

Description

Title of Invention: AGENT FOR REDUCING CATABOLISM OR PROMOTING ASSIMILATION OF PROTEIN

Technical Field

[0001] The present invention relates to an agent for reducing protein catabolism or promoting protein anabolism.

Background Art

[0002] Whether protein-energy wasting (PEW) occurs or not is an important problem for a patient receiving dialysis therapy for treatment of kidney disease (hereinafter referred to as dialysis patient).

Herein, the protein-energy wasting (PEW) refers to a state in which protein and energy are deficient. The protein-energy wasting (PEW), which is associated with reduction of protein in skeletal muscle, serum, or the like, is an important factor for understanding a state of a patient after a surgical operation or the onset of a disease.

As causes of the protein-energy wasting (PEW) or the like in a dialysis patient, there are given, for example, deficiencies of protein intake and energy due to reduction in appetite, loss of amino acid and protein during dialysis therapy (i.e. excretion into a dialysate), increase of muscle protein catabolism (i.e. degradation), and inflammation of skeletal muscle.

[0003] Reduction of muscle protein catabolism (degradation) or promotion of muscle protein anabolism (production) is beneficial for a diseased individual who is restricted in protein and water intake and the like, such as a dialysis patient, in view of suppression of exhaustion of physical power due to decreased muscle mass.

Hitherto, various methods for reduction of protein catabolism and the like have been known.

For example, in Patent Literature 1, there is a disclosure of a method involving using a composition containing a proteinaceous substance in the manufacture of a medicine for treating a subject (i.e. patient) having insulin resistance, in which the proteinaceous substance provides at least 24.0% of the energy value of the composition and at least 12% by weight of leucine is provided based on the proteinaceous substance.

[0004] In Patent Literature 2, there is a disclosure of a method of treating loss of muscle mass in an individual, the method involving a step of administering an effective amount of at least one kind of branched-chain amino acid (BCAA), a BCAA precursor, a BCAA metabolite, a BCAA-rich protein, or a protein engineered to increase a BCAA content to the individual, in which the at least one kind of BCAA, a BCAA precursor, a BCAA metabolite, a BCAA-rich protein, and a protein engineered to increase a BCAA content is antagonistic to protein catabolism.

In Patent Literature 3, there is a disclosure of a composition suitable for affecting recovery from fatigue caused by a vigorous

physical activity in an animal, in which the composition includes about 40% to about 80% of carbohydrate in total, and about 20% to about 40% of protein, and in which the carbohydrate includes about 4% to about 6% of easily-absorbable carbohydrate, about 10% to about 30% of maltodextrin, and about 20% to about 50% of starch.

Citation List

Patent Literature

- [0005] [Patent Literature 1] JP 2009-511576 A
 [Patent Literature 2] JP 2009-517473 A
 [Patent Literature 3] JP 2011-511070 A

Summary of Invention

Technical Problem

[0006] None of the technologies disclosed in Patent Literatures 1 to 3 described above has any effect demonstrated by a test (i.e. experimental data) in a human body.

 An object of the present invention is to provide an agent which can suppress or prevent decrease of muscle mass in an individual (i.e. a person) who has or may have nutritional disturbance, such as a dialysis patient (i.e. a patient receiving artificial dialysis), by reducing protein catabolism or promoting protein anabolism in a human body.

Solution to Problem

[0007] The inventors of the present invention have made intensive investigations to solve the above-mentioned problem, and consequently found that when an agent having, per 100 kcal of energy, a content of protein of from 0.5 g to 5 g, a content of phosphorus of from 10 mg to 50 mg, a content of sodium of from 10 mg to 100 mg, and a content of potassium of from 5 mg to 50 mg is used, an action of reducing protein catabolism or promoting protein anabolism in a human body is exhibited so that exhaustion of physical power due to decreased muscle mass may be suppressed or prevented. Thus, the present invention has been completed.

[0008] The present invention provides the following items [1] to [12].

[1] An agent for reducing protein catabolism or promoting protein anabolism, the agent having, per 100 kcal of energy, a content of protein of from 0.5 g to 5 g, a content of phosphorus of from 10 mg to 50 mg, a content of sodium of from 10 mg to 100 mg, and a content of potassium of from 5 mg to 50 mg.

[2] An agent for reducing protein catabolism or promoting protein anabolism, including a protein, a lipid, a nutritional carbohydrate (i.e. an available carbohydrate), a mineral, and water, the agent being capable of being ingested as a liquid food (i.e. a liquid diet), in which: the agent has, per 100 kcal of energy, a content of protein of from 0.5 g to 5 g, a content of lipid of from 1 g to 5 g, a content of nutritional carbohydrate of from 10 g to 20 g, a content of phosphorus of from 10 mg to 50 mg, a content of

sodium of from 10 mg to 100 mg, and a content of potassium of from 5 mg to 50 mg; and the agent has an energy per milliliter of from 1 kcal to 2 kcal.

[3] An agent for reducing protein catabolism or promoting protein anabolism according to Item [1] or [2], in which the agent includes a vitamin and has, per 100 kcal of energy, a content of calcium of from 10 mg to 50 mg, a content of magnesium of from 5 mg to 30 mg, a content of iron of from 0.2 mg to 2 mg, a content of zinc of from 0.2 mg to 2 mg, a content of vitamin A of from 10 µgRE to 100 µgRE, and a content of vitamin D of from 0.1 µg to 0.5 µg.

[4] An agent for reducing protein catabolism or promoting protein anabolism according to any one of Items [1] to [3], in which a single dose of the agent is from 100 milliliters to 300 milliliters.

[5] An agent for reducing protein catabolism or promoting protein anabolism according to any one of Items [1] to [4], in which the agent is for use by (i.e. is to be administered to) a dialysis patient.

[0009] [6] An agent for reducing protein catabolism or promoting protein anabolism according to any one of Items [1] to [5], in which the agent for reducing protein catabolism or promoting protein anabolism is for oral administration to a subject (i.e. a person) having a value of 0 or more, the value being obtained by subtracting a value of amino acid concentration in arterial blood in a non-ingestion state of the agent from a value of amino acid concentration in arterial blood 3 hours after ingestion of the agent.

[7] A use of an agent having, per 100 kcal of energy, a content of protein of from 0.5 g to 5 g, a content of phosphorus of from 10 mg to 50 mg, a content of sodium of from 10 mg to 100 mg, and a content of potassium of from 5 mg to 50 mg, for reducing protein catabolism or promoting protein anabolism.

[8] A use of an agent including a protein, a lipid, a nutritional carbohydrate, a mineral, and water, the agent being capable of being ingested as a liquid food, for reducing protein catabolism or promoting protein anabolism, in which: the agent has, per 100 kcal of energy, a content of protein of from 0.5 g to 5 g, a content of lipid of from 1 g to 5 g, a content of nutritional carbohydrate of from 10 g to 20 g, a content of phosphorus of from 10 mg to 50 mg, a content of sodium of from 10 mg to 100 mg, and a content of potassium of from 5 mg to 50 mg; and the agent has an energy per milliliter of from 1 kcal to 2 kcal.

[9] A use of an agent according to Item [7] or [8], for reducing protein catabolism or promoting protein anabolism, in which the agent includes a vitamin and has, per 100 kcal of energy, a calcium content of from 10 mg to 50 mg, a magnesium content of from 5 mg to 30 mg, an iron content of from 0.2 mg to 2 mg, a zinc content of from 0.2 mg to 2 mg, a vitamin A content of from 10 µgRE to 100 µgRE, and a vitamin D content of from 0.1 µg to 0.5 µg.

[10] A use of an agent according to any one of Items [7] to [9], in which a single dose of the agent is from 100 milliliters to 300 milliliters.

[11] A use of an agent according to any one of Items [7] to [10] for a dialysis patient.

[12] A use of an agent according to any one of Items [7] to [11], in which the use of an agent includes use for oral administration to a subject having a value of 0 or more, the value being obtained by subtracting a value of amino acid concentration in arterial blood in a non-ingestion state of the agent from a value of amino acid concentration in arterial blood 3 hours after ingestion of the agent.

Advantageous Effects of Invention

[0010] According to the agent of the present invention for reducing protein catabolism or promoting protein anabolism (hereinafter sometimes referred to as agent of the present invention), decrease of muscle mass in an individual who has or may have malnutrition, such as a dialysis patient, can be suppressed or prevented through reduction of protein catabolism or promotion of protein anabolism in a human body.

Description of Embodiments

[0011] An agent of the present invention for reducing protein catabolism or promoting protein anabolism has, per 100 kcal of energy, a content of protein of from 0.5 g to 5 g, a content of phosphorus of from 10 mg to 50 mg, a content of sodium of from 10 mg to 40 mg, and a content of potassium of from 5 mg to 50 mg.

The contents of protein and the like are described in detail

below.

The content of protein is from 0.5 g to 5 g, preferably from 1 g to 5 g, more preferably from 2 g to 4.5 g, and particularly preferably from 3 g to 4 g per 100 kcal of energy of the agent of the present invention. When the content is less than 0.5 g, it is difficult to give a sufficient amount of protein to an individual who ingests the agent. When the content is more than 5 g, in the case where the individual who ingests the agent is an individual who is restricted in protein intake, such as a dialysis patient, the amount of protein to be ingested is excessively large, and hence the degree of improvement of a kidney function or the like in the individual who ingests the agent may be lowered.

[0012] The content of phosphorus (P) is from 10 mg to 50 mg, preferably from 20 mg to 50 mg, more preferably from 25 mg to 45 mg, and particularly preferably from 30 mg to 40 mg per 100 kcal of energy of the agent of the present invention. When the content is less than 10 mg, it is difficult to give a sufficient amount of phosphorus to an individual who ingests the agent. When the content is more than 50 mg, in the case where the individual who ingests the agent is an individual who is restricted in phosphorus intake, such as a dialysis patient, the amount of phosphorus to be ingested is excessively large, and hence the degree of improvement of a kidney function or the like in the individual who ingests the agent may be lowered.

The content of sodium (Na) is from 10 mg to 100 mg, preferably

from 20 mg to 90 mg, more preferably from 30 mg to 80 mg, and particularly preferably from 40 mg to 80 mg per 100 kcal of energy of the agent of the present invention. When the content is less than 10 mg, it is difficult to give a sufficient amount of sodium to an individual who ingests the agent. When the content is more than 100 mg, in the case where the individual who ingests the agent is an individual who is restricted in sodium intake, such as a dialysis patient, the amount of sodium to be ingested is excessively large, and hence the degree of improvement of a kidney function or the like in the individual who ingests the agent may be lowered.

[0013] The content of potassium (K) is from 5 mg to 50 mg, preferably from 10 mg to 45 mg, more preferably from 15 mg to 40 mg, and particularly preferably from 20 mg to 40 mg per 100 kcal of energy of the agent of the present invention. When the content is less than 5 mg, it is difficult to give a sufficient amount of potassium to an individual who ingests the agent. When the content is more than 100 mg, in the case where the individual who ingests the agent is an individual who is restricted in potassium intake, such as a dialysis patient, the amount of potassium to be ingested is excessively large, and hence the degree of improvement of a kidney function or the like in the individual who ingests the agent may be lowered.

In the present invention, when each of the contents of protein, phosphorus, sodium, and potassium per 100 kcal of energy falls within the range described above, an effect of reducing protein catabolism

or promoting protein anabolism can be achieved.

[0014] The agent of the present invention can contain a lipid, a nutritional carbohydrate (i.e. a carbohydrate), other minerals (except phosphorus, sodium, and potassium described below), a vitamin, and water in addition to protein, phosphorus, sodium, and potassium. In this case, the agent of the present invention can be orally ingested as a liquid food because of inclusion of water.

Preferred examples of the lipid include medium-chain triglycerides.

The content of lipid is preferably from 1 g to 5 g, more preferably from 1.5 g to 4.5 g, and particularly preferably from 2 g to 4 g per 100 kcal of energy of the agent of the present invention. When the content is less than 1 g, it is difficult to give a sufficient amount of lipid to an individual who ingests the agent. When the content is more than 5 g, the amount of lipid to be ingested is excessively large, and hence the nutritional balance necessary for the individual who ingests the agent is poor in some cases.

Examples of the nutritional carbohydrate include soluble polysaccharides (such as dextrin, oligosaccharides, or the like).

The content of nutritional carbohydrate is preferably from 10 g to 20 g, more preferably from 12 g to 18 g, and particularly preferably from 14 g to 17 g per 100 kcal of energy of the agent of the present invention. When the content is less than 10 g, it is difficult to give a sufficient amount of nutritional carbohydrate to an individual who ingests the agent. When the content is more

than 20 g, the amount of nutritional carbohydrate to be ingested is excessively large, and hence the nutritional balance necessary for the individual who ingests the agent is poor in some cases.

[0015] Examples of the other minerals (except phosphorus, sodium, and potassium) include calcium, magnesium, iron, and zinc.

The content of calcium (Ca) is preferably from 10 mg to 50 mg, more preferably from 15 mg to 45 mg, and particularly preferably from 20 mg to 40 mg per 100 kcal of energy of the agent of the present invention. When the content is less than 10 mg, it is difficult to give a sufficient amount of calcium to an individual who ingests the agent. When the content is more than 50 mg, the amount of calcium to be ingested is excessively large, and hence the nutritional balance necessary for the individual who ingests the agent is poor in some cases.

The content of magnesium (Mg) is preferably from 5 mg to 30 mg, more preferably from 5 mg to 25 mg, and particularly preferably from 10 mg to 20 mg per 100 kcal of energy of the agent of the present invention. When the content is less than 5 mg, it is difficult to give a sufficient amount of magnesium to an individual who ingests the agent. When the content is more than 30 mg, the amount of magnesium to be ingested is excessively large, and hence the nutritional balance necessary for the individual who ingests the agent is poor and the degree of improvement of a kidney function or the like may be lowered even in an individual who is restricted in magnesium intake, such as a patient with renal insufficiency (i.e. kidney failure).

[0016] The content of iron (Fe) is preferably from 0.2 mg to 2 mg, more preferably from 0.4 mg to 1.5 mg, and particularly preferably from 0.6 mg to 1.2 mg per 100 kcal of energy of the agent of the present invention. When the content is less than 0.2 mg, it is difficult to give a sufficient amount of iron to an individual who ingests the agent. When the content is more than 2 mg, the amount of iron to be ingested is excessively large, and hence the nutritional balance necessary for the individual who ingests the agent is poor in some cases.

The content of zinc is preferably from 0.2 mg to 2 mg, more preferably from 0.3 mg to 1.5 mg, and particularly preferably from 0.5 mg to 1.2 mg per 100 kcal of energy of the agent of the present invention. When the content is less than 0.2 mg, it is difficult to give a sufficient amount of zinc to an individual who ingests the agent. When the content is more than 2 mg, the amount of zinc to be ingested is excessively large, and hence the nutritional balance necessary for the individual who ingests the agent is poor in some cases.

[0017] Examples of the vitamin include vitamin A, vitamin D, vitamin E, vitamin B1, vitamin B2, and vitamin C.

The content of vitamin A is preferably from 10 µgRE (retinol equivalent) to 100 µgRE, more preferably from 20 µgRE to 80 µgRE, and particularly preferably from 40 µgRE to 80 µgRE per 100 kcal of energy of the agent of the present invention. When the content is less than 10 µgRE, it is difficult to give a sufficient amount

of vitamin A to an individual who ingests the agent. When the content is more than 100 µgRE, the degree of improvement of a kidney function or the like may be lowered in an individual who is restricted in vitamin A intake, such as a patient with renal failure.

The content of vitamin D is preferably from 0.05 µg to 0.5 µg, more preferably from 0.05 µg to 0.3 µg, and particularly preferably from 0.1 µg to 0.2 µg per 100 kcal of energy of the agent of the present invention. When the content is less than 0.05 µg, it is difficult to give a sufficient amount of vitamin D to an individual who ingests the agent. When the content is more than 0.5 µg, the degree of improvement of a kidney function or the like may be lowered in an individual who is restricted in vitamin D intake, such as a patient with renal failure.

[0018] Vitamin E, vitamin B1, vitamin B2, vitamin C, and the like may be appropriately blended by reference to an amount generally needed for a human body.

The content of vitamin E is generally from 0.5 mg to 2 mg per 100 kcal of energy of the agent of the present invention.

The content of vitamin B1 is generally from 0.05 mg to 0.2 mg per 100 kcal of energy of the agent of the present invention.

The content of vitamin B2 is generally from 0.05 mg to 0.2 mg per 100 kcal of energy of the agent of the present invention.

The content of vitamin C is generally from 2 mg to 10 mg per 100 kcal of energy of the agent of the present invention.

In the present invention, a dietary fiber, a sweetening agent

(e.g. palatinose), an emulsifier, or the like can be further blended as a component constituting a solid content, as needed.

[0019] The content of water is such an amount that an energy per milliliter of the agent of the present invention is preferably from 1 kcal to 2 kcal, more preferably from 1.2 kcal to 1.9 kcal, and particularly preferably from 1.4 kcal to 1.8 kcal. When the value is less than 1 kcal, the burden to kidney is increased in an individual who is restricted in water intake, such as a patient with renal failure, and hence it is not preferred for improvement of the disease in some cases. When the value is more than 2 kcal, the content of water is excessively low even in an individual who is restricted in water intake, such as a patient with renal failure, and hence it may be difficult to satisfactorily maintain body functions.

[0020] As a preferred exemplary embodiment of the present invention, there is given an agent including a protein, a lipid, a nutritional carbohydrate, a mineral, and water, in which: the agent has, per 100 kcal of energy, a content of protein of from 0.5 g to 5 g, a content of lipid of from 1 g to 5 g, a content of nutritional carbohydrate of from 10 g to 20 g, a content of phosphorus of from 10 mg to 50 mg, a content of sodium of from 10 mg to 100 mg, and a content of potassium of from 5 mg to 50 mg; and the agent has an energy per milliliter of from 1 kcal to 2 kcal.

In this exemplary embodiment, it is more preferred that the agent have, per 100 kcal of energy, a content of calcium of from

10 mg to 50 mg, a content of magnesium of from 5 mg to 30 mg, a content of iron of from 0.2 mg to 2 mg, a content of zinc of from 0.2 mg to 2 mg, a content of vitamin A of from 10 µgRE to 100 µgRE, and a content of vitamin D of from 0.1 µg to 0.5 µg.

According to those preferred exemplary embodiments, an effect of reducing protein catabolism or promoting protein anabolism can be further enhanced.

[0021] The single dose (i.e. dose per administration) of the agent of the present invention is preferably from 100 milliliters to 300 milliliters, more preferably from 100 milliliters to 250 milliliters, still more preferably from 100 milliliters to 200 milliliters, particularly preferably from 100 milliliters to 150 milliliters, and most preferably from 120 milliliters to 130 milliliters. When the value is less than 100 milliliters, the amount of water to be ingested is excessively small even in an individual who is restricted in water intake, such as a patient with renal failure, and hence it may be difficult to satisfactorily maintain body functions. When the value is more than 300 milliliters, the burden to kidney is increased in an individual who is restricted in water intake, such as a patient with renal failure, and hence it is not preferred for improvement of the diseased condition in some cases.

The agent of the present invention is preferably used for a dialysis patient.

[0022] It is preferred that the agent of the present invention

be used as an agent for oral administration to an individual who has a value of 0 or more, the value being obtained by subtracting a value of amino acid concentration in arterial blood in a non-ingestion state of the agent from a value of amino acid concentration in arterial blood 3 hours after ingestion of the agent.

As a method for determining whether the agent of the present invention should be used or not, there is given a method involving calculating a value obtained by subtracting a value of amino acid concentration in arterial blood in a non-ingestion state of the agent from a value of amino acid concentration in arterial blood a predetermined period (e.g. 1 hour to 5 hours) after ingestion of the agent, and determining that in the case where the calculated value is 0 or more, the agent of the present invention is used, and in the case where the calculated value is less than 0 (i.e. negative), the agent of the present invention is not used.

[0023] The agent of the present invention can be used as an agent for reducing protein catabolism or promoting protein anabolism, specifically an agent for suppressing or preventing decrease of muscle mass in an individual who has or may have nutritional disturbance, such as a dialysis patient. The agent of the present invention can also be used as an agent for non-therapeutic use for reducing protein catabolism or promoting protein anabolism, specifically an agent for non-therapeutic use for suppressing or preventing decrease of muscle mass in an individual who has or may have nutritional disturbance, such as a dialysis patient.

Examples

[0024] The present invention is hereinafter described by way of Examples. The present invention is not limited to Examples to be described below, and various embodiments can be adopted as long as the embodiments are encompassed in the scope of claims for a patent.

[0025] [Ingestion of Agent of the Present Invention and Blood Sampling in Subject]

The following experiment involving 10 dialysis patients as subjects was performed.

The subjects each visited to a clinic after taking breakfast, ingested one pack of "Meiji Renalen MP" (trade name; manufactured by Meiji Co., Ltd.), and then received dialysis treatment for 3 hours. After completion of this 3-hour dialysis, venous blood and arterial blood samples were collected from each of the subjects.

In another week, the subjects each visited to the clinic after taking breakfast, and received dialysis treatment for 3 hours without ingestion of "Meiji Renalen MP". After completion of this 3-hour dialysis, venous blood and arterial blood samples were collected from each of the subjects.

[0026] The volume, energy and main components per pack of "Meiji Renalen MP" are as follows.

- | | |
|-------------|----------|
| (1) Volume: | 125 mL |
| (2) Energy: | 200 kcal |

(3) Main components and contents thereof

Protein (lactoprotein):	7.0 g
Lipid (including medium-chain triglycerides):	5.6 g
Nutritional carbohydrate (dextrin):	29.8 g
Sodium:	120 mg
Potassium:	60 mg
Calcium:	60 mg
Magnesium:	30 mg
Phosphorus:	70 mg
Iron:	1.76 mg
Zinc:	1.50 mg
Chlorine:	20 mg
Vitamin A:	120 µgRE
Vitamin D:	0.26 µg
Vitamin E:	2.0 mg
Vitamin B1:	0.20 mg
Vitamin B2:	0.24 mg
Vitamin B6:	1.26 mg
Vitamin C:	10.0 mg
Dietary fiber:	2.0 g
Water:	94.4 g

[0027] [Measurement of Amino Acid Concentration in Collected
Blood Sample]

An amino acid concentration in the collected blood sample was measured by the following method.

After collection of a blood sample, according to an ordinary method, plasma was separated from the blood sample. The separated plasma was put into a container containing EDTA disodium and cryopreserved until measurement. The content in the container was thawed before measurement, and the thawed content was taken at a volume of 0.5 milliliter, deproteinized, and then centrifuged (12,000 rpm, 10 minutes) with two repetitions. The supernatant was divided, and then a reaction reagent (trade name: Amino Tag Wako for amino acid autoanalysis, manufactured by Wako Pure Chemical Industries, Ltd.) was added to the supernatant, mixed and warmed to derivatize free amino acid, as a target component. Subsequently, the derivatized free amino acid was analyzed using a high performance liquid chromatography-mass spectrometry system (trade name: LCMS2020, manufactured by Shimadzu Corporation) to detect amino acid concentrations (25 types) in the blood samples. At this time, "Inertsil ODS-3" (trade name; dimensions: $\phi 2.1 \times 100$ mm, manufactured by GL Sciences Inc.) was used as a column for liquid chromatography.

[0028] [Calculation of Values a to d]

Based on the amino acid concentrations in the collected blood samples, values a to d were calculated from the following equations.

Value a="amino acid concentration in arterial blood in the case of ingesting the agent of the present invention"- "amino acid concentration in arterial blood in the case of not ingesting the

agent of the present invention" in each of the subjects

Value b="amino acid concentration in venous blood in the case of ingesting the agent of the present invention"- "amino acid concentration in arterial blood in the case of ingesting the agent of the present invention" in each of the subjects

Value c="amino acid concentration in venous blood in the case of not ingesting the agent of the present invention"- "amino acid concentration in arterial blood in the case of not ingesting the agent of the present invention" in each of the subjects

Value d=Value b-Value c

[0029] Value a represents an amount of increase of amino acid concentration in arterial blood by administration of the agent of the present invention for each of the subjects, and indicates promotion of protein anabolism.

Value b and Value c represent degrees of protein catabolism in the cases of ingesting (Value b) and not ingesting (Value c) the agent of the present invention, respectively. The fact that those values are positive values indicates that protein catabolism is promoted, and the fact that those values are negative values indicates that protein anabolism is promoted (in other words, protein catabolism is reduced). More specifically, when Value b (in the case of ingesting the agent of the present invention) is taken as an example, blood flows from an artery to a vein and hence the fact that the value obtained by subtracting an amino acid concentration in arterial blood from that in venous blood is a negative value

indicates that protein anabolism (i.e. synthesis from an amino acid) is promoted in a peripheral tissue (i.e. muscle which receives nutrient supply). On the other hand, the fact that the value obtained by subtracting an amino acid concentration in arterial blood from that in venous blood is a positive value indicates that protein catabolism (i.e. degradation to an amino acid) is promoted in a peripheral tissue (i.e. muscle which receives nutrient supply).

The fact that Value d is a negative value indicates that reduction of protein catabolism (i.e. promotion of protein anabolism) is caused by ingestion of the agent of the present invention.

[0030] [Relationship between Value d and Frequencies]

The number of combinations of the subjects (10) and types of amino acids (25) is 250. Each of those 250 combinations is counted as one frequency. In 244 frequencies except 6 frequencies which could not be measured due to a measure-operative problem (i.e. below detection sensitivity), Values d were classified into segments with a scale of 10 based on (a) Value d in the case where all of Values a were included (regardless of whether Value a was a negative value or not; 244 frequencies), (b) Value d in the case where Value a was less than 0 (i.e. negative), and (c) Value d in the case where Value a was 0 or more. Frequencies included in those segments were examined. The results are shown in Table 1.

[0031] [Table 1]

Segment of Value d	Frequency		
	All of Values a	a<0	a≥0
-60 or more and less than -50	1	0	1
-50 or more and less than -40	1	0	1
-40 or more and less than -30	0	0	0
-30 or more and less than -20	6	2	4
-20 or more and less than -10	17	3	14
-10 or more and less than 0	68	27	41
0 or more and less than 10	123	66	57
10 or more and less than 20	12	5	7
20 or more and less than 30	10	6	4
30 or more and less than 40	0	0	0
40 or more and less than 50	1	1	0
50 or more and less than 60	3	1	2
60 or more and less than 70	0	0	0
70 or more and less than 80	2	1	1
Total	244	112	132

[0032] In Table 1, in the case where Value a is less than 0 (i.e. negative), the total of frequencies of Values d included in segments of less than 0 (i.e. negative) is 32 (see part A in Table 1), and 28.6% in terms of ratio in all of values a of less than 0 (112). In the case where Value a is less than 0, the total of frequencies of Values d included in segments of 0 or more is 80 (see part B in Table 1), and 71.4% in terms of ratio in all of values a of less than 0 (112).

In the case where Value a is 0 or more, the total of frequencies

of Values d included in segments of less than 0 (i.e. negative) is 61 (see part C in Table 1), and 46.2% in terms of ratio in all of Values a of 0 or more (132). In the case where Value a is 0 or more, the total of frequencies of Values d included in segments of 0 or more is 71 (see part D in Table 1), and 53.8% in terms of ratio in all of Values a of 0 or more (132).

[0033] The difference in distribution of Values d between the case of Value a of less than 0 (i.e. negative) and the case of Value a of 0 or more can be discussed as described below.

In the subject having such a result that the amino acid concentration in arterial blood is high (in other words, Value a is a positive value) or comparable (in other words, Value a is 0) in the case of ingesting the agent of the present invention as compared to the case of not ingesting the agent of the present invention, the ingestion of the agent of the present invention increases the frequency (i.e. possibility) indicating reduction of protein catabolism (in other words, Value d is a negative value) to near 50% (46.2%).

[0034] On the other hand, in the subject having such a result that the amino acid concentration in arterial blood is low (in other words, Value a is a negative value) in the case of ingesting the agent of the present invention as compared to the case of not ingesting the agent of the present invention, even when the agent of the present invention is ingested, the frequency (i.e. possibility) indicating reduction of protein catabolism (in other words, Value d is a negative

value) is as low as 28.6%.

Statistically, significant association between stratification by Value a (i.e. division into two segments at zero) and an effect of reducing protein catabolism (i.e. whether Value d is a negative value or not) was found (m×n-type contingency table test: $p=0.0183$).

[0035] Thus, when the agent of the present invention is administered to an individual having a value of 0 or more, the value being obtained by subtracting a value of amino acid concentration in arterial blood in a non-ingestion state of the agent from a value of amino acid concentration in arterial blood 3 hours after ingestion of the agent, an excellent effect of reducing protein catabolism or promoting protein anabolism is obtained in particular. This excellent effect is sufficiently confirmed by a test involving an actual dialysis patient as described above.

[0036] As described above, it is confirmed that the agent of the present invention has an excellent effect of reducing protein catabolism or promoting protein anabolism. The agent of the present invention includes components which have been sufficiently ingested as foods and hence can be provided as a food as well as a medicine. Therefore, a medicine and a food having an action of preventing a kidney disease, such as renal failure, based on the action of reducing protein catabolism or promoting protein anabolism can also be provided.

Claims

[Claim 1] An agent for reducing protein catabolism or promoting protein anabolism, the agent having, per 100 kcal of energy, a content of protein of from 0.5 g to 5 g, a content of phosphorus of from 10 mg to 50 mg, a content of sodium of from 10 mg to 100 mg, and a content of potassium of from 5 mg to 50 mg.

[Claim 2] An agent for reducing protein catabolism or promoting protein anabolism, comprising a protein, a lipid, a nutritional carbohydrate, a mineral, and water, the agent being capable of being ingested as a liquid food, wherein:

the agent has, per 100 kcal of energy, a content of protein of from 0.5 g to 5 g, a content of lipid of from 1 g to 5 g, a content of nutritional carbohydrate of from 10 g to 20 g, a content of phosphorus of from 10 mg to 50 mg, a content of sodium of from 10 mg to 100 mg, and a content of potassium of from 5 mg to 50 mg; and

the agent has an energy per milliliter of from 1 kcal to 2 kcal.

[Claim 3] An agent for reducing protein catabolism or promoting protein anabolism according to claim 1 or 2, wherein the agent comprises a vitamin and has, per 100 kcal of energy, a content of calcium of from 10 mg to 50 mg, a content of magnesium of from 5 mg to 30 mg, a content of iron of from 0.2 mg to 2 mg, a content

of zinc of from 0.2 mg to 2 mg, a content of vitamin A of from 10 µgRE to 100 µgRE, and a content of vitamin D of from 0.05 µg to 0.5 µg.

[Claim 4] An agent for reducing protein catabolism or promoting protein anabolism according to any one of claims 1 to 3, wherein a single dose of the agent is from 100 milliliters to 300 milliliters.

[Claim 5] An agent for reducing protein catabolism or promoting protein anabolism according to any one of claims 1 to 4, wherein the agent is for use by a dialysis patient.

[Claim 6] An agent for reducing protein catabolism or promoting protein anabolism according to any one of claims 1 to 5, wherein the agent for reducing protein catabolism or promoting protein anabolism is for oral administration to a subject having a value of 0 or more, the value being obtained by subtracting a value of amino acid concentration in arterial blood in a non-ingestion state of the agent from a value of amino acid concentration in arterial blood 3 hours after ingestion of the agent.