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(54) [Title of the Invention] Medicine for Improvement of Dementia Symptoms

(57) [Abstract]
[Objective] To smoothly improve the symptoms of dementia and provide a medicine for said improvement without side effects.
[Structure] A medicine for improvement of dementia symptoms that has as a characteristic the inclusion of docosahexaenoic acid (DHA).
[Effect] The medicine improves the following ailments caused by dementia: loss of will, delirium, worsening of human relationships, loitering, manic psychological episodes and/or the reduction of powers of calculation, reduction of judgment, and reduction in the intellectual capacities and functioning of the higher functions.

[Scope of Claims]
[Claim 1] A medicine for improvement of dementia symptoms being characterized by including as an active ingredient DHA.
[Claim 2] A medicine for improvement of dementia symptoms of claim 1 that treats an adverse psychological state that is dementia.
[Claim 3] A medicine for improvement of dementia symptoms of claim 2 working to reduce will loss, delirium, worsening of human relationships, manic states, and/or loitering.
[Claim 4] A medicine for improvement of dementia symptoms of claim 1 working to reduce the loss of higher functions and of judgment brought about by dementia.
[Claim 5] A medicine for improvement of dementia symptoms of claim 1 working to reduce the loss of intellectual capacity, loss of facilities of calculation, loss of judgment, and/or loss of higher function due to dementia.

[Detailed Description of the Invention]
[0001]
[Industrial Field of Use] The present invention is in relation to a medicine for the betterment of mental symptoms that accompany dementia, and in particular relates to a medicine for the improvement of dementia symptoms that includes as an active ingredient DHA.
[0002]
[Related Art] With the aging of society in recent years, the development of medicine for the treatment of dementia has become more important both medically and socially. For example, a dementia patient may suffer worsening family relationships as a result of loss of will, delirium, or trouble in interpersonal relationships, and the looking after of the patient within the family becomes difficult. This has been pointed out as the most serious cause for concern. In past years many medicines have been developed for dementia, but the results haven't always been satisfactory. Furthermore, the traditional medicine can cause headache, dizziness, reduction in sex drive, emotional disturbances, and other side effects such as damage to the stomach. It is with this that there has been great expectation for the development of a new medicine for dementia.
[0003] DHA is present in abundance in the brain and the thick mucus membranes. DHA is known to stop the functioning of arachidonic acid. Also, in addition to this, it is known that DHA contains several useful biological functions. For example, the following patent applications have been made: substance for the increase of brain function, medicine for the improvement of academic performance, medicine for improvement of memory, dementia prevention substance, substance for the treatment of dementia, and functional food that improves brain function (Hei 2 – 49723), cholinergic agent (Hei 1 – 279830), agent for the treatment of thrombosis (Sho 57 – 35512), among others. Among these, patent application Hei 2 – 49723 shows that DHA can aid in the improvement of academic ability as well as increasing memory performance, and also acts to prevent the formation of platelet aggregation. However, this application said nothing more and did not hint at the specific application of DHA to dementia. Also, Application Hei 1 – 279830 is in relation to the increase of transmission volume to the brain of physostigmine, a cholinesterase antagonist, via the DHA.
[0004]
[Problem Solved by the Invention] The present invention provides a medicine to improve with the symptoms of dementia without providing side effects.
[0005]
[Method of Solving the Problem] The inventors of the present invention gave DHA, widely known for being a health food, to dementia patients, whereupon the symptoms of the dementia were immediately lessened, and based on that discovery gathered to file this application.
[0006] In other words, the present invention provides a medicine for the improvement of dementia symptoms that includes DHA.
[0007] The medicine for the improvement of dementia symptoms of the present invention is applied to psychological states accompanying dementia from multiple infarction, brain blood vessel function, brain damage, or Alzheimer's disease (such as loss of will, delirium, worsening of human relationships, mania, loitering, etc.) or the reduction in intellectual capabilities (for example a reduction in the powers of calculation, a reduction in judgment, or a reduction in higher order functions).
[0008] The DHA used in the present invention is an isolated acid, and refers to salt, ester, glyceride, phospholipids, choline compounds, ascorbic acid compounds, amino acid compounds. As for the oil that includes the DHA, an inclusion ratio of 10% or more DHA (as an isolated acid) within general fatty acids. As an example of such an oil, the fish oil extracted from blue backed fish such as Japanese pilchard, mackerel, horse mackerel, salmon, and Pacific saury, the fish oil from large ocean fish eye oil, such as that of the tuna or the shipjack tuna, oil coming from microorganisms, krill oil, and oil from industrial products extracted from the livers of Pacific cod and dolphins.
[0009] The medicine for the improvement of the symptoms of dementia of the present invention may be administered either orally or non-orally. For oral administration, powder, granule, capsule, lozenge, and other solid forms of administration are acceptable. Alternatively, the medicine may be administered as syrup, elixir, and other liquid forms. Also, for non-oral administration an injection can be given. By adding these forms of manufacturing to the approved medicine that is the active portion of the drug the medicine may be manufactured in the normal fashion. Furthermore, it is also possible to turn the medicine into extended release tablets via publicly known methods. When using those manufacturing helper substances the DHA levels within the medicine for the improvement of the symptoms of dementia of the present invention is between 10 and 100 % by weight, and preferably between 50 and 100 % by weight.
[0010] An appropriate manufacturing helper substance will be used in the above in accordance with the administration method, for example, internal use substances (oral medicine), injection use substances (injected medicine), adhesive administration substances (buccal, troche, and suppositories).
[0011] For example, in oral and adhesive administration excipients (example: starch, milk sugar, crystal cellulose, milk calcium, metakei acid aluminum acid magnesium, waterless silicic acid), collapse agents (example: carboxymethylcellulose, carboxymethyl cellulose calcium), lubricants (example: sterin acid magnesium, talc), coatings (example: hydroxyl methyl

cellulose, sugar, hydroxyl propyl cellulose), and taste making agents, and other production substances may be used.

[0012] In order to manufacture granules, wet or dry droplets are formed, and in order to produce pills, it is permissible to form the tablets with the powder and granules either left as they are or with additional stearic acid magnesium, talc, or other lubricant. These granules or tablets are coated with a stomach settling agent such as hydroxypropyl – methyl cellulose phthalate or methacrylic acid or methacrylic acid methyl copolymer, among others, and coating is made using stomach setting agent or ethyl cellulose, carnauba wax, hardened oil, or other substance. By doing so a durable pharmaceutical product may be produced. Also, in order to produce the medicine in capsule form, the powder or granules are filled into a hard capsule or the active ingredients are coated with a gelatin film either as is or after being melted into gelatin, polyethelyn glycol, sesame oil, olive oil, or other oil. In this way it is possible to generate a soft capsule.

[0013] In order to produce liquid medicine for oral administration, the active ingredient and a sweetener such as refined sugar, sorbitol, glycerol are dissolved in water, a clear syrup, essential oil, and ethanol are added making an elixir-like medicine, or alternatively gum arabic, tragacanth gum, polysorbate 80, carboxymethyl cellulose (CMC), or another such substance is added and an emulsion or a suspension is produced. This is also acceptable. Flavor agents, color changing agents, and/or preservatives may be added to the liquid solutions discussed herein, according to taste.

[0014] Also, stable production medicine components are used for injectable medicine, such as solution from water soluble injectable medicine and melted helper substances (example injection use distilled water, biological salt water, or propylene glycol), suspension substances (example: polysorbate 80 or other surfactant), pH regulation substances (example: organic acid or its metal salt).

[0015] In order to produce injection-use medication, the active ingredients are mixed with salts, sodium hydroxide, emulsion, emulsion natrium, dibasic sodium phosphate, sodium dihydrogen-phosphate, and other pH adjusting agents, sodium chloride, grape sugars, and other tonicity adjusting agents in injection use distilled water. The solution is sterilized and poured into an ampoule. Alternatively, mannitol, dextrin, cyclo-dextrin, gelatin, and other substances are added, fired into crystals under vacuum conditions, and placed into a form to be melted at the time of injection. To the active ingredients are added lecithin, polysolvent 80, polyoxyethylene hydrogenated castor oil, and other substances, melted into water and made into an injectable solution.

[0016] Additionally, water or oil soluble medicines or soluble helper substances (example: alcohol, fatty acid esters), adhesives (example: carboxy vinyl polymer multi-sugars), emulsifiers (example: surfactants), and other substances are used as ingredients in externally administrable medicine. In producing rectally administered medicine the active ingredients and cocoa butter, fatty acid salts, monoglycerides and other suppository use substances are humidified, melted, poured into a mold, hardened, and frozen. Alternatively, the active ingredient could be melted in polyethylene glycol, soybean oil, or other oil, and thereafter coated in a gelatin film.

[0017] Additionally, the medicine for the improvement of dementia symptoms of the present invention with the above listed characteristics may be produced using publicly known manufacturing methods, for example as stipulated in version 10 of the Pharmacy Act of Japan, noted in the manufacturing addendum, or a method that has appropriately modified the aforementioned method.

[0018] In particular, the medicine for the improvement of dementia of the present invention administration of a high purity concentration of DHA (for example, 90% or above) via a soft capsule is desirable because of the ease of administration.

[0019] The amount of DHA administered in the medicine to prevent the symptoms of dementia of the present invention will vary based on the body weight and health conditions of the patient, but in general, the dose will range from 100 to 2000 mg / person with between one and several administrations per day.

[0020] Below we explain the present invention in detail by following an embodiment of the present invention.

[0021]

[Embodiments]

Embodiment 1. Test to measure level of psychological improvement

The targets of this test were 13 cranial blood vessel related dementia patients and 5 Alzheimer's related dementia patients. In addition to traditional treatments, 10 – 20 capsules including 70 mg of DHA each were administered (hereinafter referred to as the "DHA Administration Group"), and the results of the test were compared before administration and 6 months after administration. Also, a group that continued traditional pharmaceutical treatments (hereinafter referred to as the "Unchanging Administration Group"; 24 individuals) were targeted for the same test and the variance from the DHA Administration Group was observed. The results appear in Table 1.

[0022]

[Table 1]

Table 1. Level of Improvement in Psychological State

	Recovered	Somewhat Recovered	No Change	Worsened
Cranial Blood Vessel Dementia	9	1	2	1
Alzheimer's Dementia	0	5	0	0

[0023] To further break down the content of the "improvements" seen in the cranial blood vessel related dementia patients, 2 cases of improvement in delirium were seen, 3 cases of greatly improved ambition were observed, 3 cases of improved loitering were observed. Also, among the Alzheimer's dementia patients we observed 1 case each of improved ambition, human relationships, and manic states, respectively, for a total of 3 observed improvements. The Unchanging Administration Group did not show any change in symptoms in this same period, and all cases were evaluated to have no change.

[0024] Embodiment 2. Test to measure improvement of loss of intellectual capacity. The calculation skills, judgment, and higher functions of the same test group as test 1 were evaluated. This test was a simple evaluation of intellectual abilities. Also, a course correction and pathfinding test was administered as a simple measure of motor control. The test was administered twice, once before administration of DHA and once 6 months after the administration of DHA. The results were statistically aggregated. The results are shown in Table 2.

[0025]

[Table 2]

Table 2. Level of Improvement of Intellectual Abilities

	DHA Admin Group		Unchanged Group	
Intellectual Ability	Preadmin (at test start time)	6 months post – admin	Pre-admin	6 months post - admin
Calculation Abilities Total	6.2 +- 3.3	6.9 +- 3.0	3.4 +- 2.4	3.1 +- 3.3
Judgment Total	4.6 +- 3.0	5.5 +- 3.3	4.1 +- 2.9	2.6 +- 2.4
Higher Function Total	5.1 +- 2.9	6.0 +- 2.9	3.6 +- 3.3	2.4 +- 2.8

[0026] Note that in both the motor and IQ tests, improvements were seen after the administration of DHA.

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