

COMPOSITION FOR AMELIORATING PERIPHERAL NERVE
DISORDER CAUSED BY ANTICANCER AGENT

CROSS-REFERENCE TO RELATED APPLICATIONS

5 [0001]

This application is based upon and claims the benefit of priority from Japanese Patent Application No. 2016-161457 filed on August 19, 2016; the entire contents of which are incorporated herein by reference.

10

BACKGROUND OF THE INVENTION

Field of the Invention

[0002]

Nowadays, the number of deaths from cancer has been increasing steadily worldwide, and researches on the effective treatment method therefor have been continued. There are roughly three categories of cancer treatment methods, namely surgical therapy, chemotherapy, and radiation therapy, and a variety of methods using an anticancer agent are widely used as chemotherapy. In recent years, a platinum drug (platinum formulation), as well as a vinca alkaloid drug and a taxane-based drug are frequently used in the treatment using an anticancer agent.

[0003]

25 Meanwhile, an anticancer agent such as a platinum drug, a vinca alkaloid drug, and a taxane-based drug may develop peripheral nerve disorder, such as numbness or pain of limbs, and dysaesthesia, as side effects during use (Non-Patent Literature 1). The peripheral nerve disorder caused by an anticancer agent may take a long time to recover even after withdrawal of use of the anticancer agent, and may diminish appetite significantly, and therefore there is a risk for remarkable deterioration of the quality of life (QOL) of the patient. Further, when peripheral nerve disorder appears, in order to prevent its aggravation, it becomes inevitable in many cases to reduce the dose of the anticancer agent, or even

30

35

discontinue administration thereof. Therefore, such peripheral nerve disorder caused by an anticancer agent has been recognized as a serious problem in treating cancer (Non-Patent Literature 2). In particular, when an anticancer agent treatment is effective in treating cancer, or when it is performed as a postoperative adjuvant therapy, it is desirable to continue the treatment while controlling the symptoms of the peripheral nerve disorder (Non-Patent Literature 1). Therefore, establishment of a method for ameliorating peripheral nerve disorder is an extremely important task in continuing the therapy with an anticancer agent. Further, it is necessary to maintain the nutritional status of a patient who has lost much of its appetite during the treatment with an anticancer agent. However, any effective method has not yet been found to date.

15 [0004]

Under such circumstances, methods which have been attempted to prevent aggravation of peripheral nerve disorder are roughly divided into two groups (Non-Patent Literature 2). One is the method to prevent aggravation of peripheral nerve disorder by decreasing the dose of an anticancer agent, discontinuing administration of the same, or extending the drug holidays. Although discontinuation of the administration of an anticancer agent is the only reliable method to stop peripheral nerve disorder, it is possible that the peripheral nerve disorder persists after discontinuation of administration, or even it is aggravated. The other is a method to reduce peripheral nerve disorder by a combination with a drug therapy for preventing onset or progression of peripheral nerve disorder, or by practice of self-care (Non-Patent Literature 2). In a drug therapy to alleviate peripheral nerve disorder, it is common to use an antidepressant drug (amitriptyline hydrochloride), an antiepileptic drug (carbamazepine), an antiarrhythmic drug (mexiletine), intravenous administration of electrolytes (magnesium, or calcium), a vitamin B12 formulation (mecobalamin), amino acids (acetyl-L-carnitine), a herbal medicine "Gosha-jinkigan", or the like (Non-Patent Literature 1

and 2). However, these drug therapies are used merely attempting to alleviate symptoms empirically, and their effects are limited. Furthermore, use of such drugs in the treatment of peripheral nerve disorder is not covered by Japanese health insurance, and therefore it is preferable to restrain the use of the drugs from the viewpoint of reduction of economic burden on the patient.

Citation List

Non-Patent Literature

10 [0005]

[Non-Patent Literature 1] Oishi Ryozo, *et al.*, Fukuoka Acta Medica, 104 (5), 171-180, 2013

[Non-Patent Literature 2] Arakawa Kazuhiko, *et al.*, Japanese Journal of Pharmaceutical Palliative Care and Sciences, 4, 1-13, 15 2011

SUMMARY OF THE INVENTION

[0006]

The present invention has recently been found that, when a patient to whom an anticancer agent is administered ingests a specific composition, peripheral nerve disorder caused by administration of an anticancer agent may be effectively ameliorated. Furthermore, it has been found that nutrition supply to a patient being treated with an anticancer agent may be effectively performed in addition to the amelioration of peripheral nerve disorder by using the above composition. The present invention has been completed based on such findings.

[0007]

Accordingly, an object of the present invention is to provide a means for effectively ameliorating peripheral nerve disorder caused by administration of an anticancer agent. Another object of the present invention is to perform effectively nutrition supply to a patient being treated with an anticancer agent in addition to the amelioration of peripheral nerve disorder.

35 [0008]

According to the present invention, the following

inventions are provided.

(1) A composition for ameliorating peripheral nerve disorder caused by administration of an anticancer agent, comprising a milk protein hydrolysate, and a protein derived from fermented milk as a protein component; a medium-chain fatty acid or its triglyceride, and an n-3 fatty acid as a fat component; and isomaltulose as a carbohydrate component.

(2) The composition according to (1), wherein the milk protein is at least one selected from the group consisting of casein, a milk protein concentrate (MPC), a whey protein concentrate (WPC), a whey protein isolate (WPI), α -lactalbumin, β -lactoglobulin, and lactoferrin.

(3) The composition according to (1) or (2), wherein the milk protein hydrolysate is a whey protein hydrolysate.

(4) The composition according to any one of (1) to (3), wherein the content of the milk protein hydrolysate is from 0.5 to 3.0 g per 100 kcal of the composition.

(5) The composition according to any one of (1) to (4), wherein the protein derived from fermented milk is derived from fresh cheese.

(6) The composition according to any one of (1) to (5), wherein the protein derived from fermented milk is derived from fermented milk having fermented skimmed milk using *Lactobacillus bulgaricus*, *Streptococcus thermophilus*, or a combination thereof.

(7) The composition according to any one of (1) to (6), wherein the content of the protein derived from fermented milk is from 0.5 to 6 g per 100 kcal of the composition.

(8) The composition according to any one of (1) to (7), wherein the medium-chain fatty acid is a medium-chain fatty acid having 8 to 14 carbon atoms.

(9) The composition according to any one of (1) to (8), wherein the content of the medium-chain fatty acid or its triglyceride is from 0.01 to 2 g per 100 kcal of the composition.

(10) The composition according to any one of (1) to (9), wherein the n-3 fatty acid comprises one or more fatty acids

selected from docosahexaenoic acid and eicosapentaenoic acid.

(11) The composition according to any one of (1) to (10), wherein the content of the n-3 fatty acid is from 0.05 to 2.2 g per 100 kcal of the composition.

5 (12) The composition according to any one of (1) to (11), wherein the content of the isomaltulose is from 1 to 15 g per 100 kcal of the composition.

(13) The composition according to any one of (1) to (12), further comprising an n-6 fatty acid as a lipid component,
10 wherein the weight ratio of the n-6 fatty acid to the n-3 fatty acid is from 1 to 3.

(14) The composition according to any one of (1) to (13), further comprising at least one component selected from dietary fiber, vitamins, and minerals.

15 (15) The composition according to any one of (1) to (14) which is a beverage.

(16) A method for ameliorating peripheral nerve disorder caused by administration of an anticancer agent comprising a step of having a subject in need ingest an effective amount of a
20 composition according to the present invention.

(17) Use of a composition comprising a milk protein hydrolysate and a protein derived from fermented milk as a protein component; a medium-chain fatty acid or its triglyceride, and an n-3 fatty acid as a fat component; and isomaltulose as
25 a carbohydrate component in a manufacture of a composition for ameliorating peripheral nerve disorder caused by administration of an anticancer agent.

[0009]

According to the present invention, peripheral nerve
30 disorder caused by administration of an anticancer agent can be remarkably ameliorated. Furthermore, according to the present invention, it is possible to effectively supply nutrition to a patient on top of amelioration of peripheral nerve disorder. According to the present invention, it is possible to continue a
35 treatment with an anticancer agent while maintaining and improving the QOL of a patient receiving an anticancer drug

treatment.

BRIEF DESCRIPTION OF THE DRAWINGS

[0010]

FIG. 1 is a diagram showing a change in the Grade of
5 adverse events of peripheral nerve disorder in a cancer patient
(one person) under treatment with an anticancer agent, who
has ingested the composition according to the present
invention.

FIG. 2 is a diagram showing a change in the Grade of
10 adverse events of peripheral nerve disorder in another cancer
patient (one person) under treatment with an anticancer agent,
who has ingested the composition according to the present
invention.

DETAILED DESCRIPTION OF THE INVENTION

15 [0011]

The composition according to the present invention
comprises a milk protein hydrolysate, and a protein derived
from fermented milk as a protein component; a medium-chain
fatty acid or its triglyceride, and an n-3 fatty acid as a fat
20 component; and isomaltulose as a carbohydrate component. It
is an unexpected fact that when the above components are
blended in the composition, an excellent ameliorating effect for
peripheral nerve disorder caused by administration of an
anticancer agent can be realized.

25 [0012]

Protein component

The protein component according to the present
invention comprises a milk protein hydrolysate, and a protein
derived from fermented milk.

30 There is no particular restriction on the milk protein
according to the present invention insofar as the advantageous
effects of the present invention are not compromised, and
examples thereof include casein, a milk protein concentrate
(MPC, also called total milk protein (TMP)), a whey protein, such
35 as whey, α -lactalbumin (α -La), and β -lactoglobulin (β -Lg), a
whey protein concentrate (WPC), a whey protein isolate (WPI),

and lactoferrin. A hydrolysate of the milk protein may be, if necessary, modified in terms of the physical characteristics, such as solubility, viscosity, gelling property, thermal stability, and emulsion stability, and physiological characteristics by
5 modifying an amino acid residue, or otherwise. Further, the milk protein hydrolysate according to the present invention may be, if necessary, fractionated and a fraction not exceeding a predetermined molecular weight may be used. The molecular weight of the milk protein hydrolysate is preferably 50,000 or
10 less, more preferably 30,000 or less, and further preferably 10,000 or less.

[0013]

As the milk protein hydrolysate according to the present invention, for example, one obtained by hydrolyzing any of the
15 above milk proteins with an enzyme is used. There is no particular restriction on the enzyme that hydrolyzes a milk protein, insofar as it does not interfere with advantageous effects of the present invention, and various proteases including endoprotease and exoprotease, a roughly purified product
20 containing the protease, disrupted bacterial cells containing the protease, and the like may be used. These may be used singly, or a combination of plural kinds thereof may be also used. Examples of various proteases include proteases derived from animals, such as pepsin, trypsin, chymotrypsin and pancreatin,
25 proteases derived from plants, such as papain, bromelain, and actinidine, and proteases derived from microorganisms. As these proteases, commercially available proteases may be used. Examples of commercially available endoproteases include Alcalase (registered trademark) derived from *Bacillus*
30 *licheniformis*, Esperase (registered trademark) derived from *Bacillus lentus*, Neutrase (registered trademark) derived from *Bacillus subtilis*, Protamex (registered trademark) derived from *Bacillus amyloliquefaciens*, and trypsin (PTN (registered trademark)) derived from porcine pancreas, which are all sold
35 by Novozymes A/S. Examples of commercially available exoproteases include Flavourzyme (registered trademark)

derived from *Aspergillus oryzae*, and carboxypeptidase derived from porcine or bovine viscera. In order to hydrolyze the milk protein according to the present invention, it is preferable to use a combination of Alcalase derived from *Bacillus licheniformis* and trypsin (PTN) derived from porcine pancreas.

[0014]

A whey protein hydrolysate, which is an embodiment of the milk protein hydrolysate according to the present invention can be prepared, for example, by the following method.

10 A whey protein isolate (WPI) containing protein at a dry weight of about 90% by weight is dissolved in water such that the content of protein becomes 8% by weight. The obtained WPI aqueous solution is heated at 85°C for 2 min to denature the whey protein. The aqueous solution after the denaturation treatment, to which Alcalase 2.4 L derived from *Bacillus*
15 *licheniformis* is added to 2% by weight based on the weight of the whey protein, is incubated at 55°C for 3 hours. Thereafter, trypsin (PTN 6.0S) derived from porcine pancreas was added to 3% by weight based on the weight of the whey protein and the
20 solution was incubated at 55°C for 3 hours. The obtained reaction solution is centrifuged at 20,000 × g for 10 min, and the supernatant treated with an ultrafiltration membrane having a cutoff molecular weight of 10,000, and the fraction having passed through the ultrafiltration membrane is regarded as a
25 whey protein hydrolysate.

[0015]

As the milk protein hydrolysate according to the present invention, commercially available ones may be used. Examples of the commercially available milk protein hydrolysate include
30 Peptigen IF-3080, Peptigen IF-3090, Peptigen IF-3091 and Lacprodan DI-3065 (all produced by Aria Foods Ingredients S.A.), WE 80BG (produced by FrieslandCampina Domo), Hyprol 3301, Hyprol 8361 and Hyprol 8034 (all produced by Kerry Group plc), Tatua 2016 and HMP 406 (both produced by Tatua
35 Co-Operative Dairy Co., Ltd.), Whey Hydrolysate 7050 (produced by Fonterra Co-operative Group Limited), and BioZate

3 (produced by Davisco Foods International, Inc.).

[0016]

5 The content of the milk protein hydrolysate in the composition according to the present invention may be adjusted appropriately depending on the contents of other ingredients, the pathology, disease condition, age, and body weight of the subject to be administered with the composition, purpose, or the like. Although there is no particular restriction on the content of the milk protein hydrolysate in the composition,
10 insofar as it does not interfere with advantageous effects of the present invention, specifically it is from 0.5 to 3.0 g per 100 kcal of the composition, preferably from 0.9 to 3.0 g, and more preferably from 1.2 to 2.0 g.

[0017]

15 As the protein derived from fermented milk according to the present invention, a protein contained in fermented milk may be used. Examples of the fermented milk include farm animal milk, such as cow milk, buffalo milk, goat milk, ewe milk, and horse milk, skimmed milk, semi-skimmed milk,
20 reconstituted whole milk, reconstituted skimmed milk, and reconstituted semi-skimmed milk of these farm animal milks, and those obtained by fermenting a liquid raw material for fermented milk, which has been prepared by combining one or more raw materials for fermented milk, such as butter and
25 cream produced from these farm animal milk, using bacteria, such as lactic acid bacteria and bifidobacteria, the raw material. Examples of the lactic acid bacteria and bifidobacteria used in the fermentation include *Lactobacillus bulgaricus*, *Streptococcus thermophilus*, *Streptococcus lactis*, *Streptococcus cremoris*,
30 *Streptococcus diacetylactis*, *Enterococcus faecium*, *Enterococcus faecalis*, *Lactobacillus casei*, *Lactobacillus helveticus*, *Lactobacillus acidophilus*, *Lactobacillus rhamnosus*, *Lactobacillus plantarum*, *Lactobacillus murinus*, *Lactobacillus reuteri*, *Lactobacillus brevis*, *Lactobacillus gasseri*, *Bifidobacterium longum*, *Bifidobacterium bifidum*, and *Bifidobacterium breve*.
35 In this regard, in addition to the lactic acid bacteria and

bifidobacteria, bacteria belonging to the genus *Propionibacterium* may be used in combination in producing the fermented milk.

[0018]

5 Examples of the fermented milk used according to the present invention include yoghurt, and cheese. As the cheese, fresh cheese which has not been ripened is preferable, and examples of fresh cheese include cottage cheese, quark cheese, string cheese, Neuchatel cheese, cream cheese, mozzarella
10 cheese, ricotta cheese, and mascarpone cheese.

[0019]

 The protein derived from fermented milk according to the present invention may be a protein prepared using any of fermented milk insofar as it does not interfere with
15 advantageous effects of the present invention, however it is preferably a protein prepared using quark, or a fermented milk obtained by fermenting skimmed milk with either or both in combination of *Lactobacillus bulgaricus* and *Streptococcus thermophilus*, or is more preferably a protein prepared using
20 fermented milk obtained by fermenting skimmed milk with a combination of *Lactobacillus bulgaricus* and *Streptococcus thermophiles*.

[0020]

 Quark, which is an embodiment of fermented milk for
25 preparing a protein derived from fermented milk according to the present invention, may be produced, for example, by the following method.

 Bovine skimmed milk is sterilized with heat, then inoculated with lactic acid bacteria (mixture of *Lactobacillus*
30 *bulgaricus* and *Streptococcus thermophilus*) as a starter for fermentation at 0.5 to 5% (w/w), and fermented. When the pH of bovine skimmed milk reaches approximately 4.6 by fermentation, bovine skimmed milk separates into curd and whey. The curd obtained by separating whey is cooled to yield
35 quark. The composition of the thus yielded quark is, for example, a total solid content between 17 and 19% (w/w), a

protein between 11 and 13% (w/w), a fat at less than 1% (w/w), a carbohydrate between 2 and 8% (w/w), and lactose at less than 2% (w/w). Quark may also be yielded by inoculating lactic acid bacteria as a starter to perform fermentation, and then adding rennet to curdle quark. In this regard, as the lactic acid bacteria functioning as a starter, it is also possible to use a mixture of *Lactococcus lactis* and/or *Lactococcus cremoris*, and bacteria belonging to the genus *Leuconostoc*, such as *Leuconostoc mesenteroides*.

[0021]

The content of the protein derived from fermented milk in the composition according to the present invention may be adjusted appropriately depending on the contents of other ingredients, the pathology, disease condition, age, and body weight of the subject to be administered with the composition, purpose, or the like. Specifically, the content of the protein derived from fermented milk in the composition according to the present invention is from 0.5 to 6.0 g per 100 kcal of the composition, preferably from 2.0 to 6.0 g, and more preferably from 2.5 to 4.5 g. Meanwhile, there is no particular restriction on the method of adding the protein derived from fermented milk according to the present invention to the composition, insofar as it does not interfere with advantageous effects of the present invention, and the fermented milk such as yogurt, and quark may be added as it is into the composition, or the protein derived from fermented milk separated from the fermented milk may be added into the composition.

[0022]

Fat component

The fat component according to the present invention comprises a medium-chain fatty acid or its triglyceride, and an n-3 fatty acid.

As the medium-chain fatty acid according to the present invention, a medium-chain fatty acid having 8 to 14 carbon atoms is preferable. In addition, part or all of the medium-chain fatty acid according to the present invention is

preferably contained in the form of a medium-chain fatty acid triglyceride (MCT: Medium-chain triglyceride). MCT is quickly absorbed in the body and converted to energy, and therefore it has a character to resist accumulation as fat in the body.

5 Examples of fats and oils containing MCT include fats and oils obtained from a palmae plant, such as palm oil, palm kernel oil, and coconut oil, and oils and fats containing a medium-chain fatty acid. The composition according to the present invention may contain a medium-chain fatty acid or its triglyceride as it is,
10 or in the form of fat or oil.

[0023]

Examples of the n-3 fatty acid according to the present invention include docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), α -linolenic acid, and docosapentaenoic acid (DPA),
15 and α -linolenic acid, DHA, and EPA are preferable, and DHA and EPA are more preferable. Examples of fats and oils containing an n-3 fatty acid include fish oil, Siso oil, linseed oil (flaxseed oil), perilla oil, rapeseed oil, soybean oil, and canola oil (salad oil). The composition according to the present invention may
20 contain an n-3 fatty acid as it is, or in the form of fat or oil.

[0024]

The composition according to the present invention may contain another fatty acid in addition to the medium-chain fatty acid or its triglyceride, and the n-3 fatty acid.

25 [0025]

Examples of such other fatty acid include oleic acid, palmitic acid, palmitoleic acid, linoleic acid, stearic acid, linolenic acid, and arachidonic acid, and an n-6 fatty acid such as linoleic acid is preferable. Examples of oils and fats
30 containing another fatty acid include an edible oil, such as a high-oleic sunflower oil, rapeseed oil, olive oil, a high-oleic safflower oil, soybean oil, corn oil, and palm oil. The composition according to the present invention may contain such other fatty acid as it is, or in the form of fat or oil.

35 [0026]

According to a preferred embodiment of the present

invention, the weight ratio of an n-6 fatty acid to an n-3 fatty acid in the composition according to the present invention is preferably from 1 to 3, more preferably from 1.5 to 2.5, further preferably from 1.8 to 2.2, and still further preferably from 1.9 to 2.1.

[0027]

The composition according to the present invention may contain one or more publicly known phospholipids, such as a milk phospholipid, lecithin derived from soybean, and egg yolk lecithin. The phospholipid according to the present invention can be fractionated from raw materials derived from milk, soybean, egg, *etc.* and purified. Also, a commercially available phospholipid may be used insofar as advantageous effects of the present invention may be obtained.

[0028]

As the phospholipid according to the present invention, a milk phospholipid is preferable. A milk phospholipid (also called milk lecithin) is composed of sphingomyelin (SM), phosphatidyl choline (PC), phosphatidyl ethanolamine (PE), phosphatidyl inositol (PI), phosphatidyl serine (PS), lysophosphatidyl choline (LPC), and localized only in milk fat globule membrane (MFGM). The component composition of the MFGM phospholipid fraction is described, for example, in Bulletin of Japan Dairy Technical Association, Vol. 50: pp.58-91, 2000.

[0029]

The content of the phospholipid in the composition according to the present invention may be adjusted appropriately depending on the contents of other ingredients, the pathology, disease condition, age, and body weight of the subject to be administered with the composition, purpose, or the like. A preferable content of the phospholipid per 100 kcal of the composition is from 1 to 15 g, from 1 to 10 g, from 2 to 10 g, from 3 to 10 g, from 4 to 10 g, from 5 to 10 g, from 6 to 10 g, from 7 to 10 g, or from 7 to 9 g.

[0030]

Carbohydrate component

The composition according to the present invention comprises isomaltulose as a carbohydrate component. Isomaltulose is a substance represented by CAS Registry No. 13718-94-0, and chemical formula $C_{12}H_{22}O_{11}$.

5 [0031]

Isomaltulose is commercialized under the registered trade name of Palatinose (registered trademark), and is contained in commercially available products, such as Palatinose syrup, reconstituted Palatinose, and Palatinose starch syrup.
10 Isomaltulose itself may be added to the composition according to the present invention, or the above products containing isomaltulose may be added.

[0032]

The composition according to the present invention may
15 contain a carbohydrate other than isomaltulose. Examples of a carbohydrate other than isomaltulose include sucrose, glucose, fructose, honey, and dextrin.

[0033]

The content of the carbohydrate in the composition
20 according to the present invention may be adjusted appropriately depending on the contents of other ingredients, the pathology, disease condition, age, and body weight of the subject to ingest the same, purpose, or the like. The preferable content of the carbohydrate per 100 kcal of the
25 composition is from 1 to 25 g, from 1 to 22 g, from 2 to 20 g, from 4 to 18 g, from 4 to 16 g, from 6 to 16 g, from 8 to 14 g, from 10 to 14 g, from 1 to 15 g, from 1.5 to 12 g, from 2 to 10 g, from 3 to 9 g, from 4 to 8 g, or from 5 to 7 g.

[0034]

30 In the composition according to the present invention, the weight ratio of the protein component to the lipid component is preferably from 0.3 : 1 to 3 : 1, and more preferably from 1.4 : 1 to 2 : 1.

[0035]

35 In the composition according to the present invention, the weight ratio of the protein component to the carbohydrate

component is preferably from 1 : 2 to 1 : 20, and more preferably 1 : 2 to 1 : 4.

[0036]

5 In the composition according to the present invention, the weight ratio of the lipid component to the carbohydrate component is preferably from 1 : 3 to 1 : 7, and more preferably from 1 : 4 to 1 : 6.

[0037]

Additional nutritional component

10 The nutritional composition, flavor, form, pH, osmotic pressure, etc. of the composition according to the present invention may be adjusted by adding at least one, or a combination of two or more additional nutrients. There is no particular restriction on the additional nutrient according to the
15 present invention insofar as it does not interfere with advantageous effects of the present invention, and examples thereof include an amino acid, a dietary fiber, vitamins, minerals, an organic acid, an organic base, a fruit juice, flavors, artificial sweeteners (such as aspartame), and moisture.

20 [0038]

Dietary fibers may be classified into a water-soluble dietary fiber and an insoluble dietary fiber, and both of them can be used. Examples of the water-soluble dietary fiber include non-digestible oligosaccharide, non-digestible dextrin,
25 lactitol, raffinose, pectin, and guar gum. Examples of the insoluble dietary fiber include cellulose, hemicellulose, lignin, chitin, chitosan, soybean dietary fiber, wheat bran, pine fiber, corn fiber, and beet fiber.

[0039]

30 There is no particular restriction on the content of dietary fiber in the composition according to the present invention, and the content may be adjusted appropriately depending on the contents of other ingredients, the pathology, disease condition, age, and body weight of the subject to ingest the same, purpose,
35 or the like. The preferable content of the dietary fiber per 100 kcal of the composition is from 0.5 to 10 g, from 0.5 to 8 g,

from 0.5 to 6 g, from 0.5 to 4 g, from 0.5 to 2 g, or from 1 to 2 g.

[0040]

Preferable examples of vitamins include vitamin A,
5 vitamin B1, vitamin B2, vitamin B6, vitamin B12, vitamin C,
vitamin D, vitamin E, vitamin K, niacin, folic acid, biotin,
pantothenic acid, and a combination of part or all of them, and
biotin is more preferable.

[0041]

10 The component of the vitamins in the composition
according to the present invention may be adjusted
appropriately depending on the contents of other ingredients,
the pathology, disease condition, age, and body weight of the
subject to ingest the same, purpose, or the like. The
15 preferable content of the vitamins per 100 kcal of the
composition is from 1 to 200 μg , from 10 to 200 μg , from 20 to
100 μg , from 30 to 100 μg , from 40 to 100 μg , or from 40 to 60
 μg . The preferable content of biotin per 100 kcal of the
composition is from 0.5 to 20 μg , from 0.5 to 10 μg , from 1 to
20 10 μg , from 2 to 10 μg , from 4 to 10 μg , from 5 to 9 μg , from
6.5 to 8 μg , or from 7 to 8 μg .

[0042]

Preferable examples of the minerals include sodium,
chlorine, potassium, sulfur, magnesium, calcium, phosphorus,
25 iron, iodine, manganese, copper, zinc, selenium, chromium,
molybdenum, or a combination of part or all of them, but
sodium, zinc, copper, or a combination thereof is more
preferable.

[0043]

30 The content of the minerals in the composition according
to the present invention may be adjusted appropriately
depending on the contents of other ingredients, the pathology,
disease condition, age, and body weight of the subject to ingest
the same, purpose, or the like. The preferable content of the
35 minerals per 100 kcal of the composition is from 10 to 900 mg,
from 30 to 800 mg, from 40 to 700 mg, from 100 to 600 mg,

from 150 to 550 mg, from 200 to 500 mg, from 250 to 500 mg, or from 300 to 500 mg. The preferable sodium content per 100 kcal of the composition is from 10 to 150 mg, from 20 to 130 mg, from 30 to 110 mg, from 40 to 100 mg, from 50 to 90 mg, from 60 to 80 mg, or from 65 to 75 mg. The preferable zinc content per 100 kcal of the composition is from 0.01 to 30 mg, from 0.05 to 15 mg, from 0.05 to 10 mg, from 0.1 to 7 mg, from 0.3 to 5 mg, from 0.5 to 2.5 mg, or from 0.5 to 1.5 mg. The preferable copper content per 100 kcal of the composition is from 0.002 to 20 mg, from 0.004 to 15 mg, from 0.006 to 10 mg, from 0.008 to 5 mg, from 0.01 to 1 mg, or from 0.03 to 0.07 mg.

[0044]

The content of water in the composition according to the present invention per 100 kcal of the composition is from 1 to 99 g, from 10 to 99 g, from 30 to 99 g, from 50 to 99 g, from 70 to 99 g, from 75 to 99 g, from 80 to 99 g, or from 80 to 90 g.

[0045]

There is no particular restriction on the form of the composition according to the present invention, insofar as it does not interfere with advantageous effects of the present invention, and it may be a liquid, a paste, a solid, a powder, or the like, but it is preferably a liquid.

[0046]

There is no particular restriction on the pH of the composition according to the present invention, and it may be, for example, from pH 2 to pH 6, and preferably from pH 3 to pH 5.

[0047]

There is no particular restriction on the osmotic pressure of the composition according to the present invention, and it is, for example, approximately from 300 to 1000 mOsm/L, and preferably approximately from 300 to 750 mOsm/L.

[0048]

When measured at room temperature, the viscosity of

the composition according to the present invention is, for example, approximately from 5 to 100 cp (1 cp = 0.001 Pa·s), and preferably less than 80.

[0049]

5 There is no particular restriction on the calorie of the composition according to the present invention, and it is, for example, approximately from 0.5 to 2 kcal/mL, and preferably from 1 to 1.5 kcal/mL.

[0050]

10 There is no particular restriction on the method for preparing the composition according to the present invention, and the preparation may be carried out by blending the above-mentioned components and homogenizing the same by a publicly known method. In this regard, in the preparation
15 method according to the present invention, it is preferable to apply a publicly known sterilization treatment (heating, etc.) to the composition or each component according to the present invention. Therefore, an aspect of the present invention provides a method for producing a composition for ameliorating
20 peripheral nerve disorder caused by administration of an anticancer agent, comprising a step of blending a milk protein hydrolysate, and a protein derived from fermented milk as a protein component; a medium-chain fatty acid or its triglyceride, and an n-3 fatty acid as a fat component; and isomaltulose as
25 a carbohydrate component, into a composition; and if desirable a step of homogenizing and heating the composition. The numbers of the sterilization step and the homogenization step are not particularly limited, and each may be performed a plurality of times as described later. Although there is no
30 particular restriction on the order of the blending step, the homogenization step, and the sterilization step, it is preferable to carry out the homogenization step after the sterilization step. When the composition is used in a powder form, a homogenized product may be, for example, spray-dried, or freeze-dried.

35 [0051]

 The preparation method according to the present

invention will be described below by way of more specific examples.

In a preferable example of the preparation method according to the present invention, firstly, hot water is stirred in
5 a tank, into which components other than vitamins are one by one added, mixed, and stirred in consideration of easiness of mixing and diffusion to form a mixed liquid. The order of addition that facilitates mixing and diffusion of raw materials may vary depending on the amount and characteristics of the
10 raw materials, and they may be added at one time, or dividedly in various orders, and, for example, there is a method, by which a carbohydrate, a protein, a fat, and minerals are added in this order. There is another method example, in which part of carbohydrates, a protein, another carbohydrate, minerals, and a
15 fat are added in this order. Further, in still another method example, a fat, a protein, a carbohydrate, and minerals are added in this order. The mixed liquid is sterilized with heat by means of steam injection, and then homogenized with a homogenizer (homogenized at two pressures) to form a
20 homogenized liquid. To this homogenized liquid, vitamins, a flavor (fragrance), *etc.* are added and mixed to form a final mixed liquid. The final mixed liquid is sterilized with heat by means of steam injection (two-stage sterilization), and then homogenized with a homogenizer (homogenized at two
25 pressures) to yield a composition according to the present invention.

[0052]

The mixing conditions in the preparation method according to the present invention may be appropriately set
30 corresponding to the type, proportion, properties, *etc.* of the components and composition, and the mixing temperature in mixing the proteins is, for example, in a range of 2°C to 70°C, preferably 55°C or less, more preferably in a range of 5 to 55°C, further preferably 40 to 55°C, still further preferably 40 to 53°C,
35 still further preferably 40 to 50°C. It is preferable to set the mixing temperature in handling a protein in a range of 2°C to

70°C, for the sake of preventing a protein from curdling, and of dissolving or dispersing the protein in water or the like.

[0053]

In the sterilization step according to the present invention, it is preferable to perform a publicly known high temperature sterilization treatment. In the sterilization step, for example, the temperature may be in a range of 100 to 150°C, and the holding time may be in a range of 1 to 30 sec, preferably 115 to 145°C and 1 to 20 sec, more preferably 120 to 145°C and 1 to 10 sec, and further preferably 125 to 140°C and 1 to 5 sec.

[0054]

In performing high-temperature sterilization, the pressure on the mixed liquid may be adjusted (positive or negative pressure). In doing so, for example, the sterilization pressure is set in a range of about 1 to 10 kg/cm² for the purpose of preventing the mixed liquid from boiling, etc. In other words, at the high-temperature sterilization according to the present invention such a pressure may be applied in addition to high temperature (heating). Examples of a high-temperature sterilization apparatus include a plate heat exchanger, a tubular heat exchanger, a steam injection sterilizer, a steam infusion sterilizer, and an electric heating sterilizer.

[0055]

According to the present invention, it is preferable to sterilize the mixed liquid and then homogenize it. Homogenization after sterilization is preferable for mitigating viscosity increase associated with heating at the time of sterilization. In this case the number of times of homogenization carried out after the sterilization may be one or two or more times. For example, when the second sterilization is performed after performing the first sterilization on the mixed liquid, the first homogenization may be performed after the second sterilization. Meanwhile, when the first sterilization is performed on the mixed liquid, which is then homogenized, and the second sterilization is further performed thereon, the second

homogenization may be performed after the second sterilization. Further, in a case where the mixed liquid is sterilized and then homogenized, however a second sterilization is not performed, the second homogenization may be performed directly.

5 [0056]

The homogenization step may be carried out using a publicly known homogenizer. There is no particular restriction on the preferable conditions of the homogenization step, insofar as it does not interfere with advantageous effects of the present invention, and, for example, when the temperature is set
10 between about 10 and 60°C and the flow rate is set between about 100 and 10000 L/h, the pressure is from 10 to 100 MPa, preferably from 20 to 80 MPa, more preferably from 30 to 70 MPa, and further preferably from 20 to 50 MPa.

15 [0057]

In the preparation method according to the present invention, a homogenized liquid (liquid obtained by homogenizing a sterilized liquid) may be sterilized again before or after filling the container. Specifically, a method by which a
20 homogenized liquid is, if necessary, sterilized again with heat, and cooled, and then sterile filling is performed (for example, a method combining a UHT sterilization method and an aseptic filling method), or a method by which a can or a soft bag is filled with the liquid, which is then sterilized by retort
25 sterilization (for example, by a retort method, or an autoclave method), may be applied.

[0058]

If desired, the composition according to the present invention obtained as above may be further formulated using a
30 pharmaceutically acceptable additive, and such an embodiment is also included in the present invention. Examples of the pharmaceutically acceptable additive include an excipient, a binder, a disintegrant, a lubricant, an odor ameliorating agent, a solubilizing agent, a suspending agent, a coating agent, a
35 solvent, and an isotonicizing agent.

[0059]

The composition according to the present invention is favorably used in any form among a pharmaceutical product, a food and beverage, a nutritional composition, a supplement, a food for special dietary uses, a food with nutrient function claims, a health food, a pharmaceutical additive, a food with function claims, and a food additive.

[0060]

According to the present invention, peripheral nerve disorder caused by administration of an anticancer agent can be effectively ameliorated by having a subject ingest the composition. Therefore, another aspect of the present invention provides a method for ameliorating peripheral nerve disorder caused by administration of an anticancer agent, in which a subject in need is made to ingest an effective dose of a composition of the present invention. In this regard, the term "amelioration" according to the present invention includes not only a treatment of an established pathology or symptom, but also prevention of a pathology or symptom that may be established in the future.

[0061]

The term "subject" according to the present invention is not particularly limited, but is preferably a mammal, more preferably a human, a domestic animal species, a wild animal, or the like, further preferably a human, and still further preferably a human cancer patient.

[0062]

There is no particular restriction on the anticancer agent according to the present invention insofar as it may cause peripheral nerve disorder, and a publicly known anticancer agent may be applied, and examples thereof include anticancer agents for leukemia, malignant lymphoma, myeloma, lung cancer, breast cancer, colon cancer, hepatocellular carcinoma, gastrointestinal stromal tumor, and renal cell carcinoma. More specific examples of an anticancer agent according to the present invention include an anticancer agent that damages microtubules to cause peripheral nerve disorder. Preferable

examples of such an agent include taxane-based drugs, such as paclitaxel, and docetaxel; and vinca alkaloid drugs, such as vincristine, vinblastine, vindesine, and vinorelbine. Further, there is an anticancer agent that injures neurons to cause axonopathy which causes peripheral nerve disorder. Good examples of such an agent include platinum drugs, such as oxaliplatin, carboplatin, cisplatin, and nedaplatin.

[0063]

Good examples of the peripheral nerve disorder caused by an anticancer agent include a pain, such as tingling, and burning pain, numbness of a distal portion of the extremities, abnormal sensation such as burning sensation, hyperesthesia such as hypersensitivity to cold stimulus, dysesthesia such as sensory extinction or sensory paralysis, and sense of discomfort, sensory motor ataxia, and muscular weakness. The peripheral nerve disorder by an anticancer agent according to the present invention includes not only peripheral nerve disorder caused by monotherapy using one kind of anticancer agent, but also peripheral nerve disorder occurring in a multidrug therapy in which a plurality of drugs having different functional mechanisms are administered in combination, or in a biochemical modulation therapy in which the combination or the administration method of drugs are optimized so that drugs having different functional mechanisms develop the maximum effectiveness.

[0064]

The method of ingestion of the composition according to the present invention by a subject may be either of a peroral or parenteral method, and the form of ingestion may be in either of a form of a pharmaceutical product, or a form of a non-pharmaceutical product such as a food or drink.

[0065]

When the composition according to the present invention is ingested as a pharmaceutical product, for example, enteral, or peroral administration by means of a transnasal tube, a gastric fistula, an intestinal fistula, or the like, of an enteral

nutrient, a liquid medicine, or the like may be used, and also an administration form, in which a formulation, such as tablets, capsules, granules, powders, and syrups, is prepared, may be used.

5 [0066]

When the composition according to the present invention is ingested as a food or drink, examples of its form may include milk, soft drink (such as a fruit juice type beverage, or a milk shake type beverage), fermented milk, yogurt, cheese, bread,
10 biscuit, cracker, pizza crust, formulated milk powder, fluid diet, food for patient consumption, nutritious food, frozen food, food composition, processed food, and other commercially available foods. The composition may also be a soluble powder that can be reconstituted before use.

15 [0067]

There is no particular restriction on the timing of ingestion of the composition according to the present invention, insofar as it does not interfere with advantageous effects of the present invention, and the composition according to the present
20 invention may be favorably ingested before the administration of an anticancer agent, during the administration period of an anticancer agent, and/or after the administration of an anticancer agent. The composition according to the present invention may be ingested appropriately before meals, after
25 meals, between meals and/or before bedtime. Also, the composition according to the present invention may be used in place of meal or as a food supplement.

[0068]

The effective dose of the composition according to the
30 present invention may be appropriately adjusted depending on the sex, symptom, condition, body weight and the like of a subject, and a suitable effective dose in terms of calorie per day is from 10 to 3000 kcal, from 50 to 2500 kcal, from 50 to 2000 kcal, from 100 to 2000 kcal, from 100 to 1500 kcal, from 100 to
35 1250 kcal, from 100 to 1000 kcal, from 150 to 850 kcal, from 150 to 650 kcal, or from 200 to 600 kcal. Also, a suitable

effective dose of the composition according to the present invention in terms of the solid content weight per day is from 2 to 665 g, from 11 to 555 g, from 11 to 445 g, from 22 to 445 g, from 22 to 335 g, from 22 to 280 g, from 33 to 190 g, from 33 to 145 g, or from 45 to 135 g. In this regard, a suitable effective dose of the composition according to the present invention in terms of the solid content weight may be appropriately adjusted within a range of 0.5 to 135 g per patient at one time. Further, the composition according to the present invention may be ingested 1 to 3 times a day, for 1 week or longer (preferably about 1 month to 12 months).
[0069]

Another aspect of the present invention provides use of a composition comprising a milk protein hydrolysate and a protein derived from fermented milk as a protein component; a medium-chain fatty acid or its triglyceride, and an n-3 fatty acid as a fat component; and isomaltulose as a carbohydrate component; for ameliorating peripheral nerve disorder caused by administration of an anticancer agent. Yet another aspect of the present invention provides use of a composition comprising a milk protein hydrolysate and a protein derived from fermented milk as a protein component; a medium-chain fatty acid or its triglyceride, and an n-3 fatty acid as a fat component; and isomaltulose as a carbohydrate component; in a manufacture of a composition for ameliorating peripheral nerve disorder caused by administration of an anticancer agent. Yet another aspect of the present invention provides a combination comprising a milk protein hydrolysate, and a protein derived from fermented milk as a protein component; a medium-chain fatty acid or its triglyceride, and an n-3 fatty acid as a fat component; and isomaltulose as a carbohydrate component; for ameliorating peripheral nerve disorder caused by administration of an anticancer agent. Any of the above aspects can be implemented based on the descriptions of the composition and method according to the present invention.

EXAMPLES

[0070]

The present invention will be described in more detail below by way of the Examples, provided that the present invention is not limited thereto. Meanwhile, in the following

5 Examples, % means % by weight unless otherwise specified. Further, units and measuring methods hereunder are in accordance with the provisions of Japanese Industrial Standards (JIS) unless otherwise specified.

[0071]

10 Example 1: Preparation of test composition

Milk protein hydrolysate

A whey protein isolate (WPI, Davisco Foods International, Inc.) with a protein content of about 90% as a dry matter was dissolved in distilled water to a protein content of 8% (w/v).

15 The solution was heat-treated at 85°C for 2 min to denature the protein. The pH of this solution after heating was about 7.5. For hydrolysis, Alcalase 2.4L (enzyme, Novozymes A/S) was added at a concentration of 2.0% with respect to the substrate and left to react at 55°C for 3 hours. Next, PTN 6.0S

20 (Novozymes Japan) which is a trypsin derived from swine was added at a concentration of 3.0% with respect to the substrate, and left to react at 55°C for 3 hours. The total hydrolysis time was 6 hours. The pH at the end of the reactions was about 7.0. The yielded reaction solution was subjected to a centrifugation

25 treatment (20,000×g, 10 min), and further to a treatment with a UF membrane having a cutoff molecular weight of 10,000 (Ultrafree-MC, Millipore Corporation) to yield a milk protein hydrolysate (whey protein hydrolysate).

[0072]

30 Protein derived from fermented milk

After skimmed milk was sterilized (120°C, 30 sec), lactic acid bacteria (*Lactobacillus bulgaricus*, and *Streptococcus thermophilus*) as a starter were inoculated at about 5% (w/w) and the milk was fermented. After the pH of the yielded

35 fermented solution reached about 4.6 and the curd was formed, the whey was centrifuged using a separator, and the obtained

curd was cooled to yield a protein derived from fermented milk.
[0073]

Test composition

For obtaining 100 L of a test composition, warm water at
5 55°C was stirred in a tank, to which a protein component
(containing 2 kg of the milk protein hydrolysate, and 3 kg of the
protein derived from fermented milk), a fat component
(containing 0.59 kg of medium-chain fatty acid triglyceride, 0.2
kg of refined fish oil, and 1.91 kg of edible oil), a carbohydrate
10 component (containing 7 kg of isomaltulose), 1.2 kg of dietary
fiber, and 71 g of minerals (containing sodium, zinc, and
copper) were added and mixed. The obtained mixed liquid was
sterilized with heat using a steam injection system (135°C, 5
sec), and then homogenized with a homogenizer (15 MPa) to
15 form a homogenized liquid. To this homogenization liquid, 7.5
mg of biotin, etc. were added and mixed to yield a new mixed
liquid. The pH of the yielded mixed liquid was adjusted to 3.8
with citric acid, and the liquid was sterilized with heat again
using a steam infusion system (135°C, 5 sec), and then
20 homogenized with a homogenizer (15 MPa) to yield 100 L of the
the test composition (100 kcal/100 mL) shown in the following
Table 1 and Table 2. The total content of docosahexaenoic acid
and eicosapentaenoic acid in the test composition was 0.06 g,
and the weight ratio (n-6/n-3) of the n-6 fatty acid to the n-3
25 fatty acid in the test composition was 2.0. The n-6 fatty acid
was linoleic acid, and the n-3 fatty acid was a combination of
 α -linolenic acid, docosahexanoic acid, and eicosapentaenoic
acid.

[0074]

30 [Table 1]

Nutrient component	per 100mL
Energy	100 kcal
Protein	5 g
Lipid	2.8 g
Carbohydrate	13.3 g
Dietary fiber	1.2 g
Sodium	70 mg

Zinc	1 mg
Copper	0.05 mg
Biotin	7.5 µg
Water	84.4 g

[0075]

[Table 2]

Energy	100 kcal	
Protein	20	%
Lipid	25	%
Carbohydrate	55	%

5 [0076]

Example 2: Confirmation test of ameliorating effect of peripheral nerve disorder caused by anticancer agent

As test subjects 2 cancer patients (Case 1: female, 43 year-old, malignant lymphoma patient, stage IV; and case 2: female, 47 year-old, colon cancer patient, stage IV), who were undergoing chemotherapy, and able to attend a hospital as outpatients to continue the research by themselves, were selected. The chemotherapy was given in a cycle of about 20 days, on the first day of which an anticancer agent was instilled in a test subject.

As for the administration regimen of an anticancer agent for the malignant lymphoma patient, the R-CHOP therapy (520 mg of rituximab, 1040 mg of cyclophosphamide, and 69 mg of adriamycin, and 1.9 mg of vincristine) was used for the first 2 anticancer agent administrations, and the R-CVP therapy (520 mg of rituximab, 1040 mg of cyclophosphamide, and 1.9 mg of vincristine) was used for the last 2 anticancer agent administrations.

As for the same for the colon cancer patient, the CapeOX therapy (1200 mg of capecitabine, and oxaliplatin (L-OHP 100 mg)) was used for the first four anticancer agent administrations, and the R-CVP Cape/Bev therapy (1200 mg of capecitabine, and 270 mg of bevacizumab) was used for the last anticancer agent administration.

[0077]

During the chemotherapy, course A with ingestion of the test composition, and course B for ingesting only usual diet were provided, and the course A and the course B was alternately repeated for each test subject. Specifically, in the course A, the test subject ingested 3 bottles per day of the test composition (equivalent to 600 kcal) perorally from 3 days before implementation of the chemotherapy (implementation of instillation) to one day before the implementation, and further 1 bottle per day (equivalent to 200 kcal) perorally for 4 days from the day of chemotherapy to 3 days after the chemotherapy, and thereafter ingested usual diet perorally. On the other hand, in the course B the subjects ingested perorally normal meals before and after the chemotherapy.

15 [0078]

During the test, the test subjects rated the peripheral nerve disorder (numbness, etc.) associated with the chemotherapy into 4 Grades with reference to adverse event of ver. 4 of Common Terminology Criteria for Adverse Events (CTCAE), and recorded the results by themselves. The Grades were rated as follows. Grade 0: normal; Grade 1: light numbness or pain; Grade 2: some inconvenience due to numbness or pain, but not so much to hinder daily life; and Grade3: severe numbness or pain to hinder substantially daily life.

25 [0079]

The results were as shown in FIG. 1 and FIG. 2. Peripheral nerve disorder, which is a side effect of an anticancer agent, is accumulated every time through chemotherapy, and the Grade of adverse events of the peripheral nerve disorder does not decrease normally. However, as a result of this test, it was confirmed with respect to both of the test subjects that the Grade of adverse events of peripheral nerve disorder decreased in a case where the test composition was ingested. Specifically, with respect to the malignant lymphoma patient in FIG. 1, by using the test composition together, the rating of adverse

events decreased from Grade 2 to Grade 1 at the third infusion of the anticancer agents (day 60). With respect to the colon cancer patient in FIG. 2, in the period up to day 60, in a case where the anticancer agents were instilled (day 25) without
5 ingesting the test composition, the rating of adverse events increased from Grade 0 to Grade 2, but in a case where the anticancer agents were instilled with simultaneous ingestion of the test composition (day 4, and day 46), the increase in the
10 rating of adverse events was suppressed to from Grade 0 to Grade 1.

Further, no test subject had difficulty in ingesting the test composition due to loss of appetite, and nutrient supply with the test composition could be continued in parallel with amelioration of peripheral nerve disorder.

15

CLAIMS

1. A composition for ameliorating peripheral nerve disorder caused by administration of an anticancer agent, comprising a milk protein hydrolysate and a protein derived from fermented milk as a protein component; a medium-chain fatty acid or its triglyceride, and an n-3 fatty acid as a fat component; and isomaltulose as a carbohydrate component.
2. The composition according to claim 1, wherein the milk protein is at least one selected from the group consisting of casein, a milk protein concentrate (MPC), a whey protein concentrate (WPC), a whey protein isolate (WPI), α -lactalbumin, β -lactoglobulin, and lactoferrin.
3. The composition according to claim 1 or 2, wherein the milk protein hydrolysate is a whey protein hydrolysate.
4. The composition according to any one of claims 1 to 3, wherein the content of the milk protein hydrolysate is from 0.5 to 3 g per 100 kcal of the composition.
5. The composition according to any one of claims 1 to 4, wherein the protein derived from fermented milk is derived from fresh cheese.
6. The composition according to any one of claims 1 to 5, wherein the protein derived from fermented milk is a protein of fermented milk obtained by fermenting skimmed milk using *Lactobacillus bulgaricus*, *Streptococcus thermophilus*, or a combination thereof.
7. The composition according to any one of claims 1 to 6, wherein the content of the protein derived from fermented milk is from 0.5 to 6 g per 100 kcal of the composition.

8. The composition according to any one of claims 1 to 7, wherein the medium-chain fatty acid is a medium-chain fatty acid having 8 to 14 carbon atoms.

5

9. The composition according to any one of claims 1 to 8, wherein the content of the medium-chain fatty acid or its triglyceride is from 0.01 to 2 g per 100 kcal of the composition.

10 10. The composition according to any one of claims 1 to 9, wherein the n-3 fatty acid comprises one or more fatty acids selected from docosahexaenoic acid, and eicosapentaenoic acid.

11. The composition according to any one of claims 1 to 10, wherein the content of the n-3 fatty acid is from 0.05 to 2.2 g per 100 kcal of the composition.

12. The composition according to any one of claims 1 to 11, wherein the content of the isomaltulose is from 1 to 15 g per 100 kcal of the composition.

13. The composition according to any one of claims 1 to 12, further comprising an n-6 fatty acid as a lipid component, wherein the weight ratio of the n-6 fatty acid to the n-3 fatty acid is from 1 to 3.

14. The composition according to any one of claims 1 to 13, further comprising at least one component selected from dietary fiber, vitamins, and minerals.

30

15. The composition according to any one of claims 1 to 14 which is a beverage or fluid diet.

16. A method for ameliorating peripheral nerve disorder caused by administration of an anticancer agent, comprising a step of having a subject in need ingest an effective amount of a

35

composition according to the present invention.

17. Use of a composition comprising a milk protein hydrolysate and a protein derived from fermented milk as a protein component; a medium-chain fatty acid or its triglyceride, and an n-3 fatty acid as a fat component; and isomaltulose as a carbohydrate component in a manufacture of a composition for ameliorating peripheral nerve disorder caused by administration of an anticancer agent.

10