

DESCRIPTION

TITLE OF INVENTION: COMPOSITION FOR IMPROVING MUSCLE
FLEXIBILITY

5

TECHNICAL FIELD

[0001]

The present invention relates to a composition for
improving muscle flexibility. The present invention also
10 relates to, for example, use of quercetin and/or quercetin
glycoside for improving muscle flexibility.

BACKGROUND ART

[0002]

15 Japan with a super aging society faces challenges in
extending healthy life expectancy and improving quality of
life (QOL) while the population aged 75 and older continues
to increase along with medical advancement. One of the
factors that shortens healthy life expectancy is locomotive
20 syndrome, i.e., a condition with a high risk of requiring
nursing care due to locomotor disorders. Pain due to
aging-related locomotive disease and motor function decline
such as muscle weakness, endurance decline, and decreased
movement speed are combined with one another, leading to a
25 vicious cycle. This results in interference with
activities of daily living, possibly leading to a condition
requiring nursing care. Thus, prevention of locomotive
syndrome is the key.

[0003]

30 Motor function is not simply proportional to muscle
mass, but muscle flexibility, for example, is also known to
be involved in motor function. Thus, not only an increase
in muscle mass but also an improvement in muscle
flexibility is considered to be the key in preventing or
35 reducing motor function decline or improving motor

function.

[0004]

Quercetin is a type of flavonoids and is contained as is or in the form of glycosides in many plants including
 5 onions. PPAR- γ -activating action and the like have been reported as physiological activities of quercetin or quercetin glycosides (for example, Patent Literature 1).

CITATION LIST

10 - Patent Literature

[0005]

Patent Literature 1: JP 2017-8117 A

SUMMARY OF INVENTION

15 - Technical Problem

[0006]

Taking muscle flexibility decrease for example, it leads to difficulty in stretching and contracting muscles. An ingredient capable of improving muscle flexibility is
 20 effective in, for example, preventing or reducing motor function decline, improving motor function, or the like.

[0007]

The present invention aims to provide a composition for improving muscle flexibility.

25

- Solution to Problem

[0008]

The present inventors found that quercetin and/or quercetin glycoside (a type of flavonols) is effective in
 30 improving muscle flexibility.

[0009]

Specifically, although not limited thereto, the present invention encompasses, for example, the following composition for improving muscle flexibility.

35 (1) A composition for improving muscle flexibility,

containing quercetin and/or quercetin glycoside.

(2) The composition according to (1) above for use in at least one of reducing muscle stiffness, preventing or reducing muscle stiffness increase, improving muscle suppleness, or improving muscle elasticity.

(3) The composition according to (1) or (2) above for use in combination with exercise.

(4) The composition according to any one of (1) to (3) above, wherein the muscle is a thigh muscle.

(5) The composition according to any one of (1) to (4) above, wherein the composition is a food or beverage, a cosmetic product, or a quasi-pharmaceutical product.

(6) Use of quercetin and/or quercetin glycoside for improving muscle flexibility.

- Advantageous Effects of Invention

[0010]

The present invention can provide a composition for improving muscle flexibility.

BRIEF DESCRIPTION OF DRAWINGS

[0011]

Figure 1 is a graph showing the amount of change in muscle shear wave velocity on week 24 after the start of intervention with exercise and ingestion of test food, as compared to pre-intervention.

DESCRIPTION OF EMBODIMENTS

[0012]

The composition for improving muscle flexibility of the present invention contains quercetin and/or quercetin glycoside. Hereinafter, the composition for improving muscle flexibility of the present invention is also sometimes referred to as "the composition of the present invention". The composition of the present invention

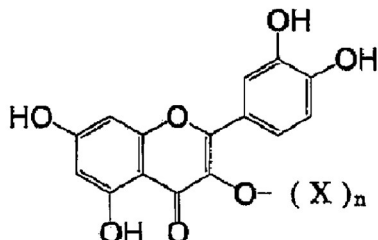
usually contains quercetin and/or quercetin glycoside as an active ingredient.

[0013]

Herein, the term "quercetin" refers to quercetin, a compound belonging to a class of polyphenols called flavonols. In the present invention, the term "quercetin glycoside" refers to a glycoside of the quercetin. Specifically, it is a collective term for a series of compounds in which one or more monosaccharides are glycosidically linked to a hydroxy group at position 3 of quercetin. A quercetin glycoside is a compound represented by the following formula. In the following formula, (X)_n represents a glycan. X represents a monosaccharide, and n is an integer of 1 or more. The quercetin glycoside may include one compound or two or more compounds.

[0014]

[Chem. 1]



[0015]

Examples of the monosaccharide of the glycan, which is glycosidically linked to quercetin and represented by X, include glucose, rhamnose, galactose, and glucuronic acid. Glucose and rhamnose are preferred. In addition, n is not limited as long as it is 1 or more, but it is preferably 1 to 16, more preferably 1 to 8. When n is 2 or more, the X moiety may contain one type of monosaccharide or multiple types of monosaccharides. In other words, when n is 2 or more, (X)_n may be a glycan containing one type of monosaccharide or a glycan containing multiple types of monosaccharides. The quercetin glycoside in the present

invention includes a quercetin glycoside obtained by treating an existing quercetin glycoside with an enzyme or the like for transglycosylation. Specific examples of the quercetin glycoside as used herein include rutin, enzyme-
5 treated rutin (enzyme-treated product of rutin), quercitrin, and isoquercitrin. In the present invention, the quercetin glycoside is particularly preferably an enzyme-treated product of rutin. Preferred examples of the enzyme-treated product of rutin include isoquercitrin
10 obtained by treating rutin with an enzyme to remove a rhamnose glycan, a product in which a glycan containing 1 to 7 glucose units are bound to isoquercitrin obtained by treating with a glycosyltransferase, and a product mainly containing a mixture thereof. In one embodiment, for
15 example, a preferred quercetin glycoside is a compound in which 1 to 8 glucose units are glycosidically linked to the hydroxy group at position 3 of quercetin (e.g., isoquercitrin or a glycoside in which 1 to 7 glucose units are bound to isoquercitrin).

20 Ingested quercetin glycoside is converted into aglycon (quercetin) by monosaccharide breakdown in the intestinal tract and is then absorbed into the body.
[0016]

In the present invention, quercetin and/or quercetin
25 glycoside may be obtained from any source and by any process. Examples of plants known to contain a large amount of quercetin and/or quercetin glycoside include buckwheat, Japanese pagoda trees, caper, apples, tea, onions, grapes, broccoli, nalta jute, raspberries,
30 cowberries, cranberries, prickly pears, leaf vegetables, and citrus fruits. Quercetin and/or quercetin glycoside can be obtained from these plants.

As long as the effect of the present invention is achieved, the quercetin and/or quercetin glycoside for use
35 in the present invention may be a naturally derived extract

of any of the above plants which has been concentrated, purified, or the like to increase the amount of quercetin and/or quercetin glycoside. For example, a concentrate or purified product of an extract containing quercetin and/or quercetin glycoside can be used. The extract can be concentrated or purified by any conventional method. In the present invention, quercetin and/or quercetin glycoside in a purified or isolated form may also be used. Quercetin and/or quercetin glycoside in a synthesized form can also be used.

[0017]

Quercetin and/or quercetin glycoside is present in natural products and food and beverages. It is a compound that has been consumed. Thus, daily ingestion of quercetin and/or quercetin glycosides, for example, is less likely to cause problems in terms of safety. The present invention can provide a composition for improving muscle flexibility, which contains a highly safe substance as an active ingredient.

[0018]

In the present invention, the term "muscle flexibility" refers to smooth stretch and contraction of muscles. It has been reported that muscle flexibility reduces with aging (for example, Muscle Nerve. 2017, Mar. 55(3), 305-315).

Muscle flexibility improvement can be rephrased as muscle stiffness (muscle stiffness level) improvement. In the present invention, the term "muscle flexibility improvement" encompasses preventing or reducing muscle flexibility decrease, maintaining muscle flexibility, enhancing muscle flexibility (increasing flexibility), and the like. The term "muscle stiffness (muscle stiffness level) improvement" encompasses preventing or reducing muscle stiffness increase, maintaining muscle stiffness, reducing muscle stiffness, and the like.

The muscle flexibility can be evaluated using muscle shear wave velocity, which is measured by shear wave elastography, as an index. The shear wave elastography is one of ultrasound elastography. It is a method of evaluating tissue hardness by applying vibrations in vivo using acoustic radiation impulses and measuring the propagation velocity distribution of shear waves generated by the vibrations (Makoto Yamakawa, Journal of Society of Biomechanism Japan, Vol. 40, No. 2 (2016), 73-78, in particular, page 74, right column, lines 10-12). A lower shear wave velocity indicates higher muscle flexibility (muscles are more supple). A higher shear wave velocity indicates lower muscle flexibility (muscles are stiffer). For example, when ingestion of a test substance resulted in a low muscle shear wave velocity or prevented or reduced an increase in muscle shear wave velocity as compared to when no test substance was ingested, the test substance is evaluated as having improved muscle flexibility or prevented or reduced muscle flexibility decrease. Thus, a substance capable of reducing the muscle shear wave velocity or preventing or reducing an increase in muscle shear wave velocity is considered to be having an action that improves muscle flexibility. In the present invention, the muscle flexibility can be confirmed by the muscle (preferably under tension) shear wave velocity described above.

[0019]

For example, the thigh muscle shear wave velocity in a fully flexed position (sitting in a kneeling position) increases with aging. As demonstrated in examples described later, ingestion of a quercetin glycoside prevented or reduced an increase in thigh muscle shear wave velocity in a fully flexed position as compared to when no quercetin glycoside was ingested. Thus, quercetin and/or quercetin glycoside has an action that improves muscle

flexibility. Quercetin and/or quercetin glycoside can be used to improve muscle flexibility. In one embodiment, quercetin and/or quercetin glycoside can be used to prevent or reduce an increase in muscle shear wave velocity or to
5 reduce the muscle shear wave velocity.

[0020]

Improving muscle flexibility can improve muscle suppleness, elasticity, and the like. In one embodiment, the composition of the present invention can be used for at
10 least one of reducing muscle stiffness, preventing or reducing muscle stiffness increase, improving muscle suppleness, or improving muscle elasticity.

Improving muscle flexibility results in effects such as increased muscle strength, increased walking ability,
15 improved balance ability, improved agility, and the like (for example, Ultrasound Med Biol. 2020 Nov; 46(11):2891-2907).

Improving muscle flexibility can also improve cutaneous muscle (for example, muscles of facial
20 expression) flexibility. As a result, an effect of improving skin elasticity can be expected.

[0021]

In one embodiment, preferably, the composition of the present invention is used in combination with exercise.
25 The composition of the present invention can be preferably used in combination with exercise for improving muscle flexibility. When the composition of the present invention is used in combination with exercise, ingestion or administration of the composition of the present invention
30 may be combined with exercise within a certain period of time. The amount of exercise, when to ingest or administer the composition of the present invention, and the like are not limited. Ingestion or administration of quercetin and/or quercetin glycoside in combination with exercise can
35 better achieve the effect of improving muscle flexibility.

The composition of the present invention when used in combination with exercise can better exert the effect of improving muscle flexibility.

The type of exercise is not limited. Examples
5 include daily exercise, aerobic exercise, strength training (e.g., resistance exercise), and stretching exercise. Only one type of exercise may be performed, or two or more types of exercise may be performed in combination. In one
10 embodiment, the exercise is preferably a combination of strength training and stretching exercise, or strength training; more preferably a combination of resistance exercise and stretching exercise, or resistance exercise; still more preferably a combination of resistance exercise and stretching exercise. In this case, the stretching
15 exercise may be performed either before or after the resistance exercise or both before and after the resistance exercise.

The resistance exercise refers to exercise with a certain resistance on muscles. Resistance may be placed on
20 muscles by any method. For example, a barbell, a machine, an adequate weight, water, an expander, a rubber tube, or the like can be used. Examples of the resistance exercise include leg extension, leg press, leg curl, chest press, squat, bench press, lateral raise, rowing, calf raise, and
25 sit-up. The resistance exercise can include one type alone or two or more types in combination. The aerobic exercise may be, for example, jogging, walking, calisthenics, aerobics, or the like.

Quercetin and/or quercetin glycoside can be used to
30 promote or enhance muscle flexibility improvement by exercise. In one embodiment, the composition of the present invention can be used to promote or enhance muscle flexibility improvement by exercise.

[0022]

35 The frequency and duration of the exercise can be,

for example, one or more times per week and five minutes or longer per time per day, (preferably, 30 minutes or longer), preferably, two or more times per week and five minutes or longer per time per day (preferably, 30 minutes or longer), more preferably three or more times per week and five minutes or longer per time per day (preferably, 30 minutes or longer). The frequency and/or duration of the exercise may be determined depending on the subject, type of exercise, and/or exercise combination. For example, in the case of aerobic exercise, the frequency and duration may be two to five days per week and about 10 to 60 minutes per time per day. In the case of resistance exercise, the frequency and duration may be one to three days per week and about 10 to 60 minutes per time per day. In the case of stretching exercise, the frequency and duration may be one to seven days per week (e.g., one to three days) and about 5 to 30 minutes per time per day.

[0023]

The exercise intensity that can be combined with the composition of the present invention is preferably 2.0 METs (e.g., walking/very slow/code 17151) or more, more preferably 2.3 METs (e.g., stretching/mild/code 02101) or more, still more preferably 3.5 METs (e.g., resistance weight training/code 02054) or more. The resistance exercise intensity is preferably 80% or less (preferably 30% or more), more preferably 60% or less (preferably 30% or more) of the repetition maximum (1RM). Preferably, the exercise load is determined depending on the subject. (For the detail of the exercise intensity, see "Revised Physical Activity METS Chart (National Institute of Health and Nutrition 2012)") and MedSci Sports Exerc. 2009 Mar; 41(3):687-708. The "codes" are described in "Revised Physical Activity METS Chart (National Institute of Health and Nutrition 2012)".)

[0024]

In the present invention, examples of the muscle as the target for muscle flexibility improvement include skeletal muscles and cutaneous muscles. Skeletal muscles are preferred. In the present invention, the site as the target for muscle flexibility improvement is not limited but is preferably a thigh muscle. In one embodiment, the composition of the present invention is preferably used for improving thigh muscle flexibility.

[0025]

The composition of the present invention is applicable for both therapeutic use and non-therapeutic use. The "non-therapeutic" is a concept that does not include medical activities, i.e., a concept that does not include methods of surgery, therapy, or diagnosis of humans.

The composition of the present invention can be provided in the form of a food or beverage, cosmetic product, pharmaceutical product, quasi-pharmaceutical product, feed, or the like. The composition of the present invention may be a food or beverage, cosmetic product, pharmaceutical product, quasi-pharmaceutical product, feed, or the like for use in improving muscle flexibility by itself, or may be a formulation or material to be added to these products.

For example, the composition for improving muscle flexibility of the present invention can be provided in the form of an agent, but it is not limited thereto. Such an agent may be provided as a composition by itself or as a composition containing the agent. In one embodiment, the composition for improving muscle flexibility of the present invention can also be referred to as a muscle flexibility improving agent.

The composition of the present invention may be either an oral composition or a parenteral composition.

Oral ingestion or administration or parenteral

administration of the composition of the present invention by or to a subject can improve muscle flexibility of the subject. The oral composition may be a food or beverage, an oral pharmaceutical product, an oral quasi-pharmaceutical product, or feed, preferably a food or beverage or an oral quasi-pharmaceutical product. The parenteral composition may be a cosmetic product, a parenteral pharmaceutical product, or a parenteral quasi-pharmaceutical product, preferably a cosmetic product or a parenteral quasi-pharmaceutical product.

[0026]

The composition of the present invention can contain optional additives and optional ingredients in addition to quercetin and/or quercetin glycoside, as long as the effect of the present invention is not impaired. Such additives and ingredients may be selected depending on the form of the composition, for example, and those generally usable in food and beverages, cosmetic products, pharmaceutical products, quasi-pharmaceutical products, feed, and the like can be used. When the composition of the present invention is provided as a food or beverage, a cosmetic product, a pharmaceutical product, a quasi-pharmaceutical product, feed, or the like, any common method can be used for the production.

[0027]

For example, when the composition of the present invention is provided as a food or beverage, ingredients usable in food and beverages (e.g., food materials and optional food additives) can be added to quercetin and/or quercetin glycoside to provide various food and beverages. The food or beverage is not limited. Examples thereof include general food and beverages, health foods, health drinks, foods with function claims, foods for specified health uses, dietary supplements, and foods for the sick. The health foods, foods with function claims, foods for

specified health uses, dietary supplements, and the like can be used in various forms of formulations such as fine granules, tablets, granules, powders, capsules, chewable tablets, dry syrups, syrups, liquid agents, beverages, and liquid foods.

[0028]

When the composition of the present invention is provided as a cosmetic product, for example, a cosmetically acceptable carrier, additive, and the like can be added to quercetin and/or quercetin glycoside. The cosmetic product may be in any product form.

[0029]

When the composition of the present invention is provided as a pharmaceutical product or a quasi-pharmaceutical product, for example, a pharmacologically acceptable carrier, an optional additive, or the like can be added to quercetin and/or quercetin glycoside to provide various dosage forms of pharmaceutical products or quasi-pharmaceutical products. Such a carrier, an additive, or the like may be any pharmacologically acceptable one that can be used in pharmaceutical products or quasi-pharmaceutical products. Examples thereof include excipients, binders, disintegrants, lubricants, antioxidants, and colorants. One or more of these can be used. The form of administration (ingestion) of the pharmaceutical or quasi-pharmaceutical product may be an oral or parenteral (transcutaneous, transmucosal, enteral, injection, or the like). When the composition of the present invention is provided as a pharmaceutical product or a quasi-pharmaceutical product, the composition is preferably an oral pharmaceutical product or quasi-pharmaceutical product (for oral administration). Examples of dosage forms for oral administration include liquids, tablets, powders, fine granules, granules, sugar-coated tablets, capsules, suspensions, emulsions, and chewable

tablets. Examples of dosage forms for parenteral administration include injection, infusion, and topical agents for skin (e.g., adhesive skin patches, creams, and ointments). The pharmaceutical product may be for non-

5 human animals.

[0030]

When the composition of the present invention is provided as feed, quercetin and/or quercetin glycoside is simply added to the feed. The feed includes feed

10 additives. Examples of the feed include feed for farm animals such as cows, pigs, chickens, sheep, and horses; feed for small animals such as rabbits, rats, and mice; and pet food for animals such as dogs, cats, and birds.

[0031]

15 The amount of quercetin and/or quercetin glycoside in the composition of the present invention is not limited and can be set according to the form or the like thereof. The amount of quercetin and/or quercetin glycoside, for example in terms of quercetin, in the composition of the present

20 invention is preferably 0.01 wt% or more, more preferably 0.1 wt% or more, and is preferably 80 wt% or less, more preferably 50 wt% or less. In one embodiment, the amount of quercetin and/or quercetin glycoside in terms of quercetin in the composition of the present invention is

25 preferably 0.01 to 80 wt%, more preferably 0.1 to 50 wt%.

The amount of quercetin and/or quercetin glycoside can be measured by a known method, such as high performance liquid chromatography (HPLC).

[0032]

30 The composition of the present invention is usually administered to or ingested by a subject. The composition of the present invention may be administered by any route, and can be ingested or administered by any method suitable to the form of the composition. In one embodiment,

35 preferably, the composition of the present invention is

orally ingested (orally administered). The administration amount (intake) of the composition of the present invention is not limited, as long as it is an amount (effective amount) that achieves the effect of improving muscle flexibility. The administration amount may be appropriately set according to the administration form, administration method, and the like.

[0033]

In one embodiment, when the composition of the present invention is ingested by or administered to a human (adult), the administration amount of quercetin and/or quercetin glycoside in terms of quercetin per 60 kg body weight per day is preferably 0.3 mg or more, more preferably 1.0 mg or more, still more preferably 10 mg or more, and is preferably 4000 mg or less, more preferably 2000 mg or less, still more preferably 1000 mg or less. In one embodiment, in the case of a human (adult), the administration amount of quercetin and/or quercetin glycoside in terms of quercetin is preferably 0.3 to 4000 mg, more preferably 1.0 to 2000 mg, still more preferably 1.0 to 1000 mg, particularly preferably 10 to 1000 mg per 60 kg body weight per day. Preferably, the above amount of the composition is ingested or administered in at least one portion per day, for example, in one to several portions (e.g., two or three portions) per day. In one embodiment, preferably, the above amount of quercetin and/or quercetin glycoside is orally ingested by or administered to a human. In one embodiment of the present invention, the composition of the present invention can be used for ingestion or administration of the above amount of quercetin and/or quercetin glycoside by or to a human per 60 kg body weight per day.

[0034]

Preferably, the composition of the present invention is continuously ingested or administered. A high effect of

improving muscle flexibility is likely to be exerted through continuous ingestion or administration of quercetin and/or quercetin glycoside. In one embodiment, the composition of the present invention is continuously
5 ingested or administered for preferably one week or more, more preferably four weeks or more, still more preferably eight weeks or more.

[0035]

The composition of the present invention can be used
10 for preventing or ameliorating a condition or disease that is likely to be prevented or ameliorated by improving muscle flexibility. Examples of such a condition or disease include conditions or diseases caused by muscle flexibility decrease and conditions or diseases that result
15 in muscle flexibility decrease. Examples of such conditions or diseases include myogenic diseases such as sarcopenia and muscular dystrophy, neurological disorders such as cerebral palsy, Parkinson's disease, and stroke (Ultrasound Med Biol. 2020 Nov; 46(11): 2891-2907). In one
20 embodiment, the composition of the present invention can be used to prevent or ameliorate abnormalities in muscles (e.g., muscle hardening) caused by conditions or diseases such as sarcopenia and muscular dystrophy, neurological disorders such as cerebral palsy, Parkinson's disease, and
25 stroke. Herein, the expression "preventing a condition or disease" encompasses preventing the onset of a condition or disease, delaying the onset, reducing the incidence rate, reducing the onset risk, and the like. The expression "ameliorating a condition or disease" encompasses helping a
30 subject recover from a condition or disease, alleviating a symptom of a condition or disease, positively reversing a condition or disease, delaying or preventing the progression of a condition or disease, and the like.

[0036]

35 The composition of the present invention may be

ingested by or administered to any subject (administration subject). The subject is preferably a human or non-human mammal, more preferably a human.

5 In one embodiment, examples of the administration subject include those needing or wanting to improve muscle flexibility and those needing or wanting to prevent or ameliorate a condition or disease caused by muscle flexibility decrease. Muscle flexibility decrease may be age-related muscle flexibility decrease, and it may be age-
10 related muscle flexibility decrease among the middle-aged and older people.

In one embodiment, examples of the administration subject in the present invention include middle-aged and older people. The middle-aged and older people include the
15 elderly. The elderly are preferred subjects among the middle-aged and older people. In the present invention, the middle-aged and older people may be those who are 40 years old and older, for example. The elderly may be those who are 60 years old and older or 65 years old and older.
20 In one embodiment, the composition of the present invention is suitably used as a composition for improving muscle flexibility for the middle-aged and older people.

The composition of the present invention may be administered to healthy people, for example, healthy
25 middle-aged and older people. For example, the composition of the present invention can be used on healthy people for purposes such as preventing a condition or disease that is likely to be prevented or ameliorated by improving muscle flexibility.

30 [0037]

The composition of the present invention may be labeled with one or more function claims based on muscle flexibility improvement. The composition for improving muscle flexibility of the present invention may be labeled
35 with one or more claims such as "enhancing muscle

flexibility", "making muscles supple", "improving muscle elasticity", and "making the body flexible".

In another embodiment, the composition of the present invention may be labeled with one or more function claims
5 such as "skin resilience", "skin firmness", "skin bounciness", "softness and resilience", and "moist and plump". The function claims may indicate that these functions can be achieved by improving muscle flexibility.

In one embodiment, preferably, the composition of the
10 present invention is a food or beverage labeled with one or more function claims described above. The function claims may be those indicating use of the composition for achieving the above functions. The labels of these function claims may be directly attached to the composition
15 or may be attached to a container or package of the composition.

[0038]

The present invention also includes the following method and use:

20 a method of improving muscle flexibility, the method including administering quercetin and/or quercetin glycoside; and

use of quercetin and/or quercetin glycoside for improving muscle flexibility.

25 The above method and use may be therapeutic or non-therapeutic. Administration (ingestion) of quercetin and/or quercetin glycoside can improve muscle flexibility. Quercetin and/or quercetin glycoside can improve muscle suppleness and/or muscle elasticity by improving muscle
30 flexibility. In one embodiment, quercetin and/or quercetin glycoside can be used for at least one selected from the group consisting of reducing muscle stiffness, preventing or reducing muscle stiffness increase, improving muscle suppleness, and improving muscle elasticity. Quercetin
35 and/or quercetin glycoside can be used, for example, for

preventing or ameliorating a condition or disease that is likely to be prevented or ameliorated by improving muscle flexibility.

[0039]

5 Preferably, quercetin and/or quercetin glycoside is used in combination with exercise for improving muscle flexibility. In the present invention, preferably, quercetin and/or quercetin glycoside is ingested or administered in combination with exercise. The muscle is
10 as described above, and thigh muscle is preferred. The exercise, its preferred embodiments, and the like are as described above.

[0040]

 In the above method and use, preferably, quercetin
15 and/or quercetin glycoside is administered to (ingested by) the subject at least once a day, for example, once to several times (for example, two or three times) per day. The quercetin and/or quercetin glycoside is as described above.

20 [0041]

 The above method and use only require use of quercetin and/or quercetin glycoside in an amount (effective amount) that achieves the effect of improving muscle flexibility. Preferred administration amounts,
25 administration subjects, administration methods, and the like of quercetin and/or quercetin glycoside are as described above for the composition for improving muscle flexibility of the present invention. The above use is preferable for humans or non-human mammals, more preferably
30 for humans. Quercetin and/or quercetin glycoside may be directly administered or may be administered in the form of a composition containing the same. For example, the composition of the present invention described above may be used. Preferably, quercetin and/or quercetin glycoside is
35 orally administered (ingested).

[0042]

Quercetin and/or quercetin glycoside can be used for production of food or beverages, cosmetic products, pharmaceutical products, quasi-pharmaceutical products, feed, or the like for use in improving muscle flexibility. In one embodiment, the present invention encompasses use of quercetin and/or quercetin glycoside for producing a composition for improving muscle flexibility. The composition for improving muscle flexibility, its preferred embodiments, and the like are as described above for the composition of the present invention.

All the academic literature and patent literature described in this description are incorporated herein by reference.

EXAMPLES

[0043]

Hereinafter, the present invention is more specifically described with reference to examples, but the present invention is not limited to these examples.

[0044]

(Example 1, Example 2, and Comparative Example 1)

<Production of test food>

Hard capsules (the size of one capsule: long diameter 19.54 mm × short diameter 6.94 mm) were produced using a quercetin glycoside (SAN EMIQ P30, San-Ei Gen F.F.I., Inc.) and an excipient to obtain a quercetin glycoside-containing food containing 200 mg of quercetin glycoside (200 mg quercetin glycoside-containing food) per six capsules and a quercetin glycoside-containing food containing 500 mg of quercetin glycoside (500 mg quercetin glycoside-containing food) per six capsules. SAN EMIQ P30 is a mixture of two or more quercetin glycosides each in which one to seven glucose units are added to quercetin. A hard capsule containing only an excipient was produced as a control food

for clinical trial. In order to prevent deterioration such as oxidation, the quercetin glycoside-containing foods and the control food were individually packaged in aluminum pouches such that each aluminum pouch contained six capsules. As many aluminum pouches as needed for the clinical trial were prepared.

[0045]

<Clinical trial>

The consent was informed to those participating in the trials, and healthy middle-aged and older people aged 50 to 74 (without an exercise habit) who agreed to the consent were subjected to a placebo-controlled, single-blind parallel-group study. The subjects were assigned into the following three groups: a group with exercise and ingestion of control food (Comparative Example 1: control food group); a group with exercise and ingestion of 200 mg quercetin glycoside-containing food (Example 1: 200 mg quercetin glycoside group); and a group with exercise and ingestion of 500 mg quercetin glycoside-containing food (Example 2: 500 mg quercetin glycoside group). Each group was subjected to intervention with exercise and ingestion of the test food for 24 weeks.

The exercise included three sets of resistance exercise per day for three days a week under the supervision of trainers (one set including four types of resistance exercise mainly for lower extremity, i.e., leg extension, leg press, leg curl, and chest press, 14 times each with load corresponding to 40% of repetition maximum (1RM)). Each type of exercise included stretching for warming up before the main exercise and stretching for cooling down after the main exercise. The 1RM measurement was performed once in four weeks, and the load weight was adjusted for each subject. Six capsules of the test food (control food or quercetin glycoside-containing food) per day were ingested with enough water or warm water.

The muscle flexibility was evaluated by measuring and quantifying the shear wave velocity using Aixplorer (Konica Minolta, Inc.) shear wave elastography mode. A lower shear wave velocity indicates higher muscle flexibility (more
 5 supple). A higher shear wave velocity indicates lower muscle flexibility (stiffer). The analysis site was the vastus lateralis muscle on the right thigh in a fully flexed position (sitting in a kneeling position). In the fully flexed position, the vastus lateralis muscle on the
 10 right thigh is in a tense condition (the muscle is stretched).

[0046]

<Analysis results>

The numbers of the analysis subjects who completed
 15 the intervention were as follows: 16 in the control food group; 16 in the 200 mg quercetin glycoside group; and 16 in the 500 mg quercetin glycoside group. In the 500 mg quercetin glycoside group, the number of subjects in analysis of the shear wave velocity on week 12 was 15
 20 because the data of one subject was missing. Table 1 shows the results of shear wave velocity (m/s) average values (the numbers in the parenthesis are standard errors). In Table 1, * denotes significant difference against the control food group (* $p < 0.05$, Dunnett's test). The
 25 results in Table 1 are the values rounded to the third decimal place.

No significant difference was found in shear wave velocity among the three groups before the intervention. Group comparison against the control food group regarding
 30 changes before and after the intervention shows that the amount of change in shear wave velocity on week 24 after the start of intervention was significantly reduced in both the 200 mg quercetin glycoside group and the 500 mg quercetin glycoside group. Figure 1 is a graph showing the
 35 amount of change in muscle shear wave velocity on week 24

after the start of intervention with exercise and ingestion of test food, as compared to pre-intervention.

[0047]

[Table 1]

5

	Measured value (average value)			Amount of change since pre-intervention	
	Before intervention	Week 12	Week 24	Week 12	Week 24
Control food group	4.66 (0.61)	4.57 (0.50)	4.41 (0.38)	-0.13 (0.28)	-0.25 (0.38)
200 mg quercetin glycoside group	5.03 (0.49)	4.67 (0.56)	4.43 (0.45)	-0.36 (0.27)	-0.60* (0.28)
500 mg quercetin glycoside group	4.97 (0.83)	4.76 (0.79)	4.36 (0.55)	-0.22 (0.49)	-0.61* (0.51)

[0048]

The muscle shear wave velocity in a fully flexed position increases with aging, i.e., muscle flexibility decreases with aging. A decrease in shear wave velocity in a fully flexed position was observed only in the quercetin glycoside ingestion group. This confirms the usefulness of ingestion of quercetin and/or quercetin glycoside on muscle flexibility.

10

CLAIMS

Claim 1. A composition for improving muscle flexibility, comprising:

5 quercetin and/or quercetin glycoside.

Claim 2. The composition according to claim 1 for use in at least one of reducing muscle stiffness, preventing or reducing muscle stiffness increase, improving muscle
10 suppleness, and improving muscle elasticity.

Claim 3. The composition according to claim 1 or 2 for use in combination with exercise.

15 Claim 4. The composition according to any one of claims 1 to 3,
 wherein the muscle is a thigh muscle.

Claim 5. The composition according to any one of
20 claims 1 to 4,
 wherein the composition is a food or beverage, a cosmetic product, or a quasi-pharmaceutical product.

Claim 6. Use of quercetin and/or quercetin glycoside
25 for improving muscle flexibility.