFA), and at least one protein, is provided. The composition improves or preserves the stability of polyunsaturated fatty acids (PUFAs). The compositions are useful for preparing dietary supplements and foods that provide health benefits.

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STABLE FATTY ACID COMPOSITIONS

Related Application

[0001] This application claims priority from a U.S. Patent application serial no. 13/951,290, filed on July 25, 2013, U.S. provisional applications, serial nos. 61/893,279, filed October 20, 2013 and 61/920,448, filed December 23, 2013, which are incorporated herein by reference.

Field of the Invention

[0001] The present invention relates to compositions that exhibit superior shelf life stability and flavor properties. The compositions contain one or more fatty acid materials and a least one protein. Thus, the compositions are useful, for example, as health care, food, and beverage compositions. The present invention is further directed to methods of stabilizing or improving such compositions as well as methods of preventing loss of flavor associated with fatty acid materials.

Background of the Invention

[0002] Fatty acids (FAs) constitute an important source of energy in humans not only during fasting but also under well-fed conditions. Some organs, *e.g.*, the brain, show a marked preference for FAs, particularly when carbohydrates supply is low. Fatty acids are classified as short-chain ($< C_7$) fatty acids (SCFAs), medium-chain (C_8-C_{12}) fatty acids (MCFAs), long-chain (C_{13}-C_{20}) fatty acids (LCFAs) and very long chain fatty acids (VLCFAs).

[0003] Developing fortified foods and supplements requires designing the extent and type of calories, extent and type dietary fuels, nutrients, and consumption timing of food products to achieve the desired effects. One approach to modulate the energy homeostasis is modulation of fatty acid metabolism by redesigning foods that have specific fatty acids that provide a specific level of calories.

[0004] Omega-3-fatty acids have been reported to provide several health benefits. Polyunsaturated fatty acids (PUFAs) represent fundamental components of phospholipids in cellular membranes. PUFAs are usually located in the sn-2 position, whereas saturated or monounsaturated fatty acids are usually bound in the sn-1 position of the phospholipid molecules. Fatty acids integrated in these positions are the healthy food of dietary fat. In recent years, there has been increased focus on the role of specific dietary fatty acids, particularly polyunsaturated fatty acids, and their effect on health and disease. The unsaturated fatty acids

such as omega-3 polyunsaturated fatty acids are known to undergo lipid oxidation or interconversion. Lipid oxidation is a complex series of chemical reactions that is initiated when oxygen interacts with unsaturated lipids. Lipid oxidation of PUFAs tends to result primary reaction products such as peroxides and conjugated dienes and secondary reaction products such as aldehydes, ketones, alcohols and hydrocarbons. Lipid oxidation causes off-flavors and aromas, which can make the product unacceptable to a consumer. Since EPA, DPA and more specifically DHA are more susceptible to oxidation than vegetable oils or certainly saturated fatty acids, shelf life of enriched products is a concern.

[0005] The scientific literature does not disclose a shelf stable or heat stable composition comprising a polyunsaturated fatty acid useful for preparing fortified foods and/or supplements. Further, the literature does not disclose that the omega-3 fatty acid can provide stability that depends on the relative content of other fatty acids and protein, as well as the purity of the overall composition and also on the presence and amount of a fatty acid (FA) and a protein. Further, there is no publication that discloses or proposes the use of a saturated fatty acid in combination with a protein to improve or increase the stability of polyunsaturated fatty acids that are useful for preparing dietary supplements or food products.

[0006] U.S. Patent No. 5,886,037 discloses a composition comprising fats, the fatty acids of said fats comprising: 55-95 wt. % of medium chain fatty acids (MCFAs); 5-25 wt. % of n-3 polyunsaturated fatty acids (n-3 PUFAs); and 0-30 wt. % of other fatty acids. U.S. Patent No. 8,283,335 discloses a lipid fraction that comprises the medium-chain fatty acids at least 4 g hexanoic acid and/or at least 5 g octanoic acid, at least 1 g eicosapentaenoic acid, and in addition more than 0.4 g of alpha-linolenic acid per 100 g fatty acids of the lipid fraction. U.S Patent No. 7,560,486 discloses an isotonic lipid-in-water emulsion free of long-chain vegetable oils, said emulsion comprising (i) 60 to 95% by weight of medium chain triglycerides (MCT), and (ii) 5 to 40% by weight of fish oil, based on the total amount by weight of MCT and fish oil lipids in the emulsion, (see, *e.g.*, col. 5, lines 5-10). U.S. Patent No. 8, 241, 672 discloses an oil-in-water emulsion of enriched fish oil and a medium chain fatty acid (MCFA) oil, wherein the enriched fish oil comprises at least 45% by weight of EPA and DHA, and at least 60% by weight of n3-FA, based on the total weight of the enriched fish oil.

[0007] There is an unmet need for more efficient compositions to prepare a dietary supplement or a food product that are stable on shelf and or against increased temperature that

prevail in distribution channels. It will be especially helpful to find a common composition useful as, *e.g.*, supplements and food products, either alone or in combination with another dietary agent.

[0008] In a surprising benefit the present invention, provides compositions having omega-3 polyunsaturated fatty acids (as defined elsewhere), which are stable against heat and/or light through use of a system comprising at least one medium chain fatty acid and at least one protein. In addition, the composition preserves the specific omega-3 content. In another aspect, the patient can obtain the health benefits of polyunsaturated fatty acid materials, which are not being widely realized due to stabilization difficulties and unacceptable oxidation profiles. The defined combinations of medium chain triglyceride (MCT) and optional protein(s), stabilize the polyunsaturated fatty acid materials over extended periods of time, for example, for at least about 90 days, and often up to about a year, additionally, stabilizing minimizing or completely removing any objectionable flavor normally associated with the polyunsaturated fatty acid.

[0009] Accordingly, the present invention provides compositions that provide extended stability for polyunsaturated fatty acid materials, as well as methods for the delivery of these unsaturated fatty acid materials without formation of degradation products such as, peroxides and/or objectionable flavors and aromas.

Summary of the Invention

[0010] In one aspect, the present invention provides a stable composition (formulation) comprising at least one medium chain triglyceride, at least one protein and least one polyunsaturated fatty acid (PUFA), and optionally a dietary carrier, or a preservative agent. The composition is useful to prepare dietary supplements and food products.

[0011] In another aspect, the present invention provides compositions comprising at least one medium chain fatty acid (MCFA), at least one polyunsaturated fatty acid (PUFA), and at least one protein, and optionally a dietary carrier, or a preservative agent. The compositions are useful to prepare dietary supplements and food products and improve or preserve the stability of polyunsaturated fatty acid (PUFA) in the composition. The compositions optionally include nutraceutically acceptable salts of the various components.

[0012] In another aspect, the polyunsaturated fatty acid (PUFA) in the compositions can be ethyl eicosapentaenoic acid (Ethyl EPA), linolenic acid (LA), arachidonic acid (AA), docosahexaenoic acid (DHA), alpha-linolenic acid (ALA), stearadonic acid (STA),

eicosatrienoic acid (ETA), docosapentaenoic acid (DPA), combinations thereof or a nutraceutically acceptable salt or derivative thereof.

[0013] In another aspect, the present invention provides a composition comprising at least one medium chain fatty acid, at least one polyunsaturated fatty acid (PUFA) and at least one protein, wherein the protein is from about 20% to about 70% by weight of the composition.

[0014] In another aspect, the present invention provides a method of producing a formulation comprising at least one medium chain fatty acid (MCFA), at least one polyunsaturated fatty acid (PUFA), at least one protein, wherein the composition comprises from about 10% to about 70% by weight of at least one medium chain triglycerides and the composition improves the stability of polyunsaturated fatty acid (PUFA) in the formulation.

[0015] In another aspect, the present invention provides a method of producing a formulation comprising at least one medium chain triglyceride, at least one protein and least one polyunsaturated fatty acid (FA), and optionally a dietary carrier, or a preservative agent, wherein the formulation is heat stable and the method comprises 1) mixing at least one medium chain triglycerides and at least one polyunsaturated fatty acid from about 5 to about 90 minutes, 2) mixing the homogenized fatty acid mixture with at least one protein from about 5 minutes to about 90 minutes

[0016] In another aspect, the present invention provides a method of producing a formulation comprising at least one medium chain triglyceride, at least one protein and least one polyunsaturated fatty acid (FA), and optionally a dietary carrier, or a preservative agent, wherein the formulation is light stable and the method comprises 1) mixing at least one medium chain triglycerides and at least one polyunsaturated fatty acid from about 5 to about 90 minutes, 2) mixing the homogenized fatty acid mixture with at least one protein from about 5 minutes to about 90 minutes.

[0017] In another aspect, the present invention provides a method of producing a formulation wherein the polyunsaturated fatty acid (PUFA) is docosahexaenoic acid and the method comprises 1) mixing at least one medium chain triglycerides and docosahexaenoic acid (DHA)from about 5 to about 90 minutes, 2) mixing the homogenized fatty acid mixture with at least one protein from about 5 minutes to about 90 minutes. Preferably, the formulation contains not more than about 10%, by weight, of eicosapentaenoic acid (EPA) and docosapentaenoic acid (DPA).

[0018] In another aspect, the present invention provides compositions wherein the amount of medium chain fatty acid is from about 35% to about 90% by weight of total fat in the composition, and the amount of polyunsaturated fatty acid is from about 10% to about 65% of by weight of total fat in the composition, and wherein the protein is at least about 50% by weight of the composition. Optionally, the composition may further contain one or more of dietary carriers, preservative agents or adjuvants.

[0019] In another aspect, the present invention provides a composition comprising at least one medium chain triglyceride, at least one protein and least one polyunsaturated fatty acid (PUFA), a protein, and optionally a dietary carrier, or a preservative agent, wherein the composition is heat stable.

[0020] In another aspect, the present invention provides a composition comprising at least one medium chain triglyceride, at least one protein and least one polyunsaturated fatty acid (PUFA), a protein, and optionally a dietary carrier, or a preservative agent, wherein the composition is light stable.

[0021] In another aspect, the present invention provides a composition wherein the polyunsaturated fatty acid (PUFA) is docosahexaenoic acid. Preferably, the composition contains not more than about 10%, by weight, of eicosapentaenoic acid (EPA) and docosapentaenoic acid (DPA). The combination can substantially preserve the stability of docosahexaenoic acid.

[0022] In another aspect, the present invention provides a composition wherein the medium chain fatty acid is caprylic acid. Preferably, the grain free composition contains not more than about 10%, by weight, of other medium chain fatty acids.

[0023] In another aspect, the present invention provides a composition wherein the medium chain fatty acid is capric acid. Preferably, the grain free composition contains not more than about 10%, by weight, of other medium chain fatty acids.

[0024] In another aspect, the present invention provides a composition wherein the polyunsaturated fatty acid (PUFA) is eicosapentaenoic acid (EPA). Preferably, the composition contains not more than about 10%, by weight, of docosahexaenoic acid (DHA) and docosapentaenoic acid (DPA).

[0025] In another aspect, the present invention provides a composition wherein the polyunsaturated fatty acid (PUFA) is Preferably docosapentaenoic acid (DPA), the composition contains not more than about 10%, by weight, of docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA).

[0026] In another aspect, the present invention provides a composition comprising up to about 50% fatty acids wherein the fatty acids comprise from about 35% to about 90% of medium chain fatty acids, by weight; from about 10% to about 65% of at least one polyunsaturated fatty acid (PUFA) by weight; at least one protein; and optionally a dietary carrier or a preservative agent; or acceptable salts or derivatives thereof, and wherein the protein is at least about 50% by weight of the composition.

[0027] In another aspect, the present invention provides a composition comprising at least one medium chain fatty acid, at least one polyunsaturated fatty acid (PUFA) and at least one protein, wherein the composition stabilizes the polyunsaturated fatty acid in the composition to light or heat.

[0028] In another aspect, the present invention provides a composition that comprises an optional additional dietary agent such as, for example, a vitamin, an amino acid, a hormone, an element, a nutrient, and the like.

[0029] In another aspect, the present invention provides a food product comprising the MCFA/PUFA/protein composition herein. The food product can be, for example, an energy bar or a beverage. The food beverages include a protein shake mix, an energy drink beverage.

[0030] In another aspect, the present invention provides a method of increasing serum ketone bodies by administering a composition comprising at least one medium chain fatty acid, at least one polyunsaturated fatty acid (PUFA) and at least one protein, wherein the composition stabilizes the polyunsaturated fatty acid in the composition to light or heat.

[0031] The details of one or more embodiments of the invention are set forth in the accompanying description below. Other features, objects, and advantages of the invention will be apparent from the description and drawings, and from the claims.

Description of the Figures

[0032] Figure 1 illustrates the docosahexaenoic acid (DHA) content at the time of formulation and from a shelf sample.

[0033] Figure 2 illustrates the total docosapentaenoic acid (DPA) acid content at the time of formulation and from a shelf sample.

[0034] Figure 3 illustrates the total Eicosapentaenoic acid (EPA) acid content at the time of formulation and from a shelf sample.

[0035] Figure 4 illustrates the total polyunsaturated fatty acid content at the time of formulation and after exposure to light of Example 9.

[0036] Figure 5 illustrates the total polyunsaturated fatty acid content at the time of formulation and after exposure to light of Example 2.

[0037] Figure 6 illustrates the change in serum triglyceride concentration from baseline to end of study.

[0038] Figure 7 illustrates the change in serum LDL concentration from baseline to end of study.

[0039] Figure 8 illustrates the change in serum HDL concentration from baseline to end of study.

[0040] Figure 9 illustrates the percent change in the mean serum concentrations of β-hydroxy butyrate.

[0041] Figure 10 illustrates the change in the mean serum concentrations of IL-6.

[0042] Figure 11 illustrates the change in the mean serum concentrations of TNF.

[0043] Figure 12 illustrates the change in the mean serum concentrations of 25-hydroxy vitamin D.

[0044] Figure 13 illustrates the concentration of caprylic and capric acid in test composition 4079, 4122 and 4123 prepared according to Example 13, 14 and 15.

[0045] Figure 14 illustrates the concentration of Docosahexaenoic acid (DHA) in test compositions 4079, 4122 and 4123 prepared according to Example 13, 14 and 15.

[0046] Figure 15 illustrates the ratio of saturated fatty acid to polyunsaturated fatty acid in test compositions 4079, 4122 and 4123 prepared according to Example 13, 14 and 15.

[0047] Figure 16 illustrates the ratio of saturated fatty acid to polyunsaturated fatty acid in test composition 4014 prepared according Example 16 and Example 17.

[0048] Figure 17 illustrates the concentration of caprylic and capric acid in test composition 4014 prepared according to Example 16 and Example 17.

[0049] Figure 18 illustrates the concentration of Docosahexaenoic acid (DHA) in test composition 4014 prepared according Example 16 and Example 17.

Detailed Description

Definitions

[0050] The following terms have the meaning as defined in this section. Although any materials and methods similar or equivalent to those described herein can be used in the practice or testing of the present invention, the preferred materials and methods are described herein. In describing and claiming the invention, unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Exemplary and preferred values listed below for radicals, substituents, and ranges are for illustrations only; they do not exclude other defined values or other values within defined ranges for the radicals and substituents.

[0051] The terms "a," "an," "the," "at least one," and "one or more" are used interchangeably. Thus, for example, a grain free composition that comprises "an" element means one element or more than one element.

[0052] The term "additive effect" as used herein means the effect resulting from the sum of the effects obtained from the individual agents.

[0053] The term "capric acid" or "capric triglyceride" used herein means the capric acid and its salts and esters of the saturated fatty acid with $CH_3(CH_2)_8COOH$ including capric triglyceride.

[0054] The term "caprylic acid" or "caprylic triglyceride" used herein means the salts and esters of the saturated fatty acid with $CH_3(CH_2)_6COOH$ including caprylic triglyceride.

[0055] The term "Heat" as used herein means a temperature that is higher than recommended for storing a product comprising at least one polyunsaturated fatty acid (PUFA).

[0056] The term " ketone bodies" as used herein means the ketone bodies generated by the metabolism of fatty acid including acetone, acetoacetic acid, and beta-hydroxybutyric acid (BHB).

[0057] The term "Light" as used herein means a light source that is higher than recommended for storing a product comprising at least one polyunsaturated fatty acid (PUFA).

[0058] The term "medium chain fatty acid (MCFA)" or "medium chain triglyceride" or "medium chain saturated fatty acid" means linear or branched saturated carboxylic acids having

four, five, six, seven, eight, nine, or ten carbon atoms either in free acid form or in their respective sales, esters including as a triglyceride.

[0059] The term "nutraceutically acceptable derivative" or "acceptable derivative" as used herein, means various equivalent isomers, enantiomers, complexes, salts, hydrates, polymorphs, esters, and the like, *e.g.*, of an active agent, a fatty acid such a polyunsaturated fatty acid (PUFA) or a medium chain fatty acid (MCFA).

[0060] The term "acceptable salt" or "nutraceutically acceptable salt" as used herein, refers to salts that retain the biological effectiveness and properties of a fatty acids such as a polyunsaturated fatty acid (PUFA), and or a medium chain fatty acid, which are not biologically or otherwise undesirable.

[0061] The term "Polyunsaturated Fatty Acid" or "PUFA" includes but is not limited to omega-3 unsaturated fatty acids such as α-linolenic acid, stearidonic acid, eicosapentaenoic acid and docosahexaenoic acid, omega-6 unsaturated fatty acids such as conjugated linoleic acid, linoleic acid, γ-linolenic acid, dihomo-γ-linolenic acid, arachidonic acid, and adrenic acid, omega-7 unsaturated fatty acids such as palmitoleic acid, vaccenic acid, and paullinic acid and omega-3 unsaturated fatty acids such as oleic acid, elaidic acid, gondoic acid, erucic acid, nervonic acid and mead acid or nutraceutically acceptable salts thereof.

[0062] The term "protein isolate" means isolated proteins. Non-limiting examples of protein sources include milk, soy, whey, wheat, tofu, collagen, pea, albumin, gelatin, caseinates, peas, hemp, and rice protein.

[0063] The disclosed stable compositions have a medium chain fatty acid (MCFA), at least one protein and at least one polyunsaturated fatty acid (PUFA), or an acceptable salt thereof, optionally an acceptable carrier, and a vitamin, an amino acid, a hormone, an element, a nutrient, intermediates of the TCA cycle, Fatty Acid Oxidation and Glycolysis.

[0064] The disclosed stable compositions can include vitamins. Non-limiting examples of vitamins include Vitamin A, Vitamin B, Vitamin C, Vitamin D, Vitamin E, Vitamin K, thiamine, riboflavin, niacin, lutein, pantothenic acid, biotin, folic acid, and the like.

[0065] The disclosed stable compositions can include amino acids. Non-limiting examples include all naturally occurring amino acids irrespective of their configuration, such as, Alanine, Arginine, Aspartic acid, Cysteine (Cystine), Glutamic acid, Glutamine, Glycine, Histidine,

Isoleucine, Leucine, Lysine, Methionine, Phenylalanine, L-Phenylalanine, Proline, Serine, Threonine, Trypophan, Tyrosine, Valine and other include Acetyl L-Carinitine Arginate, Alpha-aminoadipic acid, Alpha-amino-N-butyric acid, beta-alanine, beta-amino-isobutyric acid, Carnosine, Citrulline, gamma-amino butyric acid (GABA), hydroxyproline, 1-methylhistidine, 3-methylhistidine, N-Acetyl L-Cysteine, Ornithine amino acid, para-aminobenzoic acid (PABA), Phosphoserine, Phosphoethanolamine, Berberine, Taurine, and the like.

[0066] The disclosed stable compositions can include hormones. Non-limiting examples include all hormones for human use, such as, thyroid-stimulating hormone (TSH), follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin (PRL), growth hormone (GH), adrenocorticotropic hormone (ACTH), vasopressin, oxytocin, thyrotropin-releasing hormone (TRH), gonadotropin- releasing hormone (GnRH), growth hormone-releasing hormone (GHR H), corticotropin-releasing hormone (CRH), somatostatin, dopamine, melatonin, thyroxine (T4), calcitonin, parathyroid hormone (PTH), FGF-23 (phosphatonin), osteocalcin, erythropoietin (EPO), glucocorticoids (e.g., cortisol), mineralocorticoids (e.g., aldosterone), androgens (e.g., testosterone), Adrenalin (epinephrine), norepinephrine, Estrogens (e.g., estradiol), progesterone, human chorionic gonadotropin (HCG), androgens (e.g., testosterone), insulin, glucagon, somatostatin, Amylin, erythropoietin (EPO), Calcitriol, Calciferol, Atrial-natriuretic peptide (ANP), Gastrin, Secretin, Cholecystokinin (CCK), Fibroblast Growth Factor 19 (FGF19), Incretins, Neuropeptide Y, Ghrelin, PYY3-36, Serotonin, Insulin-like growth factor-1 (IGF-1), Angiotensinogen, Thrombopoietin, Hepcidin, Leptin, Retinol Binding Protein 4, Adiponectin, Irisin, and the like.

[0067] The disclosed stable compositions can include biologically important elements. Non-limiting examples include all elements for human consumption, such as, Sodium, Magnesium, Selenium, Manganese, Chromium, Vanadium, Phosphorus, Sulfur, Tungsten, Arsenic, Boron, Copper, Cobalt, Germanium, Silicon, Nickel, Potassium, Calcium, Iron, Iodine, and the like.

[0068] The disclosed stable compositions can include biologically important compounds. Non-limiting examples optionally include at least one intermediate of the Citric acid cycle (The citric acid cycle also known as the tri-carboxylic acid cycle (TCA cycle), or the Krebs cycle). The intermediate is selected from a group consisting of citric acid, aconitic acid, isocitric acid, α-ketoglutaric acid, succinic acid, fumaric acid, malic acid, oxaloacetic acid, and their nutraceutically acceptable salts and mixtures thereof. The precursor compounds such as 2-keto-

4-hydroxypropanol, 2,4-dihydroxybutanol, 2-keto-4-hydroxybutanol, 2,4-dihydroxy¬butyric acid, 2-keto-4-hydroxybutyric acid, aspartates as well as mono- and di-alkyl oxaloacetates, pyruvate and glucose-6-phosphate are also included in the definition of intermediates of the Citric Acid Cycle.

[0069] The term "synergistic effect" as used herein means an effect from two agents (active agents), which is greater than the additive effect that results from the sum of the effects of the two individual agents.

[0070] Suitable polyunsaturated fatty acids (PUFAs) include, but are not limited to, ethyl eicosapentaenoic acid (Ethyl EPA), linolenic acid (LA), arachidonic acid (AA), docosahexaenoic acid (DHA), alpha-linolenic acid (ALA), stearadonic acid (STA), eicosatrienoic acid (ETA), docosapentaenoic acid (DPA) or a nutraceutically acceptable salts or derivatives thereof.

[0071] A preferred polyunsaturated fatty acid (PUFA) useful for the disclosed compositions is docosahexaenoic acid and preferably the composition contains not more than about 10%, by weight, eicosapentaenoic acid (EPA).

[0072] Another preferred polyunsaturated fatty acid (PUFA) useful for the disclosed compositions is docosapentaenoic acid (DPA) and preferably the composition contains less than about 10%, combined weight of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).

[0073] Another preferred polyunsaturated fatty acid (PUFA) useful for the disclosed compositions is eicosapentaenoic acid (EPA) and preferably composition contains not more than about 10%, by weight, docosahexaenoic acid.

[0074] Suitable medium chain fatty acids useful in the disclosed compositions can be obtained from a whole food such as coconut flour, palm drupe flour, or camphor drupe flour.

[0075] In a preferred embodiment, the disclosed compositions can be grain free. The compositions have improved stability, to heat and light. The improvement in is illustrated by 1) prevention of odor formation, and 2) shelf stability data for the MCT Bars and MCT Shake Mix. Both compositions were found to be stable for at least eight months with a) sensory testing smell and feel and b) peroxide content, which was below 20 PPM, in both products

Other Health Related Uses

[0076] While not wishing to be bound by theory, it is submitted that the polyunsaturated fatty acids work by acting at different sites and aspects of diseases. This modulation is likely

influenced by the relative ratios of polyunsaturated fatty acids. PUFAs are known to increase anti-inflammatory properties, enhance the beta-oxidation in peroxisomes and improve the integrity of cell membranes. Similarly, upon administration of a medium chain fatty acid (MCFA), which is known to undergo β-oxidation in hepataocytes, generate supply ketone bodies and release them to circulation. The ketone bodies can be utilized by extra-hepatocytic cells such as neuron, retinal cells, heart, nephron, and other affected cells, or excreted from the mammal. The disclosed compositions combine the therapeutic properties of a polyunsaturated fatty acid and the properties of a medium chain fatty acid, such as anti-inflammatory properties, energy homeostasis, or membrane properties. In addition, the disclosed dispersion can be easily incorporated into å supplement or a food facilitating patient compliance. Thus, the changes expected in the levels of IL-6, TNF, and/or ketone bodies upon administering either the disclosed composition directly or the foods prepared using the disclosed compositions can provide health improvement. Increase in IL-6, TNF and Ketone bodies are reported to improve clinical symptoms associated with obesity, diabetes, rheumatoid arthritis (RA), schizophrenia, diabetic retinopathy and nonalcoholic fatty liver diseases (NALFD).

[0077] In addition, the root cause for the exacerbation of most of the modern diseases like cancer, obesity, diabetes, fatty liver & inflammatory bowel diseases and for the increased prevalence of certain genetic diseases like primary biliary cirrhosis, autism, ADHD is believed to be the modern diet. The western diet is relatively devoid of MCTs and very high in pro-inflammatory Omega-6-Polyunsaturated fatty acids. Fasting and high level of physical activity which were very common during the era when modern human genes were evolved several hundred years ago are either very uncommon or inadequate because social and technological changes. Thus, the disclosed grain free compositions and food products developed address this unmet need thereby useful for a number of diseases.

[0078] Ketone bodies are also naturally formed in the liver under conditions of prolonged fasting. Since fasting is uncommon in most developed countries and modern Western diets are relatively void of MCTs, these alternative food products provide energy to cells that do not occur naturally for most people. Dietary sources rich in MCTs include whole-fat dairy products, palm kernel oil and coconut oil. MCTs are transported directly to the liver, where they are metabolized into ketone bodies. Similarly, the presence of high dosage of omega-3-PUFAs in the food products, help improve the anti-inflammatory profile of the cells, enhance the peroxisomal -β-

oxidation and improve the membrane integrity. When taken together with carefully chosen protein, flour and isolates, MCTs and PUFAs improve the overall energy homeostasis and immunity thereby providing health benefits against a number of modern diseases as described below.

[0079] **Multiple Sclerosis (MS):** Multiple sclerosis (MS) is a disease of the central nervous system. The exact cause of Multiple Sclerosis in humans has not been determined. Multiple sclerosis (MS) is a complex disease of a heterogeneous nature. Its etiology has caused much controversy, and still remains unknown in the medical community after decades of research. The first description of MS as a neurological condition that afflicts the myelin sheath insulating long extensions of the axon conducting electrical signals from one neuron to another. MS is identified as a disease of young adulthood and does exist worldwide.

[0080] There is no known cure for MS. There are partially effective strategies are available to modify the disease course, treat exacerbations, attacks, relapses, or flare-ups, manage symptoms, improve function and safety, and provide emotional support. The treatment options for multiple sclerosis include the use of disease modifying agents with interferon beta, such as, Avonex (interferon beta-1a), Betaseron (interferon beta-1b), Rebif (interferon beta-1a), Extavia (interferon beta-1b) and others, such as, Copaxone (glatiramer acetate), Gilenya (fingolimod), Novantrone (mitoxantrone), and even a monoclonal antibody, such as, Tysabri (natalizumab). However, these treatments do not fully enhance the quality of life for people living with MS. There is recent research that reports strong evidence that axonal degeneration is a critical factor in the etiology of MS and have dysfunctional complexes I, III and IV because of electron transport system. In addition, MS is characterized by vitamin D deficiency and inflammation indicating the mitochondria function is crucial in preserving axonal integrity in both acute inflammatory and progressive stages of the disease. Since the disclosed composition comprises MCTs, PUFA, and Vitamin D, it can be helpful in producing ketone bodies that can potentially inhibit free radical production, supply anti-inflammatory eicosanoids and docosanoids and nutritional support.

[0081] **Epilepsy:** Clinical use of ketones to treat CNS disorders has been ongoing for decades in the form of the ketogenic diet. Typically, ketogenic diets are rich in fat and low in carbohydrates and proteins. Unfortunately, this combination reduces palatability. A ketogenic diet induces a decrease in blood sugar levels and an increase in ketone bodies via conversion of

fatty acids in the liver. A ketogenic diet has shown to be effective in pharmaco-resistant forms of epilepsy, including catastrophic cases of infantile spasms, the multiple seizure types associated with the Lennox-Gastaut syndrome, and certain inherited metabolic disorders. Ketogenic diets increase levels of circulating ketone bodies in the blood and have been shown to reduce seizures by more than 50%.

[0082] While a typical ketogenic diet consists of about 88% fat, about 10% protein, and about 2% carbohydrates and is a valuable adjunct in the management of epilepsy in children and adults with seizure disorder, palatability and patient compliance are major issues. Studies have shown that 53.9% of patients had a more than 75% reduction in seizure frequency 1 month and recent studies have shown that children who remained on the ketogenic diet for more than 1 year, and who had a good response to the diet, had positive outcomes at 3-year and 6-year follow ups, after initiation of the diet provided the compliance is good.

[0083] By using MCTs and PUFAs in a grain free composition with an edible solid material, the disclosed composition promotes formation of ketone bodies, improves anti-inflammatory effects and palatability considerably. Thus the disclosed dietary supplements and food products are especially useful as standard nutritional support under the supervision of a physician in the dietary management of epilepsy.

[0084] **Ophthalmic disorders:** Systemic oxidative stress, dysfunctional cellular processes and malfunctioning mitochondria are implicated in the pathogenesis of diseases such as retinopathy, AMD, cataract, glaucoma and retinitis pigmentosa. It is reported that the pathogenesis of glaucoma, AMD and Alzheimer's has common pathways. The brain, which comprises only about 2% of the body weight, is one of the highest energy demanding tissues of the human body and consumes 20% of the total oxygen and about a quarter of the total glucose used for energy supply. Within the brain, the visual system reportedly ranks amongst the highest energy-consuming systems. Thus, the visual system requires high performing energy supply system. In ophthalmic diseases, the primary defect often affects glucose metabolism, which is crucial for energy supply. For example, in proliferative diabetic retinopathy, the blood supply to the retina is reportedly reduced. Because blood transports oxygen and glucose, it is proposed the energy supply is compromised in diabetic retinopathy.

[0085] The disclosed compositions, in combination with specific agents, such as, vitamin A, Luetin, alpha-ketoglutarate, provide unique products for large market indications such as diabetic

retinopathy, age related macular degeneration, glaucoma in addition to smaller underserved markets like retinitis pigmentosa, and the like.

[0086] **Psychiatric disorders:** Unlike other organs, the brain, which is energy intensive, can only consume glucose and ketone bodies for their metabolic processes. It is being increasingly reported that disturbed energetic metabolism and/or reactive oxygen species production take part in the pathophysiology of psychiatric disorders and more specifically in schizophrenia, bipolar disorder and major depressive disorder. The TCA cycle plays a central role in the oxidation of all substrates and the function of the ATP producing oxidative phosphorylation machinery in neurons. Oxidative phosphorylation is reportedly involved in synaptic signaling and plays a role in ion homeostasis in presynaptic nerve terminals. Proteome analysis of schizophrenic patient reports eleven down-regulated and fourteen up-regulated proteins, most of them related to energy metabolism. Metabolite marker studies in schizophrenic patients strongly support the role of energy metabolism dysfunction particularly glycolysis. Similarly, recent research indicates the central role of energy metabolism, more specifically oxidative phosphorylation, and mitochondrial distress in major depressive disorders and bipolar disorders.

[0087] The disclosed compositions can generate ketone bodies for energy deficient neurons, providing ω-omega PUFA for addressing lipid, neuro-protective, and anti-oxidant deficiencies in different psychiatric disorders such as schizophrenia, MDD, bipolar disorder, and the like. In addition, clinical studies indicate long-chain ω-3 PUFAs reduce the risk of progression to a psychotic disorder and may offer a safe and efficacious strategy for indicated prevention in young people with sub-threshold psychotic states. The formulation also synergistically improves β-oxidation of fatty acids, up-regulates anti-inflammatory cytokine IL-10, and down-regulates pro-inflammatory cytokines.

[0088] Gastrointestinal and Liver Diseases: Typically, lipid and glucose metabolism are in constant equilibrium in liver. If either of them is dysfunctional, it can result in many gastrointestinal and liver diseases such as celiac disease; Whipple disease, Crohn's disease; enteritis; gluten enteropathy; intestinal lymphangiectasia; chylous ascites; chylothorax; fistulas, cholestasis, stomach or duodenum; biliary atresia; obstructive jaundice; primary biliary cirrhosis; blind loop syndrome; gastrointestinal cancer; pancreatitis; cystic fibrosis where lipid breakdown or lipid uptake is compromised, in situations in which gall bladder or pancreas is dysfunctional, or anomalies occur in the lymph flow.

[0089] It has long been recognized that liver diseases like alcoholic and nonalcoholic fatty liver diseases, primary biliary cirrhosis, chronic liver failure, nonalcoholic steatohepatitis (NASH), have dysfunctional energy metabolism characterized by increased fatty acid oxidation. There are publications that report a link between fatty liver disease and mitochondrial dysfunction, inflammation and dysfunctional mitochondrial and peroxisomal β-oxidation of fatty acid against their ω-oxidation in endoplasmic reticulum (ER). The disruption of equilibrium among gluconeogenesis, TCA cycle, fatty acid oxidation and oxidative phosphorylation and the signaling mechanisms lead to fatty liver diseases.

[0090] The disclosed compositions of MCT dispersion with large doses of eicosapentaenoic acid and docosahexaenoic acid are especially useful. MCTs are completely broken down into fatty acids by pancreatic enzymes and, unlike LCTs, MCTs can even be taken up in the absence of bile acids or pancreatic enzymes. Medium chain fatty acids (MCFAs) are delivered directly to the blood, where they are transported in a complex with serum albumin. Therefore MCTs do not induce lymph flow. In summary, MCTs are taken up more quickly, more directly and more completely in the circulation than LCTs. MCTs and PUFAs prevent triglyceride accumulation and enhance (ω-3 polyunsaturated acids) peroxisomal *β*-oxidation. In addition, the formulation also synergistically improves fatty acid oxidation, up-regulates anti-inflammatory cytokine IL-10 and down regulates pro-inflammatory cytokines. For these reasons, the compositions disclosed herein can be used in the dietary management of gastrointestinal and liver diseases.

[0091] **Inflammatory Disorders**: While the interplay between the nervous, endocrine, and immune systems is recognized to be involved in the pathophysiology of chronic inflammatory diseases (CIDs), the recent findings highlight the role of adipose and energy regulation in inflammatory diseases. Inflammatory disorders such as irritable bowel syndrome (IBS), inflammatory bowel diseases (IBD), rheumatoid arthritis, etc. are characterized by higher level of pro-inflammatory cytokines. For example, irritable bowel syndrome (IBS) is reportedly characterized by an augmented cellular immune response with enhanced production of pro-inflammatory cytokines such as IL-6, TNF-α as reported in a study of 55 IBS patients as compared to age-sex matched healthy controls. Similarly, most of the effective monoclonal antibodies approved to manage rheumatoid arthritis, *e.g.*, inhibit IL-6 and TNF-α cytokines13 improve the disease profile. A number of studies indicate that energy regulatory dysfunction/oxidative stress as a consequence of increased production of ROS and reactive

nitrogen species (RNS) is important in the pathogenesis of IBD. The disclosed dispersion of MCTs, PUFAs and edible solid food can improve fatty acid oxidation, may up-regulate anti-inflammatory cytokine IL-10, and down-regulate pro-inflammatory cytokines. In addition, MCTs generate ketone bodies, enhance anti-oxidant/ROS scavenging capabilities, and are useful in addressing energy and metabolic/lipid deficiencies in inflammatory disorders. The ketone bodies generate conditions similar to what prevails under fasting or under a low carbohydrate diet that is reported to significantly reduce symptoms of IBS.

[0092] The following Examples are for illustrating the disclosed stable composition comprising a medium chain fatty acid (MCFA), at least one protein, and at least one polyunsaturated fatty acid (PUFA), and it not intended to limit the scope of the invention. The experimental examples disclose the preparation and use of a stable composition comprising a medium chain fatty acid (MCFA), at least one protein and at least one polyunsaturated fatty acid (PUFA), for providing health benefits and the examples are just intended to be a way of illustrating but not limiting the invention.

Example 1: Exemplary Composition

[0093] For illustrative purposes, an exemplary stable composition is prepared according to standard procedures known it the art. Docosahexaenoic Acid, 3 grams (Life's DHA P35-0100 from (DSM Nutrition, NJ, USA) (3 grams)) is mixed with 10 grams of medium chain triglycerides (KIC Chemicals, NJ, USA) in a suitable container. Room temperature is maintained during the mixing process. Whey protein, (Milk Specialties, MN, USA) 17 grams, is added to the homogenized solution. The mixture is stirred until the protein is uniformly dispersed in the oil. The composition was used for the stability studies in Example 5.

Example 2: Exemplary Composition

[0094] For illustrative purposes, another representative stable composition is prepared according to standard procedures known it the art. Docosahexaenoic acid, 6 grams (Life's DHA S17-P100 (DSM Nutrition, NJ, USA) (6 grams) is mixed with 14 grams of whey protein (Milk Specialties, MN, USA) in a suitable container. Room temperature is maintained during the mixing process. Medium Chain Triglycerides, 10 grams, (KIC chemicals, NJ, USA), is added to the powder. The mixture is stirred until the ingredients uniformly mixed with one another. The composition was used for the stability studies in Example 5.

Example 3: Exemplary Composition

[0095] For illustrative purposes, yet another representative stable composition is prepared according to standard procedures known it the art. Docosahexaenoic acid, 6 grams (Life's DHA S17-P100 (DSM Nutrition, NJ, USA) (6 grams) is mixed with 14 grams of whey protein (Milk Specialties, MN, USA) in a suitable container. Room temperature is maintained during the mixing process. Medium Chain Triglycerides, 20 grams, (KIC chemicals, NJ, USA), is added to the powder. The mixture is stirred until the ingredients uniformly mixed with one another. The composition was used for the stability studies in Example 5.

Example 4: Exemplary Composition

[0096] For illustrative purposes, yet another representative stable composition is prepared according to standard procedures known it the art. 4 grams of DHA oil (Life's DHA P35-0100 from (DSM Nutrition, NJ, USA) (4 grams)) is mixed with 3 grams of medium chain triglycerides (KIC Chemicals, NJ, USA) in a suitable container. Whey protein (Milk Specialties, MN, USA), 22 grams, is added to the homogenized solution. The mixture is stirred until the protein is uniformly dispersed in the oil. The composition was used for the stability studies in Example 6.

Odor Studies - Methodology:

[0097] The German standard Olfactometry Determination of Odor Intensity VDI 3882 Part 1 (VDI, 1992) provides qualitative descriptions of odor intensity with a numerical scale that may be used in back-calculating the corresponding odor concentration. These descriptions are reproduced in Table 1. Like odor threshold determination, assessment of odor intensity is undertaken in the laboratory by odor panels. Panel members are presented with odor at concentrations without dilution and asked to rate the odor strength on the scale in Table 1. The concentration presented to the panel is known because the threshold is known from the determination described below.

[0098] The "dynamic olfactometry" method is typically used as the basis of odor management by regulatory authorities because there are no reliable instrument-based methods that can measure an odor response in a manner similar to the human nose. The dynamic olfactometry method measures odor by presenting a sample of odorous air to a panel of people at a range of dilutions and seeking responses from the panelists on whether they can detect the odor. The correlations between the known dilution ratios and the panelists' responses are then used to calculate the number of dilutions of the original sample required to achieve the odor

detection threshold. The units for odor measurement using dynamic olfactometry are "odor units" (OU) which are dimensionless and are effectively "dilutions to threshold".

[0099] The above described method was amended with intensity level 6 indicating a highly unpleasant odor and 0 indicating a highly pleasant odor. A panel of six volunteers, who had not been exposed to rancid or fishy odor prior to the beginning of panel testing, were exposed to the test (investigative) sample and to reference samples as prepared according to Examples 1, 2, 3, and 4, DHA Oil and DHA Powder were used as controls. The panelists marked the odor intensity/pleasantness from a scale of 0 to 6 as described above.

Table 1: Odor Intensity Categories.

Odor Strength	Intensity Level
Extremely strong	6
Very strong	5
Strong	4
Distinct	3
Weak	2
Very weak	1
Not perceptible	0

[00100] The results of the panel testing are shown as an average for each sample in Table 2.

Table 2: Average Rating by Panelists

	Example 1	Example 2	Example 3	Example 4	DHA Oil (Life's DHA P35-0100)	DHA Powder (Life's DHA S17-P100)
Average	2.33	3.00	2.00	3.17	4.00	4.00

Example 5: Stability Study 1

[00101] A sample composition prepared according to example 1 was subjected to a stability study as follows. A heating oven was pre-heated and allowed to stabilize at a temperature of 170° F (77° C) for 30 minutes. The composition of Example 1, 50 grams, and a Reference Sample, Life's DHA (Life's DHA P35-0100 from DSM, USA), were heated in the oven for five hours. The samples were odor tested. The Life's DHA reference sample exhibited a strong fishy and rancid odor. There was no change in the odor from the sample from the Example 1 sample, which retained the original mild sweet vanilla flavor. The investigative sample (Example 1) was analyzed for Omega-3 fatty acid profile in a commercial laboratory. The results of change in

docosahexaenoic acid (DHA), docosapentaenoic acid (DPA), and eicosapentaenoic acid (EPA) content are illustrated in Figure 1, 2 and 3. There was no loss of DHA content in the heat exposed sample. The DPA appeared to have undergone inter-conversion to DHA.

Example 6: Stability Study 2

[00102] The composition prepared according to Example 2 was subjected to a stability study as follows. The composition of Example 2, 50 grams, and a Reference Sample, Life's DHA (Life's DHA P17-P100 from DSM, USA), were placed under a standard light (Equivalent to ID65 as per ISO 10977 (1993) for three months. Then the samples were odor tested. The reference sample exhibited a strong fish and rancid odor while there was no change in odor from the sample from Example 2, which retained the original mild sweet vanilla flavor.

Example 7: Stability Study 3

[00103] The composition prepared according to Example 3 was subjected to a stability study as follows. The investigative composition of Example 3, 50 grams, and a reference sample, Fish Oil (J. R Carlson Laboratories, Inc. Arlington Heights, IL, USA), were placed in an oven, preheated to 350° F (177° C), for seven teen minutes. Then the samples were odor tested. The Fish Oil reference sample exhibited a strong fish and rancid odor while there was no change in odor from the investigative sample, which retained the original mild sweet vanilla flavor.

Example 8: Energy Bar

[00104] An energy bar comprising the disclosed stable omega-3 composition is prepared by using methods known in the art by adding the composition prepared according to Example 1, with the desired ingredients. For Example, 10 g medium chain triglyceride (KIC Chemicals, NY, USA) is mixed with 3 g of Docosahexaenoic acid (Life's DHA OilS35-0300 from DSM Nutrition, NJ, USA), 17g whey protein isolate (Milk Specialties, MN, USA) and vanilla flavor to prepare the platform composition. The platform composition is mixed with appropriate amount Chicory Root Fiber, Organic Dates, Organic Peanut Butter, Organic Cocoa, Organic Vegetable Glycerin, Organic Cashews, Raw Almonds, Organic Coconut, Organic Raisins, Organic Flaxseed, Organic Vanilla Extract, Organic Banana Flakes, and Sea Salt. The ingredients are mixed thoroughly and passed through an extruder pre-configured for desired weights. The bars are dried, pressed and packaged for further tests.

Example 9: Light Stability

[00105] The effect of light on the stability of polyunsaturated fatty acids (PUFA) was analyzed in a light exposure experiment. Polyunsaturated fatty acid (Life's DHA Oil S17-0100 from DSM Nutrition, NJ, USA), 100 g, was placed under a standard light (Equivalent to ID65 as per ISO 10977 (1993) for three months. The sample was odor tested. The Life's DHA reference sample exhibited a strong fish. The light exposed polyunsaturated fatty acid was analyzed in a commercial laboratory. The change in the total polyunsaturated fatty acid content is in Figure 4.

Example 10: Light Stability

[00106] The effect of light on the stability of Polyunsaturated Fatty Acids (PUFA) content was analyzed in a light exposure experiment. 100 g of exemplary composition of Example 2 was placed under a standard light (Equivalent to ID65 as per ISO 10977 (1993) for three months. Then the sample was odor tested. The sample exhibited a sweet vanilla flavor with very little fishy odor. The light exposed sample was analyzed in a commercial laboratory to evaluate the change in polyunsaturated fatty acid content. The change in the total polyunsaturated fatty acid content is in Figure 5.

Example 11: Accelerated Shelf Stability

[00107] Sample of the composition prepared according to Example 1 was subjected accelerated shelf stability in a commercial laboratory at 45° C. The Peroxide content was measured according to the method (AOCS CD 8B-90) as specified by the Association of American Oil Chemists (AOCS). A sensory expert conducted sensory analysis. The peroxide content was within the specification and the sample continued exhibiting the sweet vanilla flavor without any unpleasant flavor.

Example 12: Accelerated Shelf Stability

[00108] Samples of Exemplary Energy Bars prepared according Example 8 were subjected accelerated shelf stability in a commercial laboratory at 45° C. The Peroxide content was measured according to the method (AOCS CD 8B-90) as specified by the Association of American Oil Chemists (AOCS). A sensory expert conducted sensory analysis. The peroxide content was within the specification and the sample continued exhibiting the sweet vanilla flavor without any unpleasant flavor.

Example 13: Test Composition 4079

[00109] Algal docosahexaenoic acid (Algal DHA), 43 lbs (Life's DHA P35-0100 from (DSM Nutrition, NJ, USA) was allowed come to room temperature. Medium chain triglycerides 141.9 lbs (Jedwards International, MA, USA) also at room temperature. MCT oil and Algal DHA oil were mixed in a mixer, at room temperature, for 10 minutes. Whey protein, (Milk Specialties, MN, USA) 240.8 lbs and 4.3 lbs of Vanilla Extract Powder (Lochhead Manufacturing Company, MO, USA) were mixed together for 10 minutes in a separate mixer. MCT-DHA Oil was added to Whey Protein-Vanilla Extract powder over a period of 45 minutes in a slowly rotating mixer. Upon completion of the mixing, contents were spun were mixed together with constant stirring for 20 minutes till the mixture is stirred until the protein is uniformly dispersed in the oil by monitoring the homogenization. The formulation was used for evaluation as per fatty acid analysis studies.

Example 14: Test Composition 4122

[00110] A 33 labs production batch was prepared according to the Example 13 except for changes in the time period of mixing process. MCT Oil (11 lbs) and DHA Oil (3.3 lbs) were mixed for twenty minutes. The whey protein (18.2 lbs) and Vanilla Extract (0.400 lbs) were mixed for twenty minutes. The final mixing, for twenty minutes, of Whey Protein-Vanilla Extract, by gradual addition of the MCT-DHA homogenized oil provided a dispersion. Room temperature was maintained during the mixing process. The mixture was stirred until the ingredients are uniformly mixed with one another. The formulation was used for evaluation as per fatty acid analysis studies.

Example 15: Test Composition 4123

[00111] The production batch 4123 was carried according example 13 and the fatty acid profile was analyzed.

[00112] The results of fatty acid analysis of three batches 4079, 4122 and 4123 are shown in Figures 13, 14 and 15.

[00113] These examples, 13, 14, and 15, illustrate that it is important to add MCT-DHA fatty acid mixtures gradually over a period of time for two reasons. First, if the addition is either too rapid or too slow, the fatty acid distribution is not uniform and laboratory analysis show batch to batch variation. Second, uneven distribution of fatty acid around protein results in unsatisfactory polyunsaturated fatty acid stability and odor preservation. The importance of the method of

manufacturing is further illustrated in example 16, composition 4009 and example 17, composition 4014 described below.

Example 16: Test Composition 4114

[00114] The difficulty of manufacturing a stable formulation is illustrated by this example, where changes to the process resulted in a fatty acid profile that is different from the fatty acid profiles from Examples 13, 14 and 15. Algal Docosahexaenoic Acid, 3g was taken out from the freezer and Medium chain triglycerides 10g were removed from the freezer. Without bringing the ingredients to room temperature, MCT oil and Algal DHA oil were mixed in a mixer for 5 minutes. Room temperature is maintained during the mixing process. Whey protein, 17g and 0.35g of Vanilla Extract Powder were mixed together for 5 minutes in a separate mixer. MCT-DHA Oil and Whey Protein-Vanilla Extract powder were mixed together with constant stirring for 10 minutes monitoring the homogenization till the mixture is stirred until the protein is uniformly dispersed in the oil. The formulation was used for evaluation of the fatty acid profile similar to those of example 13, 14 and 15. The results are shown in figures 16, 17 and 18.

Example 17: Test Composition 4009

[00115] Following the procedures in Examples 13, 14, 15 and 16 test composition 4009 was manufactured, except the mixing was conducted for two hours.

Example 18: Exemplary Composition

[00116] The following exemplary formulation according to Table 3 is prepared, as per the process disclosed below:

Table 3

Ingredient	Quantity (mg)
Eicosapentaenoic acid	2.0
Docosahexaenoic Acid	1.32
MCT	20
Vitamin D3	0.0175
Hemp Protein	5

[00117] The process for preparing the composition of Example 18 was similar to those described for Examples 1, 2 and 3. Eicosapentaenoic acid, 2 grams, is mixed with 20 grams of

medium chain triglycerides in a suitable container. Docosahexaenoic acid, 1.32, g, of was added with the EPA-MCT fatty acid mixtures. The temperature is maintained at ≤ about 10 °C during the mixing process. Whey protein, 25 grams and 0.0175 g of vitamin D3, are added to the homogenized solution. The mixture is stirred until the protein is uniformly dispersed in the oil. The dispersion is stored in cool place maintained at ≤ about 10 °C.

Examples 19-23: Health Food Compositions

[00118] The method of preparing a standard grain free nutraceutical compositions is outlined above, the composition of MCFA, PUFA, protein content and other dietary agents fortified may vary as exemplified (examples 18-22) below in Table 4.

Table 4

Ingredient	Ex. 19	Ex. 20	Ex. 21	Ex. 22	Ex. 23
Vitamin D	1000 IU	1000 IU	2000 IU	1000 IU	5000 IU
Docosahexaenoic Acid,	2	0	1.32	2	2
Eicosapentaenoic Acid	0	2	2.1	0	0
MCFAs	15	20	20	20	5
Almond flour	15	0	0	0	0
Soy Protein	0	20	0	0	0
Rice Protein	0	0	0	0	5
Whey Protein	0	0	20	0	0
Melatonin	0	0	0	0.5	0
Hemp Protein	0	0	0	20	5
L-Carntine	1	1	0	0	1

PHARMACOLOGICAL STUDIES

EXAMPLE 24: Lipid Panel, Interleukin-6, TNF, Vitamin D and Ketone Bodies Studies

[00119] **Primary Objectives:** A study to evaluate the effect of a grain free composition on the lipid panel, serum concentrations of IL-6, TNF, vitamin D and Ketone bodies in healthy volunteers by exploring changes in the lipid a, serum concentration of IL-6, TNF, and Ketone bodies in healthy volunteers.

[00120] **Study Design:** An open label study of the effects of the disclosed compositions on the lipid panel and on the plasma concentration of ketone bodies, Interleukin-6, Vitamin D_3 and Tumor Necrosis Factor.

[00121] The study was divided into two periods: a) a baseline period of three days and b) a treatment period of seven days, with the disclosed compositions. During the baseline period, the subjects underwent a baseline characterization phase where the baseline lipid panel, IL-6. TNF and ketone bodies were determined. The during the treatment period, the subjects were administered a grain free composition prepared as disclosed Example 4 for seven days. Upon completion of treatment period, lipid panel, serum ketone bodies, 25-hydroxy vitamin D, IL-6 and TNF values were determined on day 8.

Study Arms and Medications

[00122] **Treatment Arm** (Test Composition Arm): Example 18 consisting of 20 grams of MCT, 2 grams of EPA, 1.32 grams of DHA, 2000 IU of Vitamin D_3, and 5 grams of Hemp Protein.

[00123] If a test subject had taken ω-3 Polyunsaturated Fatty Acids (PUFA), MUFA supplements within one week of being included in the trial, he/she must undergo a three days of washout period to remove the supplement from their system.

[00124] **Investigational agents**: The active ingredients in the investigational product- are Medium Chain Triglycerides, Eicosapentaenoic Acid (EPA) and Docosahexaenoic Acid (DHA). All three active agents have been extensively studied in humans.

[00125] **MCTs:** Medium chain triglycerides (MCTs) are a class of lipids in which three saturated fats are bound to a glycerol backbone. MCTs are distinguished from other triglycerides in that each fat molecule is between six and twelve carbons in length. The specific composition of MCTs used in Example 4 are below:

- Caproic Acid Triglyceride ($C_{24}H_{44}O_6$) with C_6 hydrocarbon chains; Not more than 6%;
- Caprylic Acid Triglyceride ($C_{27}H_{50}O_6$) with C_8 hydrocarbon chains: Between 55% to 85% of the composition. Generic name-Caprylic triglyceride (Other names: Tricaprylin; Octanoin, tri-; Caprylic acid triglyceride; Caprylin; Glycerol trioctanoate; Glyceryl trioctanoate; Octanoic acid triglyceride), Chemical name: 2,3-

bis(octanoyloxy)propyl octanoate, Molecular formula: $C_{27}H_{50}O_6$, Molecular weight: 470.68 and Melting point: 8-10°C;

- Capric Acid Triglyceride ($C_{29}H_{54}O_6$) with C_{10} hydrocarbon chains: Between 15% to 40% of the composition. Generic name: Capric Triglyceride, Chemical Name- 2,3 bis(decanoyloxy)propyl decanoate, Molecular Formula- $C_{29}H_{54}O_6$, Molecular Weight-425.7 and Melting point: 12-14°C;
- Lauric Acid Triglyceride ($C_{32}H_{60}O_6$) with C_{12} hydrocarbon chains: Not more than 4%;
- Eicosapentaenoic acid (EPA): EPA is a long chain, 20 carbon, omega-3 polyunsaturated fatty acid (PUFA) found in the diet such as in fish oil. Upon consumption, it undergoes demethylation of ethyl-EPA to EPA. Enterocyte uptake is followed by re-esterification, chylomicron formation and secretion into the lymph before systemic distribution. Molecular formula: $C_{20}H_{30}O_2$, Molar Weight: 302.45 g/mol and Melting point: Oil with a melting point of 54°C;
- Docosahexaenoic Acid (DHA): SHA is long chain 22-carbon atom omega -3-polyunsaturated fatty acid (PUFA) found in fish oil. Molecular formula: $C_{22}H_{32}O_2$, Molar Weight: 328.488 g/mol, Melting point: Oil with a melting point of -44°C.

[00126] **Pharmacology:** Docosahexaenoic acid (DHA) has been extensively studied in humans and animals in combination with EPA. DHA is recognized as being essential for normal development of the brain and retina during fetal development and the first two years of life. The European Food Safety Authority (EFSA) stated that the consumption of n-DHA has not been associated with adverse effects in healthy children or adults at observed intake levels. Therefore, supplemental combined intakes of EPA and DHA at doses of up to 5 g/day, and supplemental intakes of EPA alone up to 1.8 g/day, do not raise safety concerns for adults. Supplemental intakes of DHA alone up to about 1 g/day do not raise safety concerns for the general population.

[00127] **Statistical Methods:** SAS software was used for analysis performed by using the analysis of variance. The results were processed using repeated measures analysis of variance and were considered significant when $P < .05$

[00128] **Subject Population(s) for Analysis:** The all subjects were used for all study analyses. For the purposes of this study, the all-randomized population is defined as any subject randomized into the study, regardless of whether they receive study drug.

Results

- Figure 6 illustrates the change in serum triglyceride concentration from baseline to end of study.
- Figure 7 illustrates the change in serum VLDL concentration from baseline to end of study.
- Figure 8 illustrates the change in serum HDL concentration from baseline to end of study.
- Figure 9 illustrates the change in the mean serum concentrations of β-hydroxy butyrate during the study.
- Figure 10 illustrates the change in the mean serum concentrations of IL-6 during the study.
- Figure 11 illustrates the change in the mean serum concentrations of TNF during the study.
- Figure 12 illustrates the changes in serum concentration of 25-hydroxy vitamin D during the study.

[00129] The abbreviations used herein have their conventional meaning within the chemical and biological arts. The disclosures of each and every patent, patent application, and publication cited herein are expressly incorporated herein by reference in their entirety into this disclosure. In the case of any inconsistencies, the present disclosure, including any definitions therein will prevail. Illustrative embodiments of this disclosure are discussed and reference has been made to possible variations within the scope of this disclosure. These and other variations and modifications in the disclosure will be apparent to those skilled in the art without departing from the scope of the disclosure, and it should be understood that this disclosure and the claims shown below are not limited to the illustrative embodiments set forth herein.

Claims:

1. A composition comprising at least one medium chain fatty acid (MCFA), at least one polyunsaturated fatty acid (PUFA), at least one protein, and optionally a dietary carrier, or a preservative agent;

   wherein the polyunsaturated fatty acid (PUFA) in the composition has improved stability.

2. The composition claim 1, wherein the medium chain fatty acid comprises from about 35% to about 90% by weight of total fat in the composition, and the polyunsaturated fatty acid (PUFA) comprises from about 10% to about 65% of by weight of total fat in the composition, or acceptable salts thereof;

   wherein the protein is at least about 50% by weight of the composition; and

   optionally, further comprising one or more of dietary carriers, preservative agents or adjuvants.

3. The composition of claim 1 or 2, wherein the medium chain fatty acid is from a whole food such as coconut flour, palm drupe flour, or camphor drupe flour.

4. The composition of any of claims 1 - 3, wherein the polyunsaturated fatty acid (PUFA) is ethyl eicosapentaenoic acid (Ethyl EPA), linolenic acid (LA), arachidonic acid (AA), docosahexaenoic acid (DHA), alpha-linolenic acid (ALA), stearadonic acid (STA), eicosatrienoic acid (ETA), docosapentaenoic acid (DPA) or a nutraceutically acceptable salt or derivative thereof.

5. The composition of any of claims 1 - 4, wherein the polyunsaturated fatty acid (PUFA) is eicosapentaenoic acid (EPA) and composition contains not more than about 10%, by weight, docosahexaenoic acid.

6. The composition of any of claims 1 - 4, wherein the polyunsaturated fatty acid (PUFA) is docosahexaenoic acid and the composition contains not more than about 10%, by weight, eicosapentaenoic acid (EPA).

7. The composition of any of claims 1 - 4, wherein the polyunsaturated fatty acid (PUFA) is docosapentaenoic acid (DPA) and the composition contains less than about 10%, combined weight of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).

8. The composition of any preceding claim, wherein the composition comprises at least one adjuvant, preservative, antioxidant, thickening agent, chelating agent, antifungal agent, antibacterial agent, isotonic agent, flavoring agent, sweetening agent, anti-foaming agent, colorant, diluent, moistening agent, parietal cell activator, or any combination of thereof.

9. The composition of any preceding claim, wherein the medium chain fatty acid (MCFA), is caprylic acid.

10. The composition of claim 10, wherein the medium chain fatty acid (MCFA) comprises at least about 90%, by weight, of caprylic acid.

11. The composition of any of claims 1-9, wherein the medium chain fatty acid (MCFA), has from about 35% to about 90% by weight of capric acid.

12. The composition of claim 11, wherein the medium chain fatty acid (MCFA) comprises at least about 90%, by weight, of capric acid.

13. The composition of any preceding claim, wherein the composition shows improved heat stability.

14. The composition of any preceding claim, wherein the composition shows improved light stability.

15. The composition of any preceding claim, further comprising an optional dietary agent such as, for example, a vitamin, an amino acid, a hormone, an element, a nutrient, and the like.

16. A nutraceutical composition of any preceding claim, comprising from about 35% to about 90% of medium chain fatty acids, by weight; from about 10% to about 65% of at least one polyunsaturated fatty acid (PUFA) by weight; at least one protein; and optionally a dietary carrier or a preservative agent; or acceptable salts or derivatives thereof;

wherein the protein is at least about 50% by weight of the composition.

17. The composition of any preceding claim, wherein the dispersion is suitable for admixing with a food product such as a breakfast cereal snacks, drink, an ice cream, a meal, or a dessert.

18. A method of increasing serum ketone bodies by administering a composition comprising at least one medium chain fatty acid, at least one polyunsaturated fatty acid (PUFA) and at least one protein, wherein the composition stabilizes the polyunsaturated fatty acid in the composition to light or heat..

19. The composition of any preceding claim wherein the composition is solid-in-oil dispersion.

20. The composition of any preceding claim wherein the composition is grain-free.

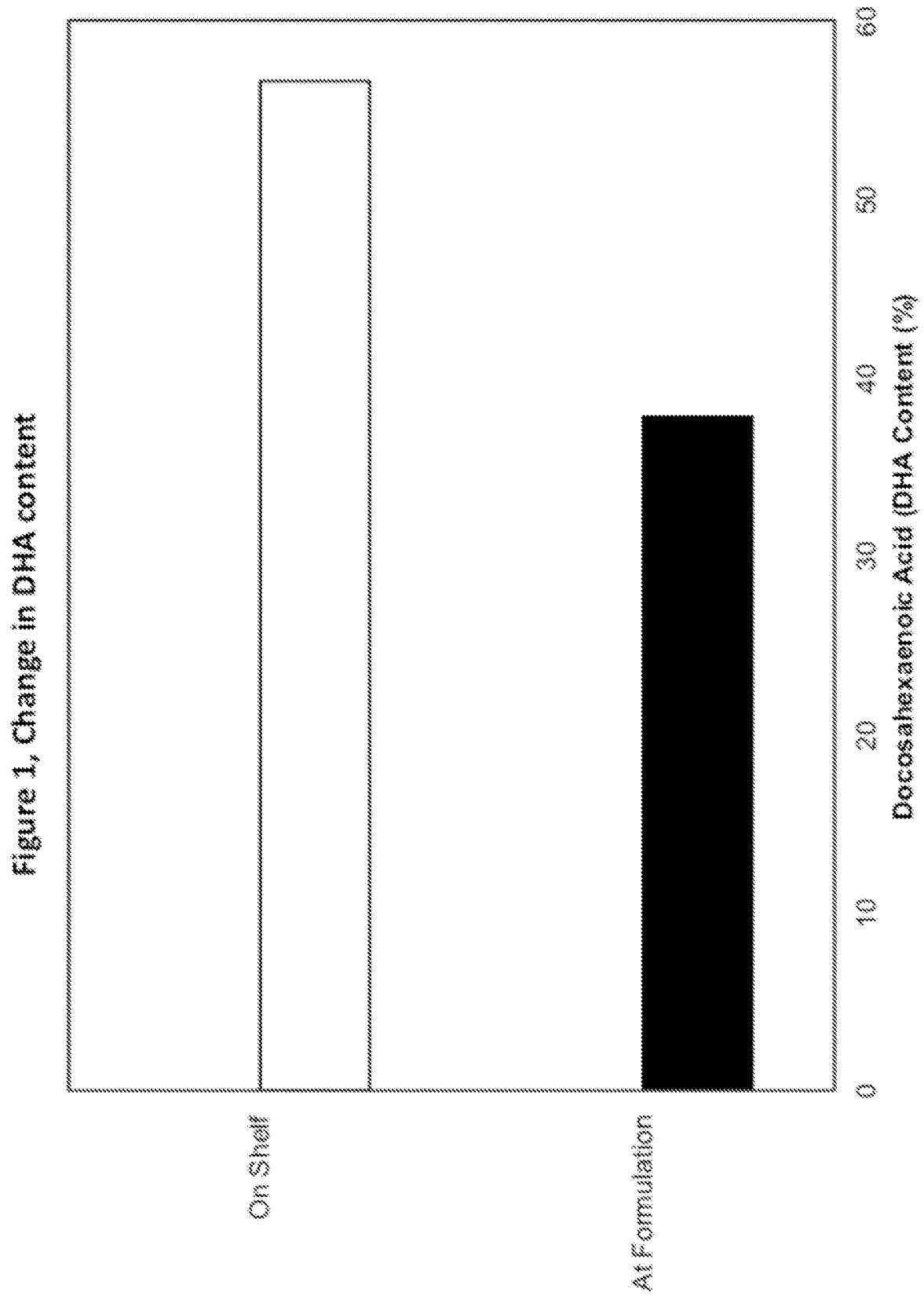


Figure 1, Change in DHA content
Docosahexaenoic Acid (DHA Content (%)
0
10
20
30
40
50
60
On Shelf
At Formulation

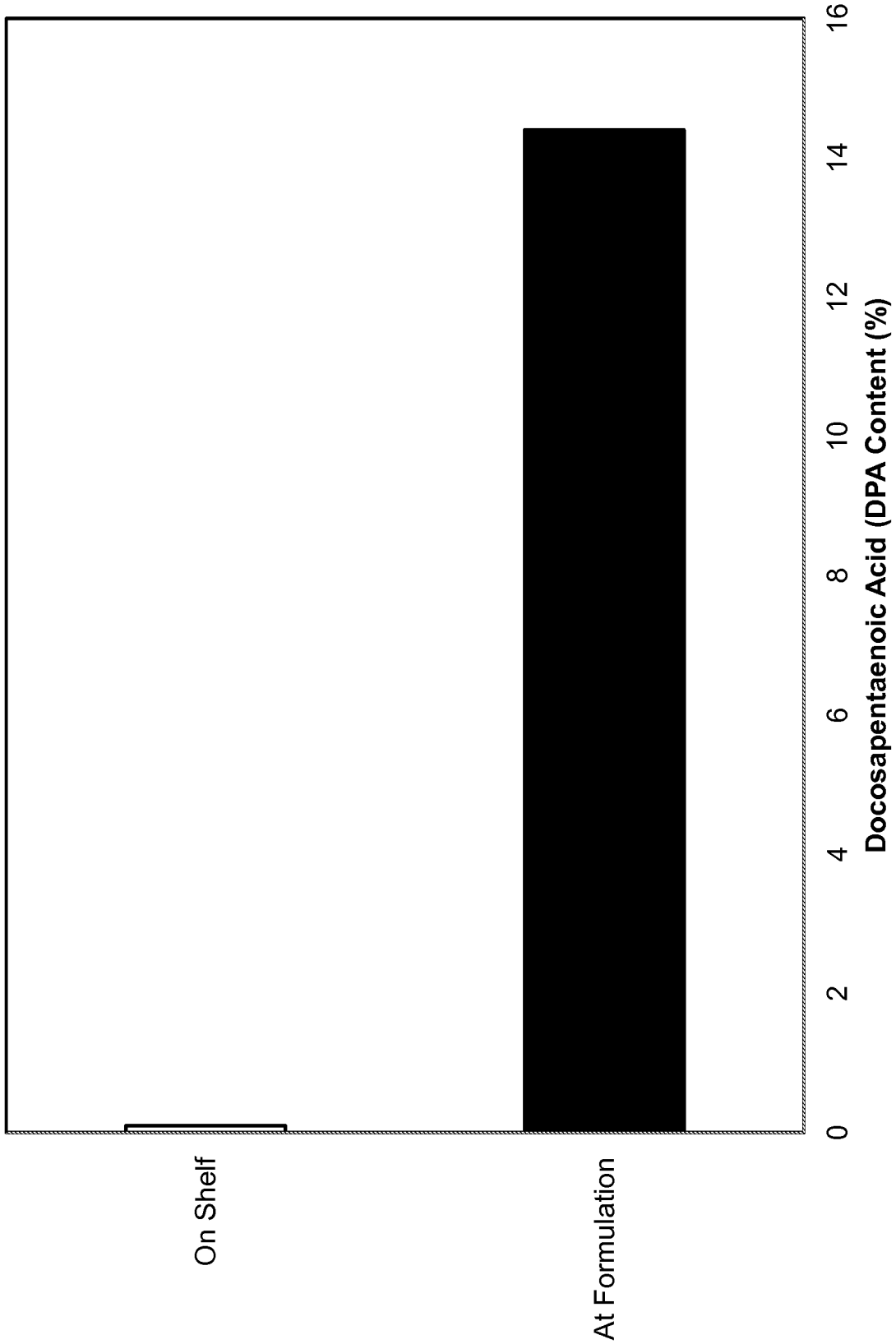


Figure 2, Change in DPA content
Docosapentaenoic Acid (DPA Content (%)
0
2
4
6
8
10
12
14
16
On Shelf
At Formulation

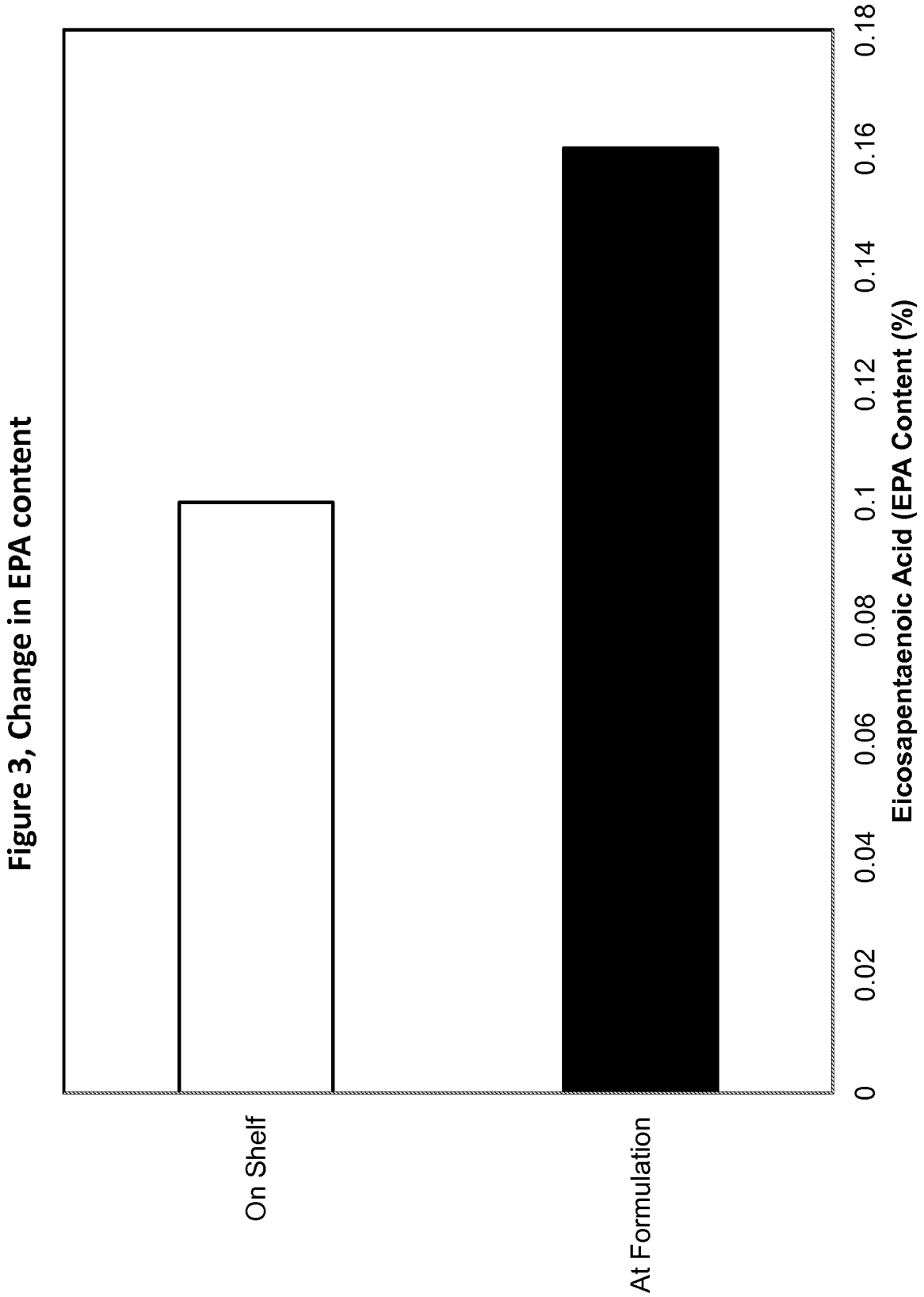


Figure 3, Change in EPA content
Eicosapentaenoic Acid (EPA Content (%)
0
0.02
0.04
0.06
0.08
0.1
0.12
0.14
0.16
0.18
On Shelf
At Formulation

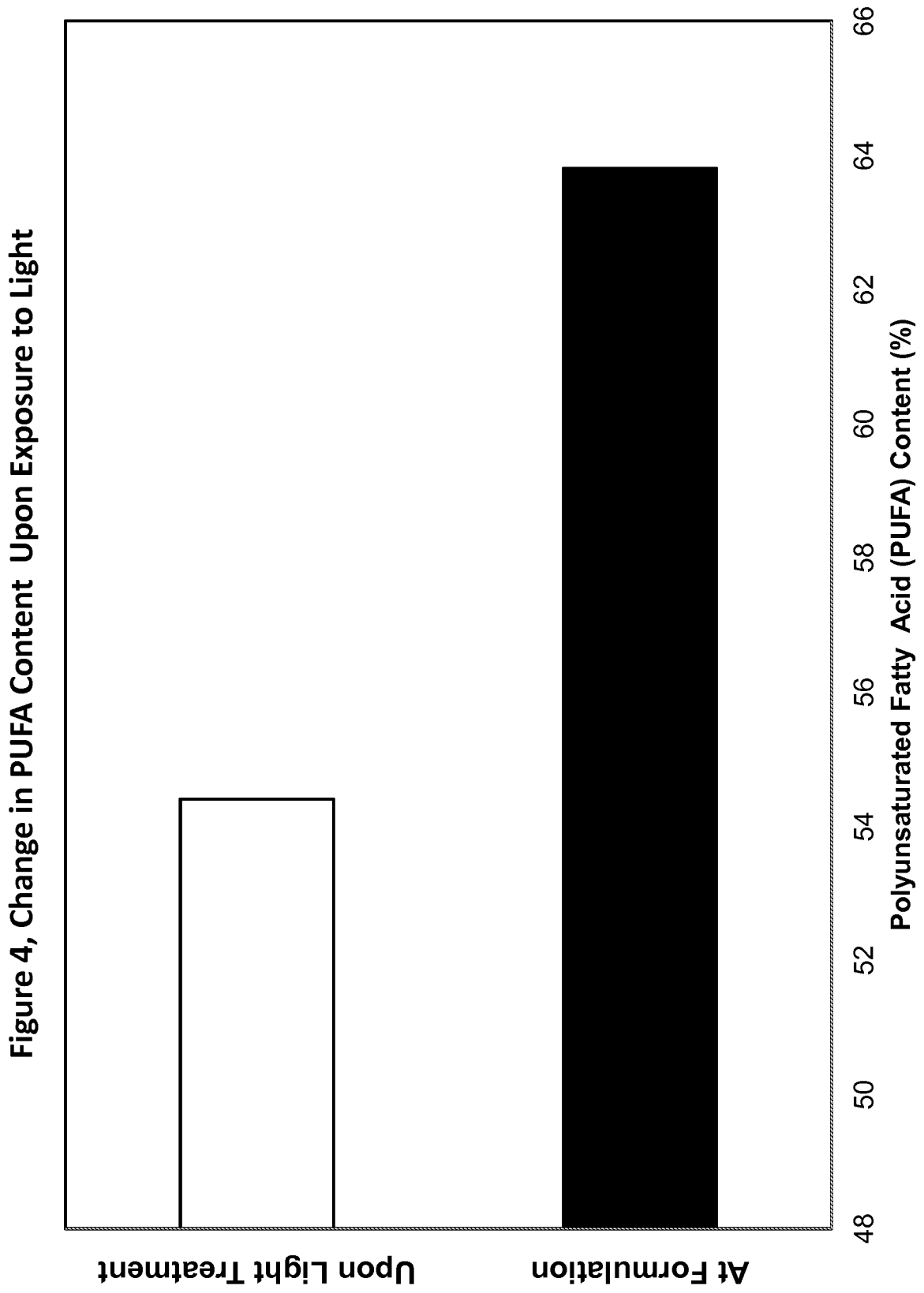


Figure 4, Change in PUFA Content Upon Exposure to Light
Polyunsaturated Fatty Acid (PUFA) Content (%)
48
50
52
54
56
58
60
62
64
66
At Formulation
Upon Light Treatment

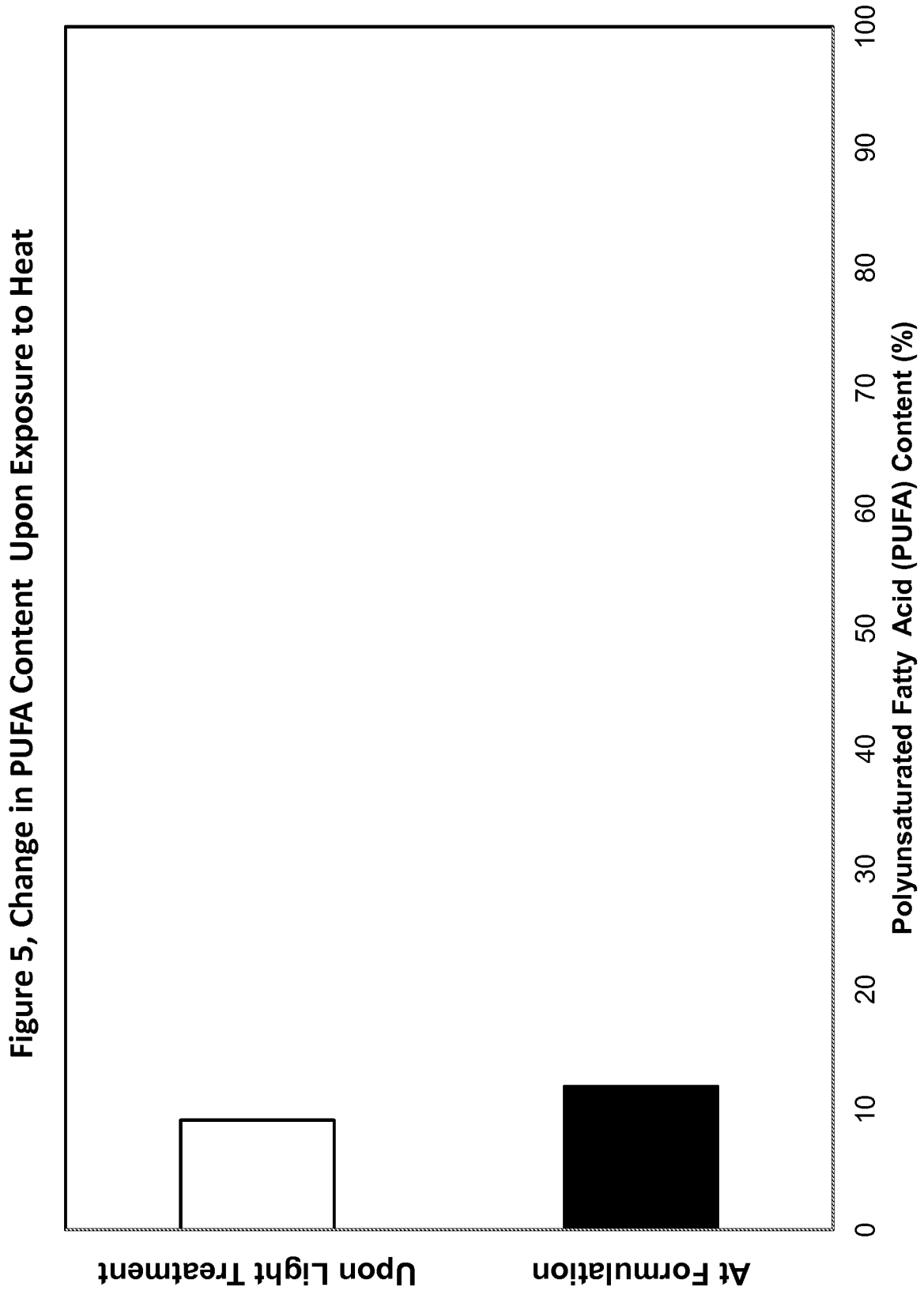


Figure 5, Change in PUFA Content Upon Exposure to Heat
Polyunsaturated Fatty Acid (PUFA) Content (%)
0
10
20
30
40
50
60
70
80
90
100
At Formulation
Upon Light Treatment

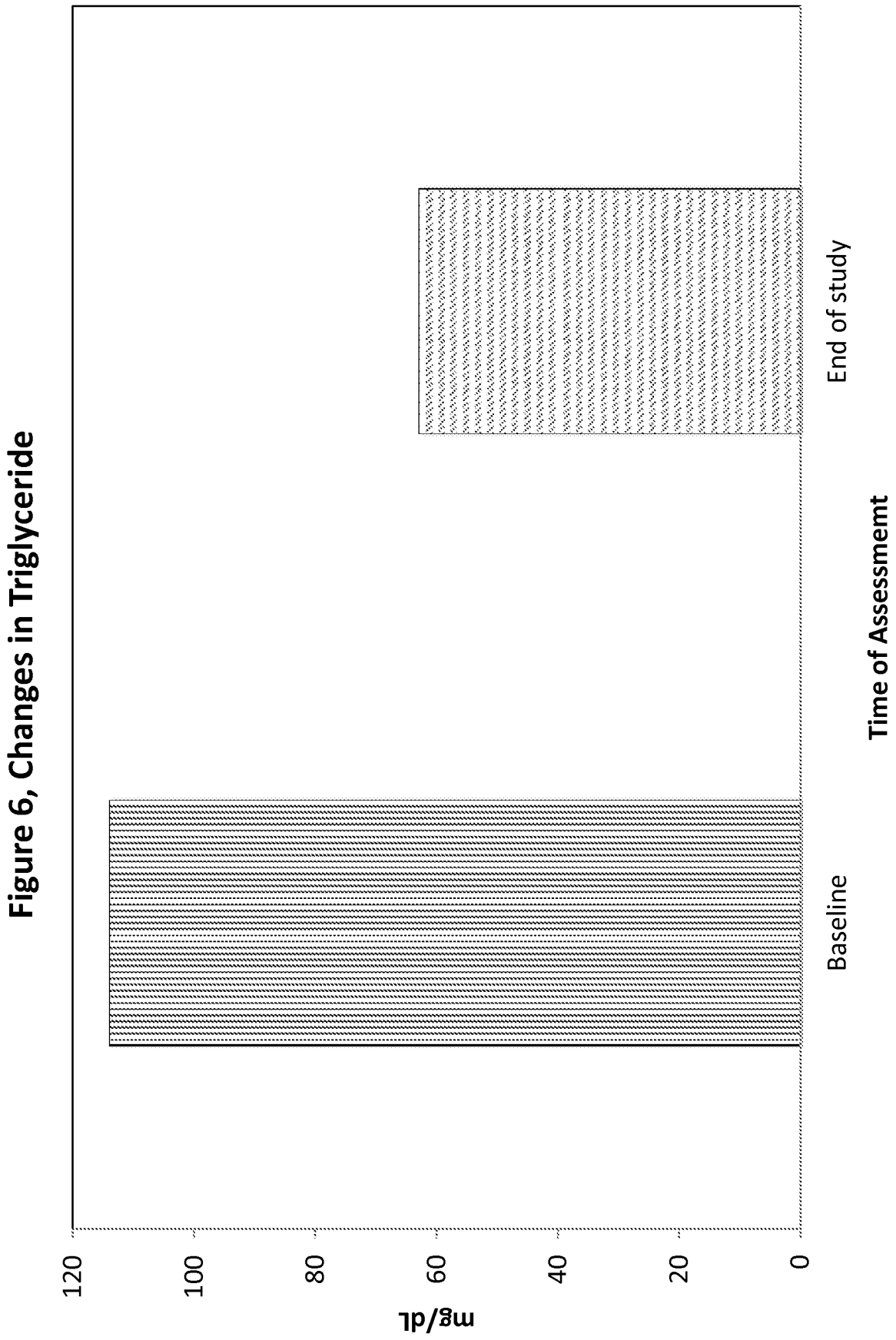


Figure 6, Changes in Triglyceride
mg/dL
120
100
80
60
40
20
0
Baseline
End of study
Time of Assessmemt

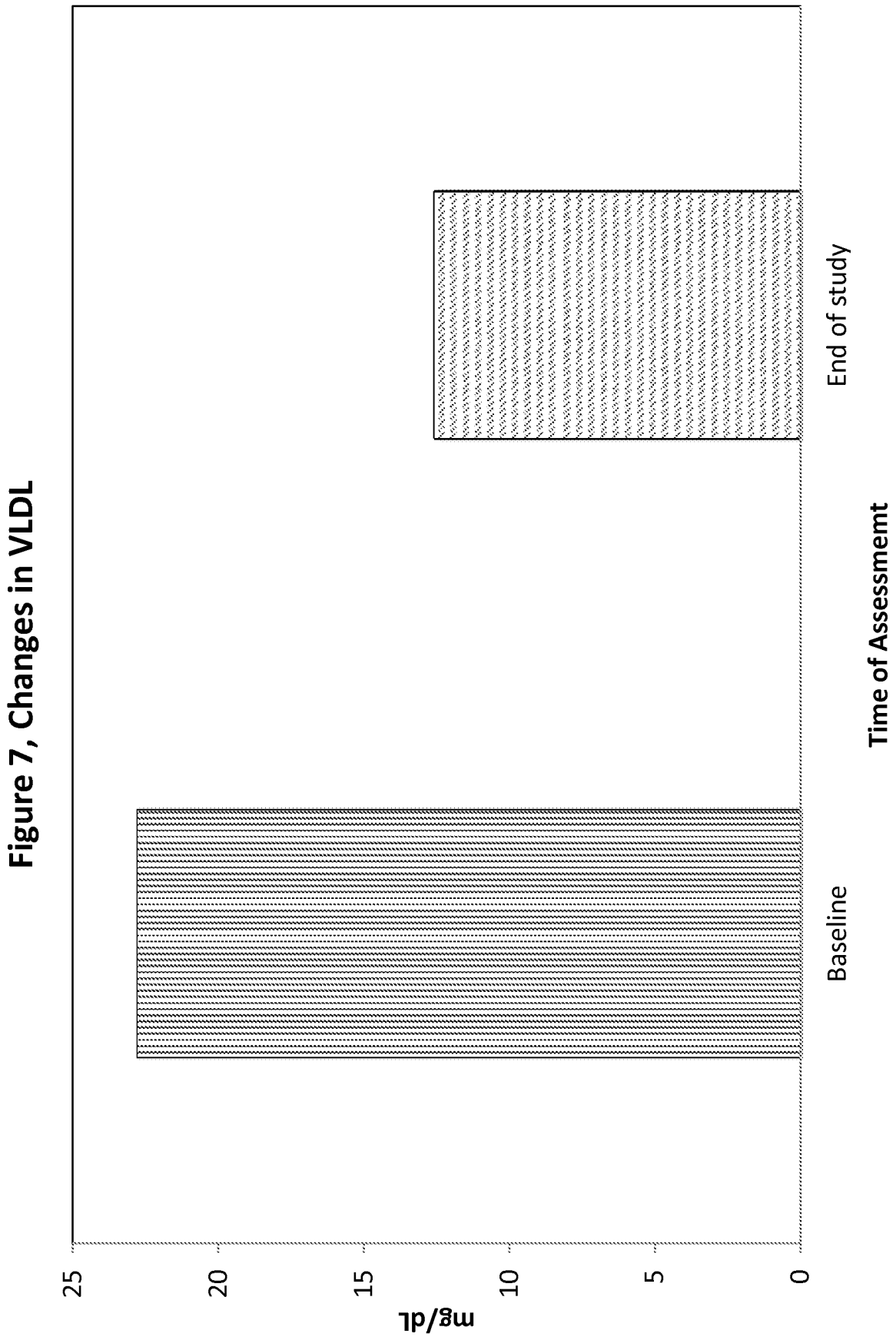


Figure 7, Changes in VLDL
mg/dL
25
20
15
10
5
0
Baseline
End of study
Time of Assessmemt

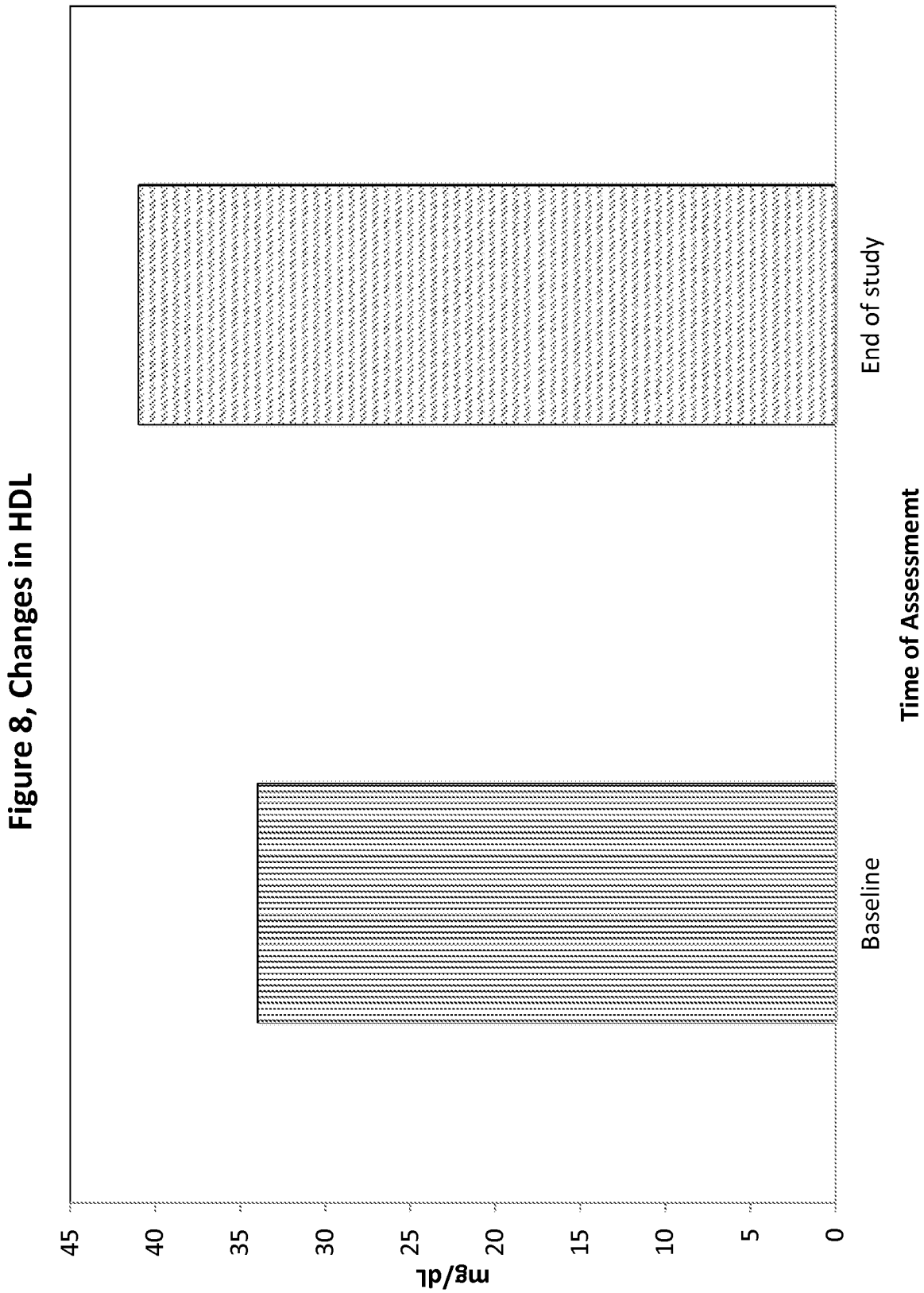


Figure 8, Changes in HDL
mg/dL
45
40
35
30
25
20
15
10
5
0
Baseline
End of study
Time of Assessmemt

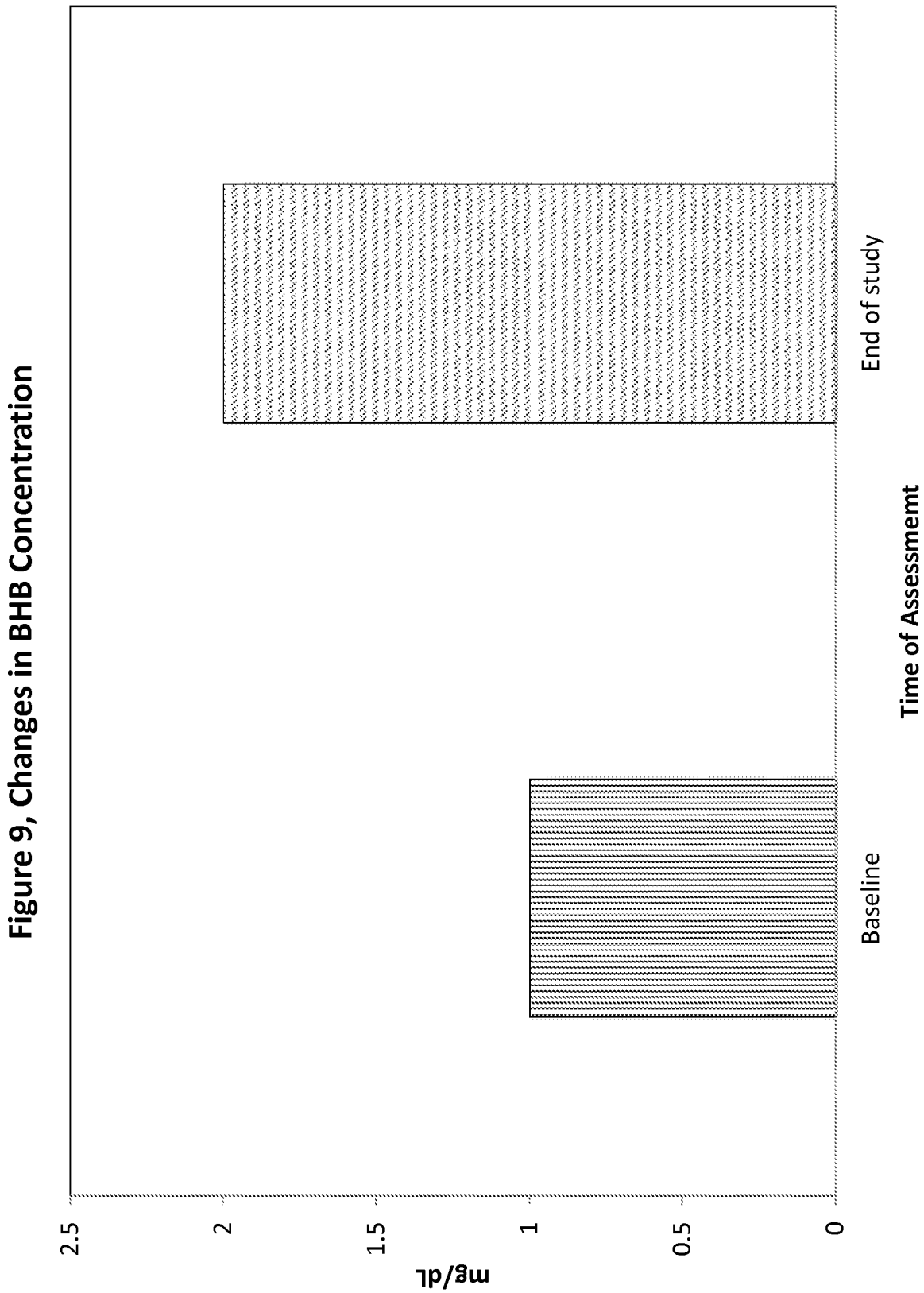
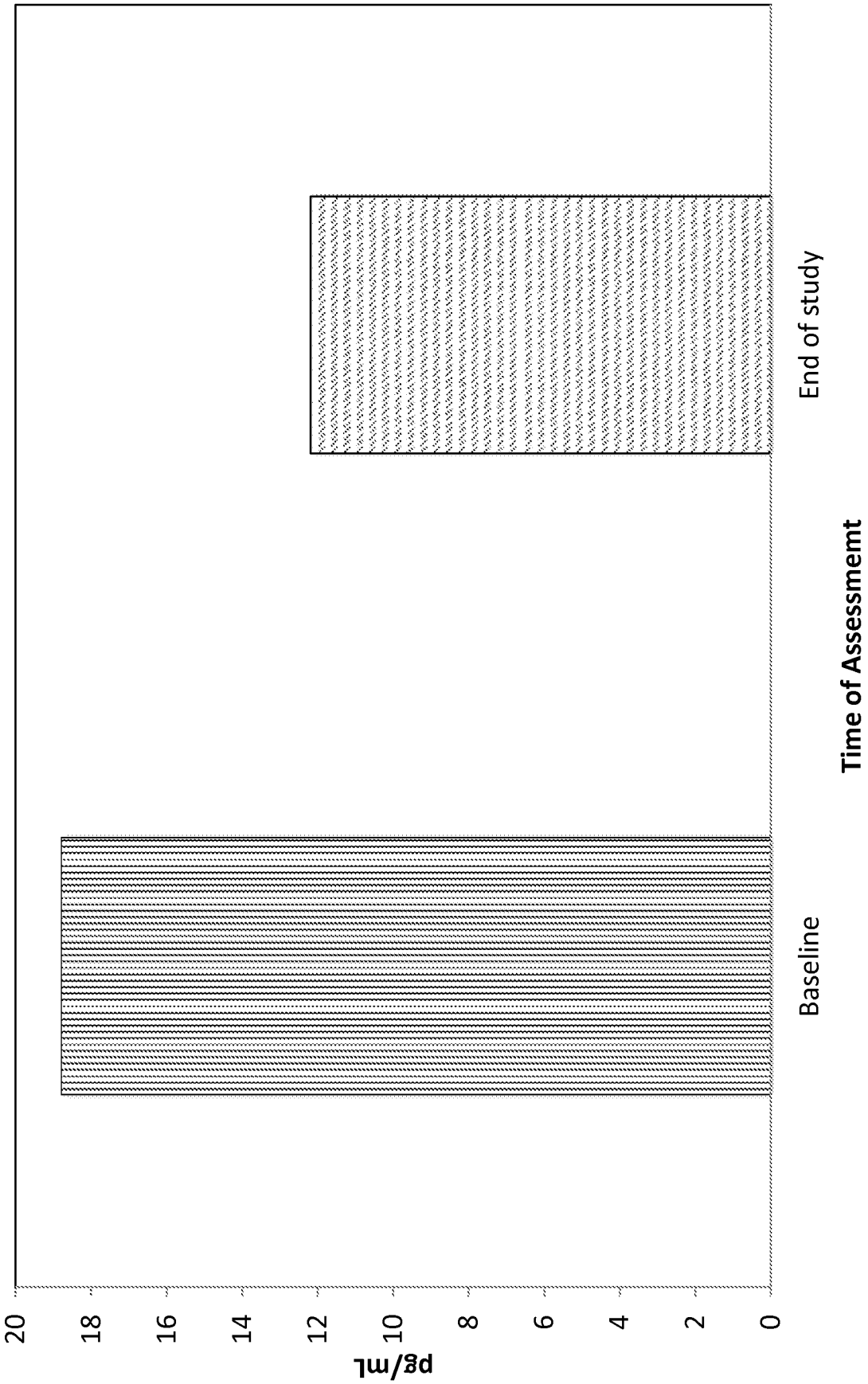


Figure 9, Changes in BHB Concentration
mg/dL
2.5
2
1.5
1
0.5
0
Baseline
End of study
Time of Assessmemt

Figure 10, Changes in IL-6



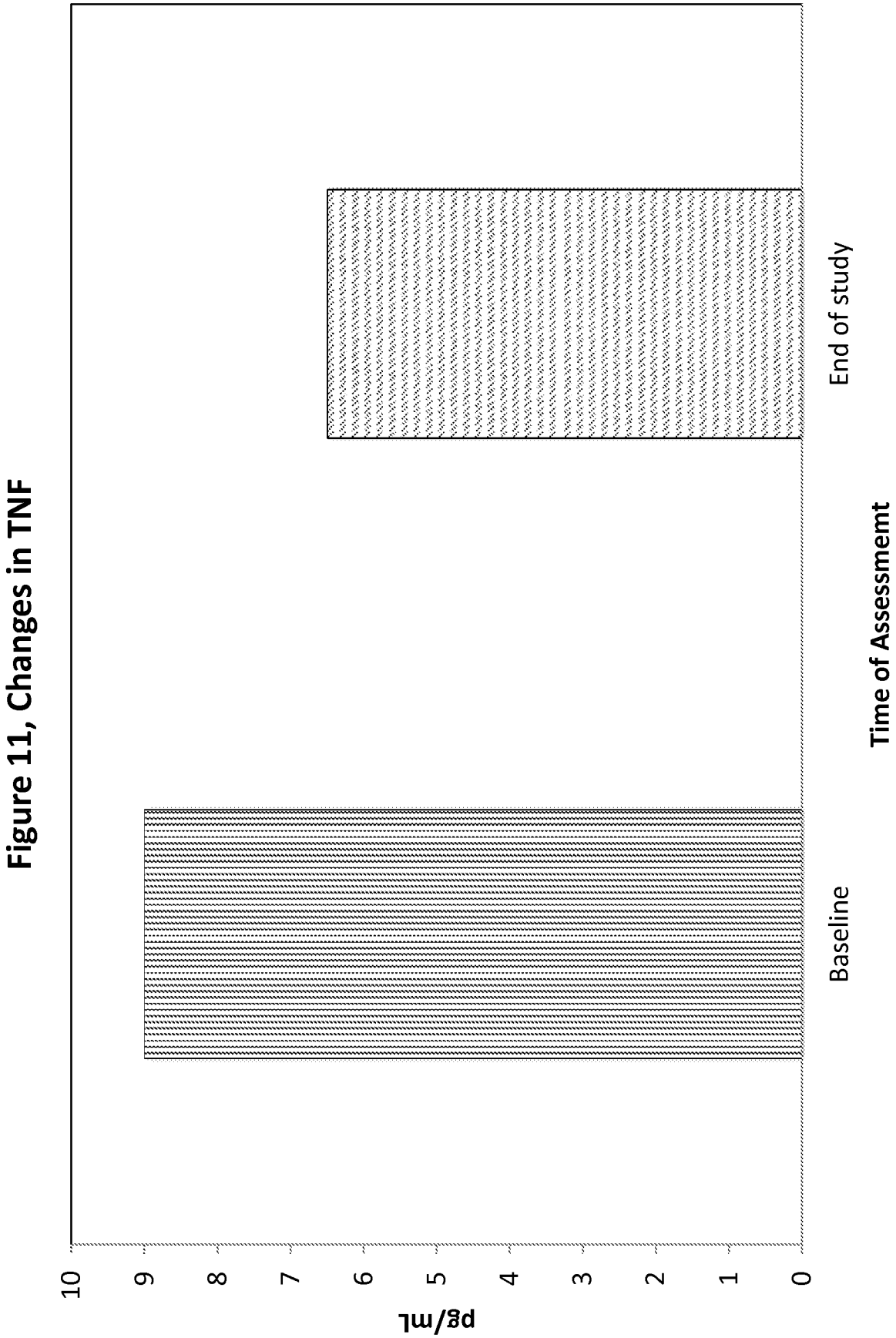


Figure 11, Changes in TNF
pg/mL
10
9
8
7
6
5
4
3
2
1
0
Baseline
End of study
Time of Assessmemt

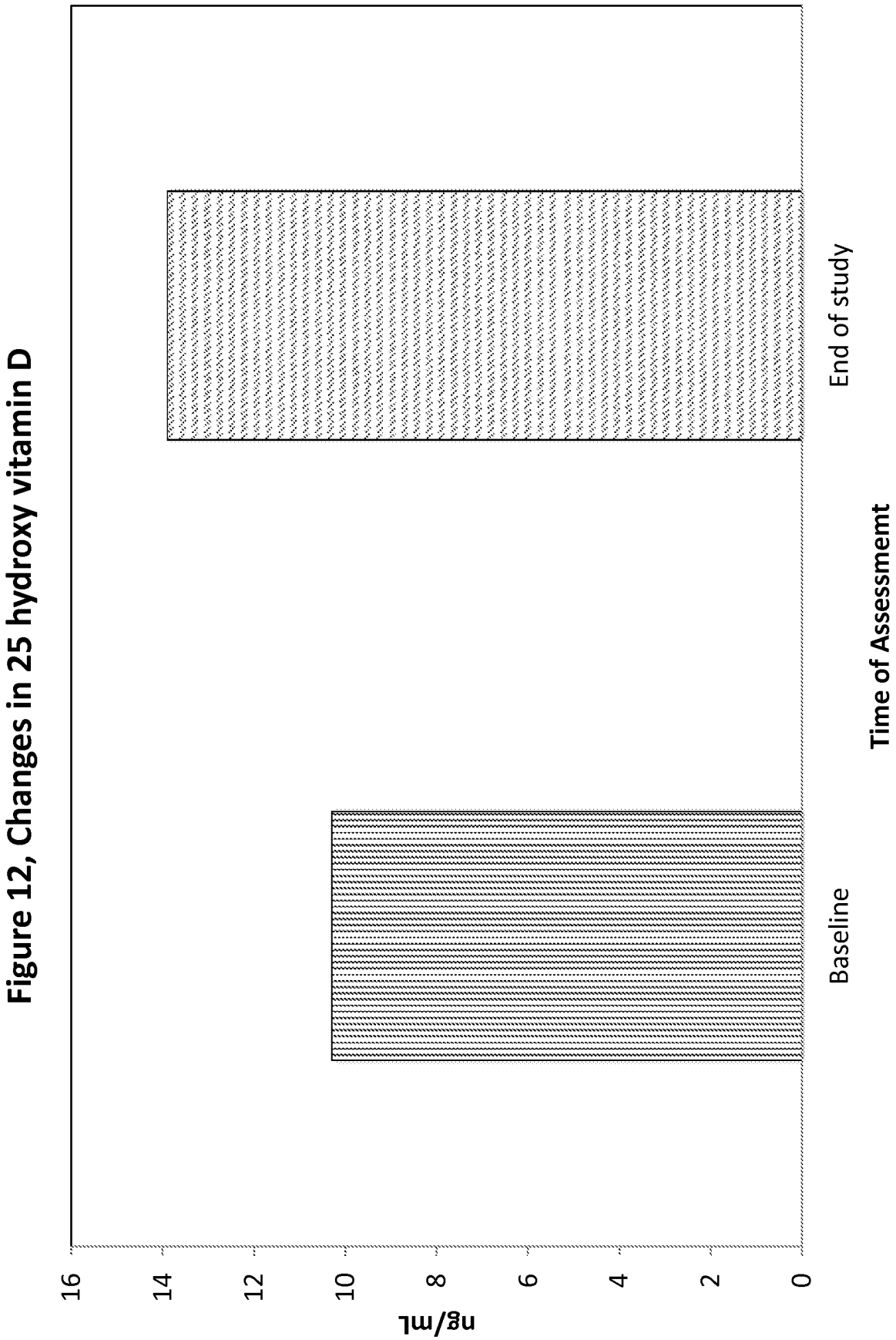


Figure 12, Changes in 25 hydroxy vitamin D
ng/mL
16
14
12
10
8
6
4
2
0
Baseline
End of study
Time of Assessmemt

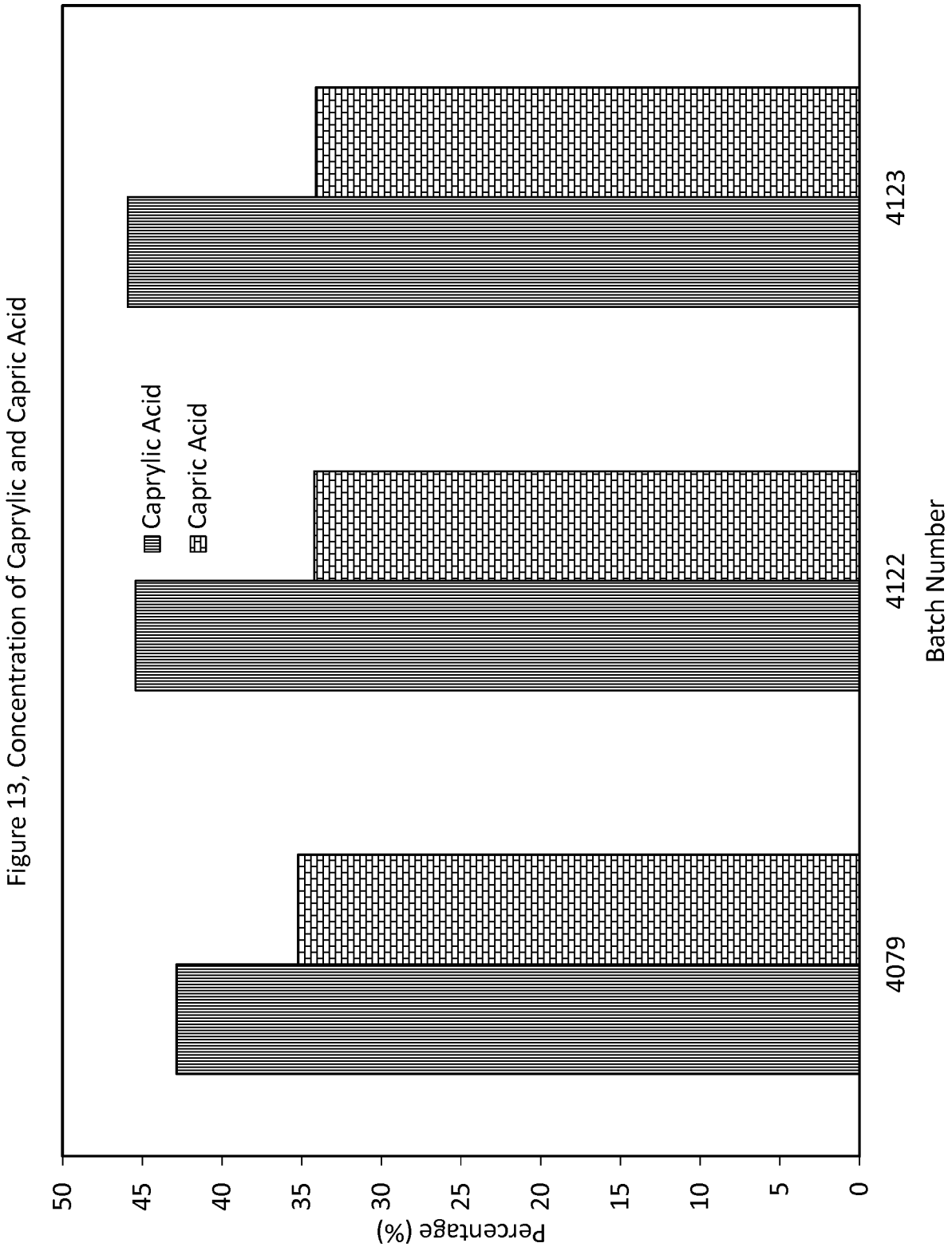


Figure 13, Concentration of Caprylic and Capric Acid

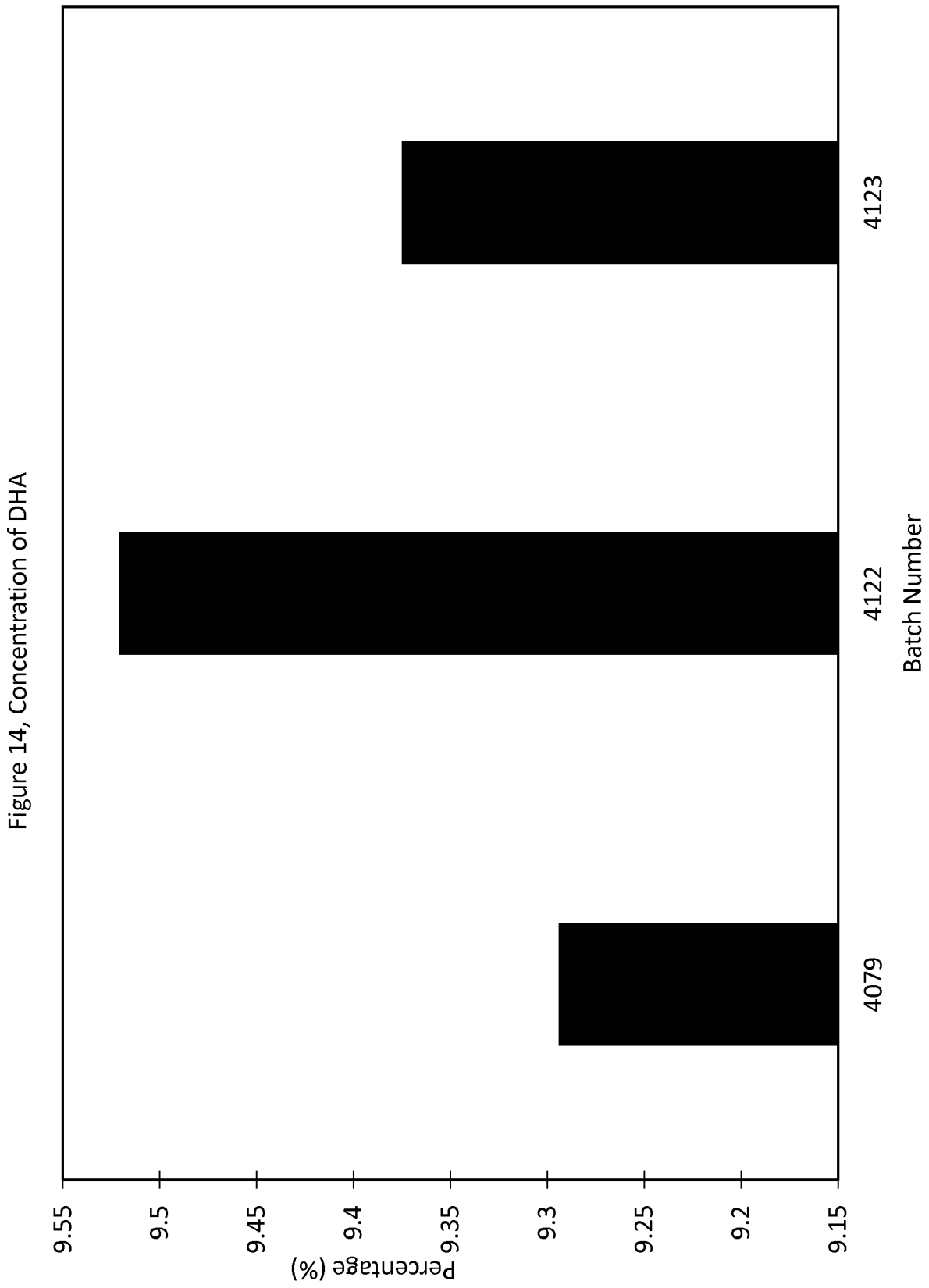


Figure 14, Concentration of DHA

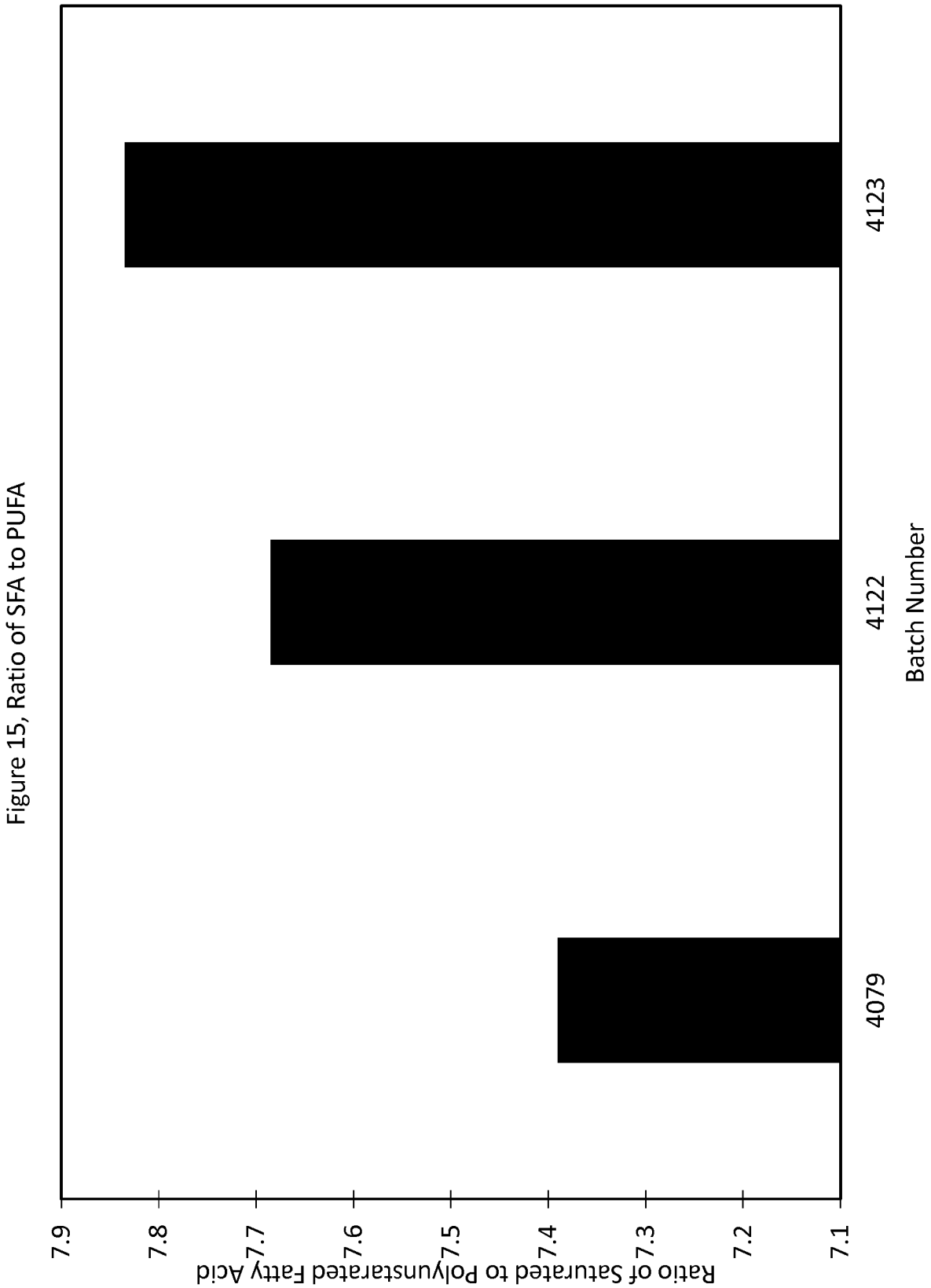


Figure 15, Ratio of SFA to PUFA
Ratio of Saturated to Polyunstarated Fatty Acid
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
4079
4122
4123
Batch Number

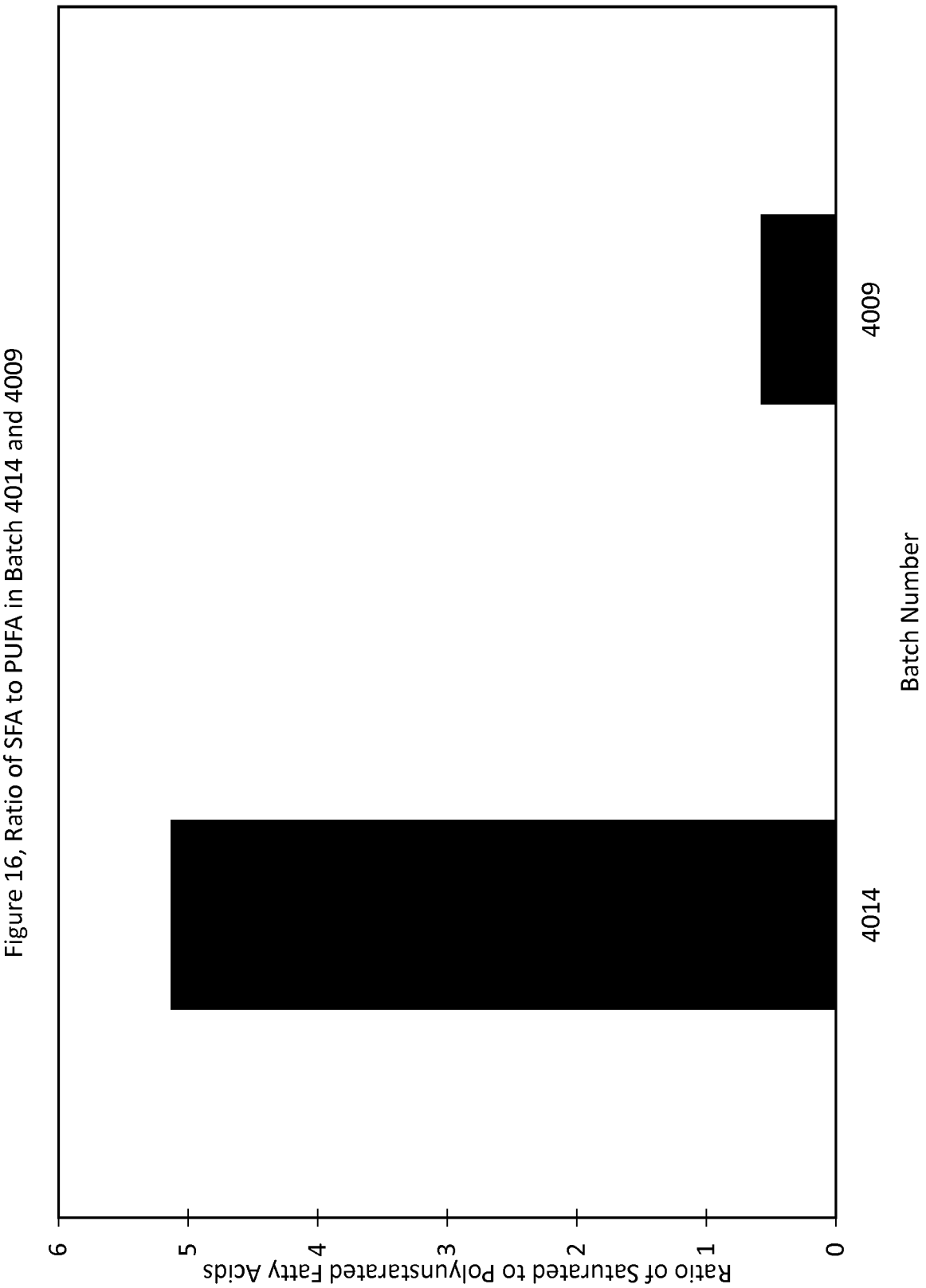


Figure 16, Ratio of SFA to PUFA in Batch 4014 and 4009

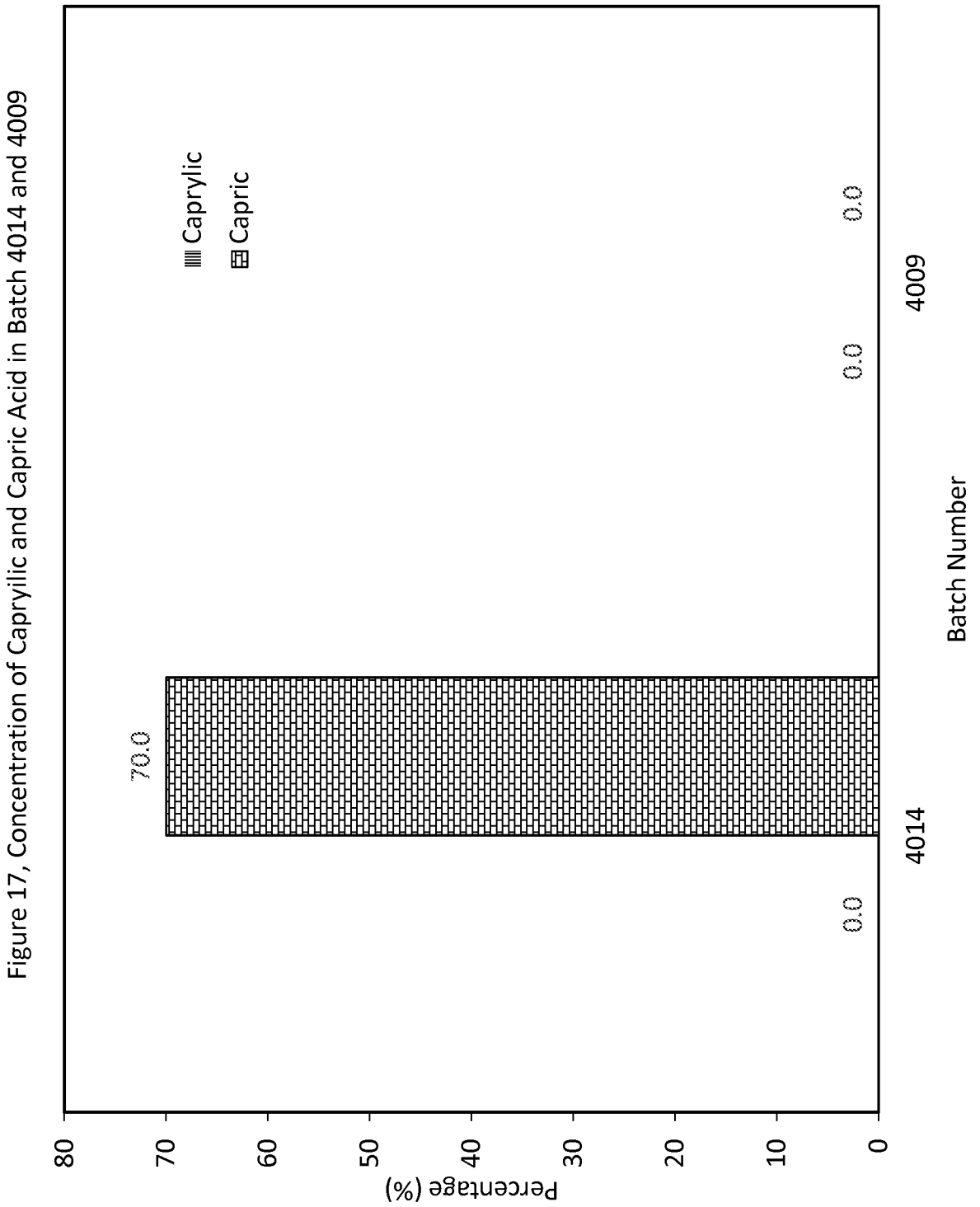


Figure 17, Concentration of Capryilic and Capric Acid in Batch 4014 and 4009

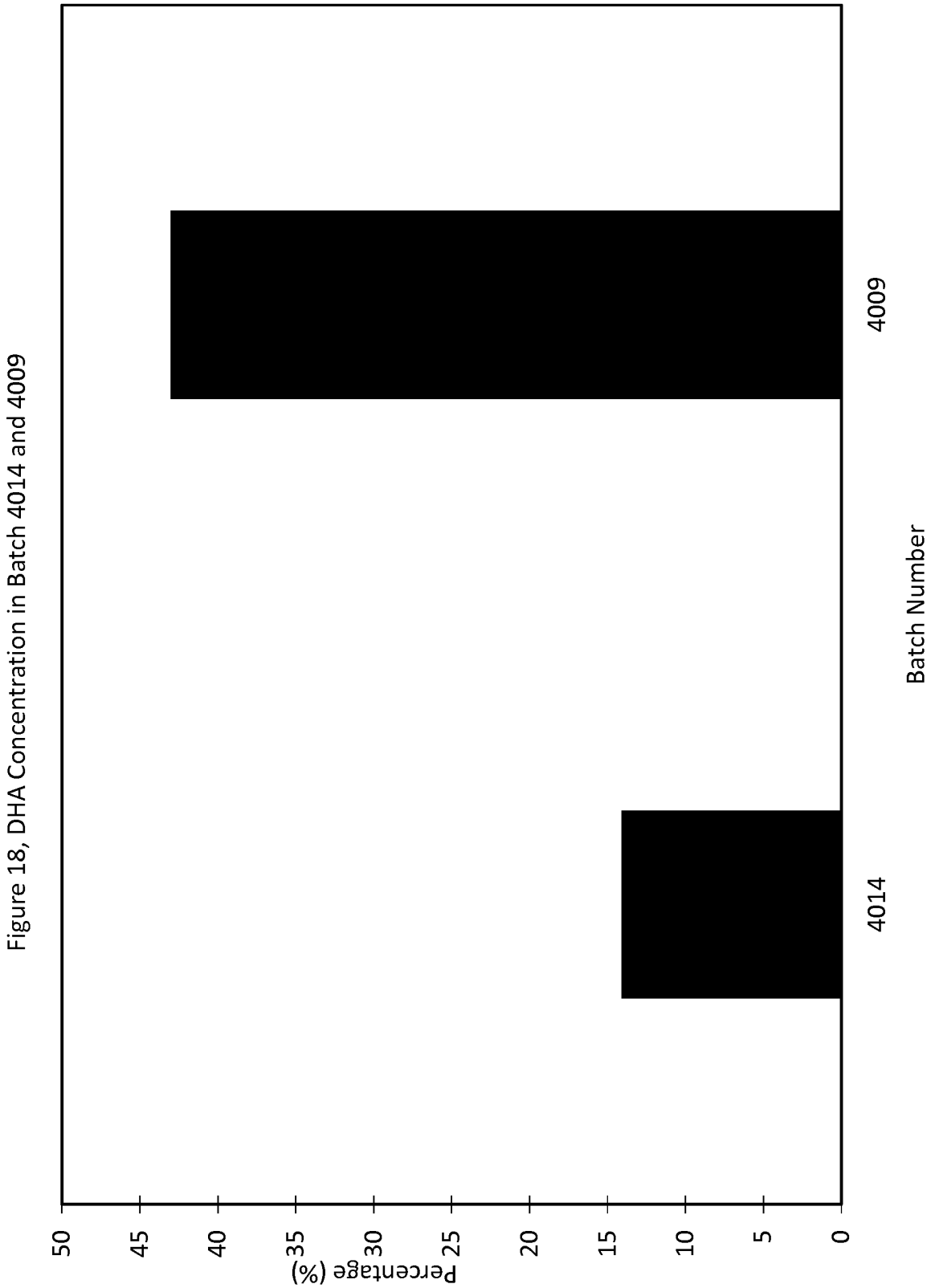


Figure 18, DHA Concentration in Batch 4014 and 4009
Percentage (%)
0
5
10
15
20
25
30
35
40
45
50
4014
4009
Batch Number