

Description

The present invention relates to a composition of matter having useful physiological and nutritional activity.

It has been recognized for many years that the mammalian body requires for its nutrition relatively large amounts of fats, carbohydrates and proteins, and by contrast relatively small amounts of vitamins and minerals; lack of these latter classes of substances has been held to be accountable for the absence of general good health as well as the incidence of various specific bodily ailments. Vitamins and minerals are normally ingested or otherwise produced from the mammalian diet, but to a certain extent may also or alternatively be produced in the body. For various reasons which may be related to the source of supply or the manufacturing processes used, foods are sometimes lacking or deficient in vitamins and/or minerals, and even where vitamins are synthesized in the body, such a process may not produce the amount required. Over a period of time there has therefore grown up the use of food supplements, or nutritional compositions, to supply the ingredients of this nature required by the body, but which are either not produced therein in sufficient amounts, or are not supplied thereto by the regular diet of the subject in sufficient amounts.

Nutritional compositions are not at the present time, however, restricted merely to a content of vitamins and minerals, as the sole active ingredients. Other materials which are intermediate in metabolic processes and which it is thought may not be produced in sufficient amounts (at least in subjects with abnormal metabolism) may also be present in nutritional compositions. Examples of such other materials are unsaturated fatty acids, such as linoleic acid, gamma-linolenic acid, dihomogamma-linolenic acid arachidonic and eicosapentaenoic acids, as well as physiologically compatible derivatives thereof, such as salts, esters and amides of such acids, which may be metabolized in the body to prostaglandins. Prostaglandins are an important group of local hormones which act within the body tissues in which they are synthesized, in roles which are not entirely understood, though they may act at least to lower blood pressure, and to induce smooth muscle to contract.

Horrobin, in *Med. Hypotheses* 6: 469-486 (1980), has also proposed that a metabolic abnormality in the synthesis of certain prostaglandins is responsible for allowing an initial cancer cell to divide indefinitely, the abnormality being in particular, inhibition of the enzyme delta-6-desaturase which converts essential unsaturated fatty acids in normal cells to prostaglandins. He has also proposed pharmaceutical compositions (see e.g. EP 0037175 published October 7, 1981 and prior patent applications referred to therein,) comprising certain unsaturated fatty acids together with other ingredients which enhance formation in the body of essential prostaglandins and therefore bypass the metabolic abnormality referred to above.

In general, fatty acids in combined form are present in animal and vegetable fats and oils, but vegetable oils such as corn, cottonseed and soya oils contain in general a higher ratio of unsaturated to saturated acids, than do animal fats. A higher proportion of polyunsaturated fatty acids (such as linoleic and linolenic acids) in the diet apparently tends to reduce the incidence of heart disease, although whether this is due to a positive effect of the polyunsaturated compounds themselves, rather than to an intake of a correspondingly lower proportion of saturated compounds (and of cholesterol which is also present in animal fats), or to a lower fat intake overall, remains uncertain. "The Modern Drug Encyclopedia, 1961, 8th Edition, page 663, under the entry "Lenic" discloses serum cholesterol depressant capsules which contain a 63:2 ratio of linolenic:linoleic acids, in the presence of a substantial amount of oleic acid."

It has now been surprisingly found in accordance with the present invention, that a combination of two naturally occurring polyunsaturated acids within a certain range of proportions, produces certain beneficial effects in the human and animal body, including memory enhancement, analgesia, sleep regulation and inhibition of the symptoms of senility. Experiments carried out by the inventor support the belief that it is the combination of these acids themselves in particular proportions which is the active factor in producing the beneficial effects just referred to; there is no evidence at the present time that such effects are connected with the metabolization of these polyunsaturated acids to other substances.

The present invention accordingly provides a composition of matter which comprises (a) from 13.0 to 27.5% by weight of a compound selected from linolenic acid and derivatives thereof, calculated as the free acid, the derivatives of linolenic acid being both physiologically hydrolyzable and pharmacologically acceptable, and (b) 87.0 to 72.5% by weight of a compound selected from linoleic acid and derivatives thereof, calculated as the free acid, the derivatives of linoleic acid being both physiologically hydrolyzable and pharmacologically acceptable.

The present invention also provides, in another aspect, a pharmaceutical formulation which comprises the composition of matter as just defined, together with at least one pharmaceutically acceptable substance selected from diluents, carriers and adjuvants.

In yet another aspect, the invention provides a nutritional composition, adapted for consumption by mammals, characterized by the presence of (i) an orally ingestible diluent or carrier, (ii) at least one compound selected from linolenic acid and physiologically non-deleterious and hydrolyzable derivatives thereof and (iii) at least one compound selected from linoleic acid and physiologically non-deleterious and hydrolyzable derivatives thereof, such that the proportion of ingredient (ii) calculated as a percentage by weight of the combined ingredients (ii) and (iii) is from 13.0 to 27.5%, each of (ii) and (iii) being calculated as free acids.

It will be appreciated that the compositions and formulations of the invention are in particular intended for administration to humans, or for human consumption, for the purpose of inducing in them at least one of the aforementioned beneficial effects.

The composition of matter according to the invention preferably comprises from 14.3 to 25.0% by weight of component (a) and 85.7 to 75.0% by weight of component (b), more preferably from 16.3 to 24.4% by weight of component (a) and 83.7 to 75.6% by weight of component (b).

In accordance with a particular embodiment of the invention, a special memory enhancement effect has been noted when the composition of matter comprises from 20.0 to 24.4% by weight of component (a) and 80.0 to 75.6% by weight of component (b), or from 18.2 to 22.2% by weight of component (a) and 81.8 to 77.8% by weight of component (b); and more particularly when the composition comprises either about 22.2% by weight of component (a) and about 77.8% by weight of component (b), or about 20.0% by weight of component (a) and about 80.0% by weight of component (b).

These preferred percentage proportions by weight are also applicable to the relationship between the at least one compound selected from linolenic acid and physiologically non-deleterious and hydrolyzable derivatives thereof, and the at least one compound selected from linoleic acid and physiologically non-deleterious and hydrolyzable derivatives thereof (calculated as the free acids), in the nutritional compositions of the invention.

Since, as has been intimated above, it is believed that the combination of linoleic and linolenic acids is the active principle per se which induces the effects mentioned, it will be appreciated by those skilled in the art that instead of the acids themselves, there may be utilized in the composition of the invention derivatives of these acids which are both physiologically hydrolyzable (to the corresponding acids) and pharmacologically acceptable. Such derivatives may for example be selected from salts, esters and amides of the respective acids.

Among suitable salts there may be mentioned the ammonium, sodium, potassium, calcium and magnesium salts as salts with substituted mono- and di-substituted amines and the analogous saturated heterocyclic compounds containing an NH group in the ring, so long as the amines and the analogues in question are physiologically acceptable. As suitable esters there may be mentioned, for example, the ethyl and glyceryl esters. Amides of the acids may also be utilized, e.g. amides of the acids with substituted mono- and di-substituted amines and with the analogous saturated heterocyclic compounds containing an NH group in the ring, so long as the amines and the analogues in question are physiologically acceptable. It will be appreciated that the latter stipulation is necessary (in the case of the amine salts, the amides and their heterocyclic analogues) since it is to be expected that such derivatives will metabolize in the body to the desired acids and the starting amines or heterocyclic compounds. It will of course be evident to a person skilled in the art how to select a particular salt, ester or amide, so as to comply with the requirements of physiologically hydrolyzing to the corresponding acids, and pharmacological acceptability.

The pharmaceutical formulation provided in accordance with the present invention may be adapted for oral, parenteral or rectal administration, and it may be in the form of dosage units. The diluents, carriers and adjuvants are those conventionally used in pharmaceutical and veterinary formulation.

For oral administration, the pharmaceutical formulations of the invention may be utilized as e.g. tablets, capsules, emulsions, solutions, syrups or suspensions. For parenteral administration, the formulations may be utilized as ampoules, or otherwise as suspensions, solutions or emulsions in aqueous or oily vehicles. The need for suspending, stabilizing and/or dispersing agents will of course take account of the fact of the solubility or otherwise of the linoleic and linolenic acids, or of their derivatives used in the formulations, in the vehicles which are used in particular embodiments. Thus, for example, where the acids themselves are used, accounts will be taken of the fact that these have a relatively low water solubility and in general a relatively high oil solubility. The formulations may additionally contain e.g. physiologically compatible preservatives and antioxidants.

The pharmaceutical formulations of the invention may also be utilized as suppositories with conventional suppository bases such as cocoa butter or other glycerides. As is well known in the pharmaceutical art, the formulations may also be made available in a depot form which will release the active composition slowly in the body, over a preselected time period.

The nutritional composition according to the invention includes as a necessary component an orally ingestible diluent or carrier; this may for example comprise a substance selected from sugar-based confectionery, a manufactured cereal, a fruit or vegetable product, a beverage or beverage concentrate, or any inert diluent, carrier or excipient known in the pharmaceutical art. It is intended generally that ingredients (ii) and (iii), as previously defined, may be used in nutritional compositions in any of the forms in which these are known and practised in the art. Thus, the nutritional compositions may take the form of, e.g., sugar-based confectionery such as candies or chocolate, breakfast cereals, fruit or vegetable purees or beverages, other beverages (including those based on carbonated water), or beverage concentrates generally (including those in the form of e.g. powders, granules, flakes or crystals, which are intended to be mixed with hot or cold water and/or milk). The nutritional compositions may also generally be in the form of powders, tablets, capsules, solutions, concentrates, syrups, suspensions, gels or dispersions. It will be evident that when the nutritional compositions take the form of dispersions or suspensions, it will usually be necessary to use an acceptable (i.e. non-toxic and otherwise suitable) dispersing or suspending agent, as is well known in the nutritional and pharmaceutical arts. When these compositions are utilized in the form of capsules, it will be evident that gelatin or other known suitable ingestible materials may be used for encapsulation.

The present invention moreover includes the nutritional compositions described herein, which are adapted for consumption by non-human, as well as human mammals.

The present invention further includes nutritional compositions which also include any of the known vitamins. Thus for example, such compositions (which may be, but need not be, in the form of aqueous suspensions) may comprise at least one water-soluble vitamin selected from thiamine, riboflavin, niacin, pyridoxine, pantothenic acid, biotin, folic acid, cobalamin and ascorbic acid. Alternatively or additionally, such compositions may comprise at least one oil-soluble vitamin selected from retinol, calciferol, tocopherol and menadione. The nutritional compositions of the present invention may also comprise in combined form at least one element selected from sodium, potassium, calcium, phosphorus, magnesium, chlorine and sulfur, and additionally or alternatively, at least one element selected from iron, copper, iodine, manganese, cobalt, zinc, molybdenum, fluorine, selenium and chromium. These compositions may also contain other natural or synthetic antioxidants.

The nutritional compositions of the present invention may also comprise other unsaturated fatty acids, such as for example those known to be metabolized in the body to prostaglandins, e.g. dihomogamma-linolenic acid, arachidonic and eicosapentaenoic acids, as well as physiologically compatible derivatives thereof, such as salts, esters and amides of such acids.

The invention will be illustrated by the following Examples.

EXAMPLE 1

TREATMENT OF EXPERIMENTAL ANIMALS

METHOD:

Subjects were male Long Evans (hooded) rats weighing initially 100 g. They were housed individually in hanging stainless steel, wire-mesh cages in a well-ventilated room at an ambient temperature of 20-22° C. Light (Vita-Lite, Dura-Test, N.J.) was provided from 06.00 h. to 18.00 h. daily. A control group of rats (Group A) was fed a diet of linoleic acid 35 mg/kg diet plus linolenic acid 0.15 mg/kg diet. Other groups of rats received the same diet, plus a daily aqueous injection of a mixture of linoleic and linolenic acids (with polyethylene glycol emulsifier), each rat receiving by injection 25 mg linolenic acid, the balance being linoleic acid. (It will be appreciated that the amounts of linoleic and linolenic acids ingested by the rats from the diet just described is insignificant compared with the amounts of these substances administered by injection.) The composition of the injected unsaturated fatty acid mixture was varied among different experimental groups; the percentage by weight of linolenic acid in the mixture was as follows (balance linoleic acid): 25.0; 22.2; 20.0; 18.2; 16.7; 15.4; and 14.3 (these groups were respectively labelled B, C, D, E, F, G and H. Otherwise expressed, the ratios by weight were respectively; 1:3; 1:3.5; 1:4; 1:4.5; 1:5; 1:5.5; and 1:6.0. Another route of administration (i.e., supplemented water or an enriched diet) was tested with closely similar results. Throughout the experiment the rats had free access to food and water. Handling of the rats was kept to a minimum, so as not to interfere with the learning.

Every week groups of rats, from each treatment regimen, were tested in the learning apparatus. The level of motor activity, pain threshold, colonic temperature and d-amphetamine-induced hypothermia were tested in different groups. The order of testing was as follows: first day, motor activity; second day, pain threshold; third day, thermoregulation.

The learning apparatus is known from the scientific literature. Briefly, a circular tank (110 cm in diameter) was filled with water (at the 40 cm level), which was made opaque by the addition of powdered milk, so that rats swimming in the tank were unable to see an escape platform (7.5 cm in diameter) submerged 2 cm below the water level. Each animal was released facing the wall in one of four predetermined starting points located every 90° around the inner perimeter. A mass-learning technique was used, and each rat was tested 8 times per day in the tanks. The order of starting points was randomly predetermined. Each rat was allowed 120 seconds to find the platform, and intertrial interval was 20 seconds. The rats were tested during 3 consecutive days. During this period the platform was in the same location in the tank. After completion of the session on day 3, the platform was removed to another location in the tank, and the performance of rats in the new position was recorded. For each of the 24 trials (8 trials x 3 days) the latency to reach the platform was recorded. A cut-off point criterion (i.e., the first trial to reach latency of 10 seconds, without increasing the latency in a later trial) was used to calculate the learning capacity of each diet group. To calculate the resistance to extinction, the time which the rats spent in the "old position" in the first trial was recorded.

The level of motor activity was assessed in an open field apparatus by recording the number of horizontal movements (infrared photobeam crossing) and rearing movements (determined from videotappings) made during the 15 minute session. The apparatus was very similar to the one previously described by Coscina et al. in 1986.

Pain threshold was measured with a hot plate (60x60 cm) heated by a thermostatic bath (Hakke, Germany) to 58 ± 0.2° C. The latency to lick the paw was recorded to the nearest 0.1 second. On the third day, the basic colonic temperature of each rat was measured (YSI telethermometer, model 43TA, Yellow Springs, Ohio). The rat was then injected with 15.0 mg/kg, i.p., d-amphetamine and placed immediately into a 4° C cold room for 1 hour.

All tests were conducted between 10.00 and 14.00 h. These were 9 rats in each experimental group. At the end of each week of the experiment, the brain of the rats was removed for biochemical analysis for a different study. All experiments were conducted "double blind," i.e., the experimenter was unaware of the diet fed to the individual subjects or which treatment the rat received. Comparisons across diets and weeks of treatment were analyzed by analysis of variance with contrast tests.

RESULTS:

TABLE 1

NUTRITIONAL FACTORS

<u>GROUP</u>	<u>FOOD INTAKE(K Cal)</u>	<u>WEIGHT GAIN</u>
A	2565 +/- 39	237 +/- 4.7
B	2575 +/- 80	230 +/- 7.0
C	2545 +/- 75	235 +/- 2.8
D	2534 +/- 68	237 +/- 4.6
E	2543 +/- 72	239 +/- 6.1
F	2562 +/- 57	235 +/- 3.3
G	2586 +/- 48	238 +/- 3.9
H	2533 +/- 61	234 +/- 5.5

Unsaturated fatty acid treatment has no effect on either the amount of food intake (in kCal) or the rate of body weight gain.

LEARNING

TABLE 2
NUMBER OF TRIALS TO REACH CRITERION (10₁)

	<u>WEEKS OF TREATMENT</u>				
<u>GROUP (P)</u>	0	1	2	3	4
A(N.S.)	19.6+/-3.3	19.0+/-3.7	20.3+/-2.5	18.5+/-2.9	19.1+/-2.7
B(N.S.)	20.1+/-4.1	18.0+/-4.0	19.9+/-4.5	17.1+/-4.0	17.0+/-3.2
C(0.01)	17.1+/-3.3	12.5+/-2.1*	10.7+/-4.1*	7.9+/-3.9*	5.6+/-2.5*
D(0.001)	18.5+/-2.0	9.3+/-2.6*	7.1+/-2.9*	6.1+/-2.8*	6.1+/-2.5*
E(0.01)	19.1+/-2.3	14.2+/-3.7*	12.8+/-3.9*	9.6+/-3.0*	9.0+/-3.4*
F(0.01)	19.5+/-3.5	16.1+/-2.6	11.2+/-1.1*	9.2+/-1.8*	7.9+/-1.0*
G(N.S.)	19.7+/-3.8	18.1+/-3.3	18.4+/-2.9	17.9+/-4.1	18.6+/-2.6
H(N.S.)	21.0+/-4.0	20.0+/-3.0	19.6+/-3.1	18.8+/-3.9	19.1+/-3.0

P	N.S.	0.01	0.01	0.01	0.01
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*) Statistically differs from Control (M+/- SEM)

Treatment with the ratios 1:3.5 to 1:5 (Groups C to F) has a significant effect on the rate of learning. The optimal ratio was 1:4 (Group D).

TABLE 3**TIME IN THE 'WRONG' LOCATION: MEANS OF THE FIRST 2 TRIALS**

		<u>WEEKS OF TREATMENT</u>				
<u>GROUP(P)</u>		0	1	2	3	4
A(N.S.)	22.9+/-3	24.3+/-4	19.0+/-3	22.3+/-4	25.1+/-4	
B(N.S.)	18.5+/-3	19.4+/-4	20.6+/-6	20.6+/-4	20.1+/-5	
C(0.001)	20.3+/-4	30.9+/-2*	35.3+/-4*	39.2+/-4*	49.4+/-3*	
D(0.01)	19.5+/-3	24.1+/-3	29.3+/-4*	36.6+/-4*	39.1+/-4*	
E(0.01)	20.8+/-4	25.1+/-4	30.1+/-3*	33.1+/-4*	36.1+/-5*	
F(0.01)	19.4+/-3	22.1+/-3	29.1+/-5*	30.1+/-5*	32.2+/-5*	
G(N.S.)	22.8+/-4	19.4+/-3	19.0+/-3	19.6+/-4	18.1+/-4	
H(N.S.)	19.1+/-5	18.7+/-5	19.9+/-4	21.1+/-3	19.6+/-5	
P		N.S.	0.01	0.001	0.001	0.001

*) Statistically differs from Control (M+/- SEM).

Unsaturated fatty acid treatment with ratios of 1:3.5 - 1:5 (Groups C to F) has a significant effect on retention of the old learning. The most effective ratio was 1:3.5 (Group C).

MOTOR ACTIVITY

TABLE 4
AT THE END OF THE 4 WEEKS' TREATMENT

	<u>GROUP</u>	<u>LINE CROSSING</u>	<u>REARING</u>
5	A	76.0+/-27	75.0+/-5.0
	B	74.0+/-30	75.5+/-5.5
10	C	70.7+/-25	76.0+/-4.5
	D	70.3+/-33	84.3+/-5.5
15	E	72.1+/-29	77.7+/-6.6
	F	74.4+/-32	74.6+/-5.1
	G	72.5+/-25	76.9+/-6.1
20	H	75.5+/-31	80.0+/-5.5
	P	N.S.	N.S.

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None of the treatment has any effect on horizontal or on vertical movement.

30 PAIN THRESHOLD

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TABLE 5**WEEKS OF TREATMENT**

<u>GROUP(P)</u>	0	1	2	3	4
A(N.S.)	7.9+/- .9	7.8+/- .8	8.0+/- .6	7.9+/- .9	8.1+/- .9
B(N.S.)	8.0+/- .8	7.9+/- .7	8.0+/- .9	8.1+/- .7	7.8+/- .7
C(0.01)	7.8+/- .6	11.9+/- .7	13.9+/- .7*	16.5+/- .6*	20.1+/- 1.1*
D(0.01)	8.1+/- .8	12.1+/- .6*	14.5+/- .6*	18.2+/- .7*	21.1+/- .9*
E(0.01)	7.8+/- .6	9.0+/- .9*	9.0+/- .8*	14.1+/- .7*	17.4+/- .7*
F(0.01)	8.1+/- .9	9.9+/- .9	11.5+/- .7	14.1+/- .7*	16.3+/- .7*
G(N.S.)	7.6+/- .7	8.0+/- .3	8.8+/- .8	8.0+/- .8	8.1+/- .9
H(N.S.)	8.0+/- .9	8.0+/- .4	8.5+/- .5	8.3+/- .7	8.3+/- .7
P	N.S.	0.05	0.01	0.01	0.01

***) Statistically differs from control (M+/-SEM).**

Unsaturated fatty acid treatments with ratios of 1:3.5 to 1:4.5 (Groups C to E) cause analgesia among rats which were placed on a hot plate (58° C). The most effective ratio seems to be 1:4 (Group D).

THERMAL RESPONSE TO D-AMPHETAMINE AT 4° C

TABLE 6**WEEKS OF TREATMENT**

GROUP (P)	0	1	2	3	4
A(N.S.)	-1.9+/-0.7	-1.8+/-0.8	-1.7+/-0.6	-1.9+/-0.7	-2.0+/-0.9
B(N.S.)	-1.9+/-0.9	-1.9+/-0.9	-1.8+/-0.7	-2.0+/-0.9	-2.1+/-0.7
C(0.001)	-2.0+/-0.5	-0.9+/-0.3*	-0.8+/-0.3*	+0.9+/-0.9*	+1.1+/-0.7*
D(0.001)	-2.0+/-0.7	-0.9+/-0.6*	+0.9+/-0.5*	+1.1+/-0.7*	+1.2+/-0.6*
E(0.001)	-1.9+/-0.8	-0.6+/-0.9*	+0.6+/-0.3*	+0.9+/-0.9*	+0.9+/-0.9*
F(0.01)	-1.9+/-0.8	-0.9+/-0.7*	-0.9+/-0.7*	+0.7+/-0.5*	+1.1+/-0.9*
G(N.S.)	-1.9+/-0.9	-2.0+/-0.7	-1.8+/-0.7	-1.8+/-1.2	-1.9+/-0.7
H(N.S.)	-2.0+/-0.9	-1.9+/-0.7	-2.1+/-0.9	-2.0+/-0.9	-2.2+/-1.1
P	N.S.	0.05	0.01	0.01	0.01

***) Statistically differs from Control (M+/-SEM)**

Unsaturated fatty acid treatment protected rats from d-amphetamine induced hypothermia at ambient temperature of 4 C°. A ratio of 1:4 (Group D) seems to be most effective.

SLEEP PARAMETERS

A small number of rats (n=6) received unsaturated fatty acids at a ratio of 1:3.5 (as in Group C) for 4 weeks. At the end of the treatment period the length of total sleeping hours and REM percentage was examined and compared with saline treated rats. A strong tendency (but not statistically significant) of longer sleeping hours (+30%) and an increase in REM periods (+18%) were found in treated rats.

THE EFFECT OF IRON DEFICIENCY ON LEARNING

Iron deficiency induced severe learning deficits both in water maze and in water tank learning. Similar deficits were obtained by brain lesions. While control rats needed 19.6+/-3.3 trial to reach the criterion of learning, iron-deficient rats needed 26.4+/-1.1 to reach the same performance. Iron-deficient rats treated for 3 weeks with 1:4 ratio (as in Group D) before training reached the criterion in 15.9+/-4.8 trial while saline treated rats had the same 27.0+/-1.2 trials to criterion.

THE EFFECT OF AGING ON LEARNING

Old male rats (20-22 months old) showed a strong deficit in learning. Among 7 non-treated rats none was able to learn the swim test. The group of old rats (n=6) was able to learn the swim test after 1:4 ratio treatment (as in Group D) of 6 weeks duration. They learned the task in 15.9+/-6.1 trials. However, due to the small number of rats, and because it is one trial without replication, it is difficult to draw positive conclusions on the effect of such treatment on old age learning deficit.

EXAMPLE II

STUDY OF HUMANS

225 mg of the composition of one embodiment of the present invention which contained 22.2% by weight linolenic acid and the balance linoleic acid, was given twice daily to 12 demented geriatric patients (male and female, mean age 76.5+/-2). A comparable group of 12 geriatric patients (similar in age and severity of dementia) was given a placebo (lemonade syrup, the vehicle of the unsaturated fatty acid mixture). The treatment length was 28 days. The study was carried out in double-blind fashion; (however, there were some differences between the treatment and the lemonade, mainly in color). The medical staff, doctors and nurses, were instructed to follow the 24 subjects and to tell by the end of the period which one was "improved" on a subjective scale. The medical staff identified correctly 10 of the 12 treated patients as improved, and none of the 11 placebo group (one of the subjects in this group has to leave the experiment because of other medical problems). The patients seemed to be improved in the following aspects: they were more cooperative; they were in a better mood; appetites improved; they were able to remember their way around the hospital, and complained less about sleep disturbances. The food intake (amount and type of food) was not controlled. However, the rate of success in identifying treated subjects was highly significant.

While the present invention has been particularly described with reference to certain embodiments, it will be apparent to those skilled in the art that many modifications and variations may be made. The invention is accordingly not to be construed as limited in any way by such embodiments, rather it is to be defined only by the claims which follow.

Claims

1. A composition of matter which consists of (a) from 13.0 to 27.5% by weight of linolenic acid and/or derivatives thereof, calculated as the free acid, said derivatives of linolenic acid being both physiologically hydrolyzable and pharmacologically acceptable, and (b) 87.0 to 72.5% by weight of linoleic acid and/or derivatives thereof, calculated as the free acid, said derivatives of linoleic acid being both physiologically hydrolyzable and pharmacologically acceptable.
2. A composition of matter according to claim 1, which consists of from 14.3 to 25.0%, preferably from 16.3 to 24.4%, more preferably from 18.2 to 22.2%, and most preferably about 20.0%, by weight of component (a), balance to make 100% component (b).
3. A composition of matter according to claim 1, which consists of from 20.0 to 24.4%, preferably about 22.2%, by weight of component (a), balance to make 100% component (b).
4. A composition of matter according to any of the preceding claims, wherein said derivatives of linolenic acid and said derivatives of linoleic acid are salts, esters and amides of the respective acids.
5. A pharmaceutical formulation which comprises ingredients (a) and (b) as identified in and in the relative percentages defined in any of the preceding claims, together with at least one pharmaceutically acceptable substance selected from diluents, carriers and adjuvants, except an oily carrier or diluent which comprises a C₈₋₁₈ saturated fatty acid, oleic acid or a derivative of these acids.
6. A pharmaceutical formulation according to claim 5, and which is adapted for oral, parenteral or rectal administration.
7. A pharmaceutical formulation according to either claim 5 or claim 6, which is in the form of dosage units.
8. A pharmaceutical formulation according to claim 5, which is in depot form which will release the active ingredients (a) and (b) slowly in the body, over a preselected time period.

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Claims

1. A composition of matter which consists of (a) from 13.0 to 27.5% by weight of linolenic acid and/or derivatives thereof, calculated as the free acid, said derivatives of linolenic acid being both physiologically hydrolyzable and pharmacologically acceptable, and (b) 87.0 to 72.5% by weight of linoleic acid and/or derivatives thereof, calculated as the free acid, said derivatives of linoleic acid being both physiologically hydrolyzable and pharmacologically acceptable.
2. A composition of matter according to claim 1, which consists of from 14.3 to 25.0%, preferably from 16.3 to 24.4%, more preferably from 18.2 to 22.2%, and most preferably about 20.0%, by weight of component (a), balance to make 100% component (b).
3. A composition of matter according to claim 1, which consists of from 20.0 to 24.4%, preferably about 22.2%, by weight of component (a), balance to make 100% component (b).
4. A composition of matter according to any of the preceding claims, wherein said derivatives of linolenic acid and said derivatives of linoleic acid are salts, esters and amides of the respective acids.
5. A pharmaceutical formulation which comprises ingredients (a) and (b) as identified in and in the relative percentages defined in any of the preceding claims, together with at least one pharmaceutically acceptable substance selected from diluents, carriers and adjuvants, except an oily carrier or diluent which comprises a C_{8-18} saturated fatty acid, oleic acid or a derivative of these acids.
6. A pharmaceutical formulation according to claim 5, and which is adapted for oral, parenteral or rectal administration.
7. A pharmaceutical formulation according to either claim 5 or claim 6, which is in the form of dosage units.
8. A pharmaceutical formulation according to claim 5, which is in depot form which will release the active ingredients (a) and (b) slowly in the body, over a preselected time period.





9. A nutritional composition, adapted for consumption by mammals, which is characterized by the presence of (i) an orally ingestible diluent or carrier, except an oily carrier or diluent which comprises a C_{8-18} saturated fatty acid, oleic acid or a derivative of these acids, (ii) linolenic acid and/or physiologically non-deleterious and hydrolyzable derivatives thereof and (iii) linoleic acid and/or physiologically non-deleterious and hydrolyzable derivatives thereof, such that the proportion of ingredient (ii) calculated as a percentage by weight of the combined ingredients (ii) and (iii) is within the range of from 13.0 to 27.5%, each of (ii) and (iii) being calculated as free acids.
10. A nutritional composition according to claim 9 and wherein said proportion is from 14.3 to 25.0%, preferably from 16.3 to 24.4, more preferably from 18.2 to 22.2, and most preferably about 20.0%.
11. A nutritional composition according to claim 9 and wherein said proportion is from 20.0 to 24.4%, preferably about 22.2%.
12. A nutritional composition according to any of claims 9 to 11, wherein said derivatives of linolenic acid and said derivatives of linoleic acid are salts, esters and amides of the respective acids.
13. A nutritional composition according to any of claims 9 to 12, wherein said orally ingestible diluent or carrier comprises a sugar-based confectionery, a manufactured cereal, a fruit or vegetable product, a beverage or beverage concentrate, a ground meat product or a vegetable analogue thereof, of any inert diluent, carrier or excipient known in the pharmaceutical art.
14. A nutritional composition according to any of claims 9 to 13, which comprises at least one of the water-soluble vitamins thiamine, riboflavin, niacin, pyridoxine, pantothenic acid, biotin, folic acid, cobalamin and ascorbic acid; the oil-soluble vitamins retinol, calciferol, tocopherol and menadione; in combined form the elements sodium, potassium, calcium, phosphorus, magnesium, chlorine and sulfur, iron, copper, iodine, manganese, cobalt, zinc, molybdenum, fluorine, selenium and chromium; unsaturated fatty acids which are known to be metabolized in the body to prostaglandins, and physiologically compatible derivatives (such as salts, esters and amides) of said fatty acids; and acceptable antioxidants, dispersing and suspending agents, and water.
15. A nutritional composition according to any of claims 9 to 14, which is in the form of a powder, tablet, capsule, solution, concentrate, syrup, suspension, gel or dispersion.
16. A composition of matter according to any of claims 1 to 4, a pharmaceutical formulation according to any of claims 5 to 8, or a nutritional composition according to any of claims 9 to 15, for use in a method of treating a human for the purpose of inducing in the human a beneficial physiological effect selected from memory enhancement, analgesia, sleep regulation and inhibition of the symptoms of senility.

Claims for the following Contracting States: GR ES

1. A process for preparing a composition of matter which comprises admixing ingredients (a) and (b) as hereinafter defined and in the proportions indicated, namely (a) from 13.0 to 27.5% by weight, based on the total weight of (a) plus (b), of linolenic acid and/or derivatives thereof, calculated as the free acid, said derivatives of linolenic acid being both physiologically hydrolyzable and pharmacologically acceptable, and (b) balance to make 100% of linoleic acid and/or derivatives thereof, calculated as the free acid, said derivatives of linoleic acid being both physiologically hydrolyzable and pharmacologically acceptable, provided that said admixing is effected in the absence of an oily carrier or diluent which comprises a C_{8-18} saturated fatty acid, oleic acid or a derivative of these acids.
2. A process according to claim 1, wherein there are admixed from 14.3 to 25.0%, preferably from 16.3 to 24.4%, more preferably from 18.2 to 22.2%, and most preferably about 20.0%, by weight of component (a), balance to make 100% component (b).
3. A process according to claim 1, wherein there are admixed from 20.0 to 24.4% by weight of component (a), preferably about 22.2%, by weight of component (a), balance to make 100% component (b).



4. A process according to any of the preceding claims, wherein said derivatives of linolenic acid and said derivatives of linoleic acid are salts, esters and amides of the respective acids.
5. A process for preparing a pharmaceutical formulation which comprises mixing together the following ingredients (a), (b) and (c), namely:
 - (a) from 13.0 to 27.5% by weight in relation to the total weight of (a) plus (b) of linolenic acid and/or derivatives thereof, calculated as the free acid, said derivatives of linolenic acid being both physiologically hydrolyzable and pharmacologically acceptable;
 - (b) 87.0 to 72.5% by weight in relation to the total weight of (a) plus (b) of linoleic acid and/or derivatives thereof, calculated as the free acid, said derivatives of linoleic acid being both physiologically hydrolyzable and pharmacologically acceptable; and
 - (c) at least one pharmaceutically acceptable substance selected from diluents, carriers and adjuvants, except an oily carrier or diluent which comprises a C₈₋₁₈ saturated fatty acid, oleic acid or a derivative of these acids.
6. A process according to claim 5, wherein the admixture is made into a form suitable for oral, parenteral or rectal administration, or/and is formed into dosage units, or is made into a depot form which will release the active ingredients (a) and (b) slowly in the body, over a preselected time period.
7. A process according to claim 6, wherein the required proportions of ingredients (a) and (b) are utilized as a preformed composition with each other, which is then admixed with ingredient (c).
8. A process according to any of claims 5 to 7, wherein component (a) constitutes from 14.3 to 25.0%, preferably from 16.3 to 24.4%, more preferably from 18.2 to 22.2%, and most preferably about 20.0%, by weight of the total combined weight of (a) plus (b), calculated as free acids.
9. A process according to any of claims 5 to 7, wherein component (a) constitutes from 20.0 to 24.4% by weight, preferably 22.2% by weight, of the total combined weight of (a) plus (b), calculated as free acids.
10. A process for making a nutritional composition, which comprising admixing ingredients including (i) an orally ingestible diluent or carrier, except an oily carrier or diluent which comprises a C₈₋₁₈ saturated fatty acid, oleic acid or a derivative of these acids, (ii) linolenic acid and/or physiologically non-deleterious and hydrolyzable derivatives thereof and (iii) linoleic acid and/or physiologically non-deleterious and hydrolyzable derivatives thereof, such that the proportion of ingredient (ii) calculated as a percentage by weight of the combined ingredients (ii) and (iii) is within the range of from 13.0 to 27.5%, each of (ii) and (iii) being calculated as free acids.
11. A process according to claim 10, wherein component (a) constitutes from 14.3 to 25.0%, preferably from 16.3 to 24.4%, more preferably from 18.2 to 22.2%, and most preferably about 20.0%, by weight of the total combined weight of (a) plus (b), calculated as free acids.
12. A process according to claim 10, wherein component (a) constitutes from 20.0 to 24.4% by weight, preferably about 22.2% by weight, of the total combined weight of (a) plus (b), calculated as free acids.
13. A process according to any of claims 10 to 12, wherein said derivatives of linolenic acid and said derivatives of linoleic acid are salts, esters and amides of the respective acids.
14. A process according to any of claims 10 to 13, wherein said orally ingestible diluent or carrier comprises a sugar-based confectionery, a manufactured cereal, a fruit or vegetable product, a beverage or beverage concentrate, a ground meat product or a vegetable analogue thereof, or any inert diluent, carrier or excipient known in the pharmaceutical art.
15. A process according to any of claims 10 to 14, wherein there is also admixed at least one additional ingredient selected from the water-soluble vitamins thiamine, riboflavin, niacin, pyridoxine, pantothenic acid, biotin, folic acid, cobalamin and ascorbic acid; the oil-soluble vitamins retinol, calciferol, tocopherol and menadione; in combined form the elements sodium, potassium, calcium, phosphorus, magnesium, chlorine and sulfur, iron, copper, iodine, manganese, cobalt, zinc, molybdenum, fluorine,



selenium and chromium; unsaturated fatty acids which are known to be metabolized in the body to prostaglandins, and physiologically compatible derivatives (such as salts, esters and amides) of said fatty acids; and acceptable antioxidants, dispersing and suspending agents, and water.

- 5 16. A process according to any of claims 10 to 15, wherein the admixture is made in the form of a powder, tablet, capsule, solution, concentrate, syrup, suspension, gel or dispersion.

Revendications

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1. Composition constituée de (a) 13,0 à 27,5 % en poids d'acide linoléique et/ou de ses dérivés, calculé sous forme d'acide libre, lesdits dérivés de l'acide linoléique étant à la fois physiologiquement hydrolysables et pharmacologiquement acceptables, et (b) 87,0 à 72,5 % en poids d'acide linoléique et/ou de ses dérivés, calculé sous forme d'acide libre, lesdits dérivés de l'acide linoléique étant à la

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2. Composition selon la revendication 1, constituée de 14,3 à 25,0 %, de préférence 16,3 à 24,4 %, en particulier 18,2 à 22,2 %, et de façon particulièrement préférée, d'environ 20,0 % en poids de composant (a), le complément à 100 % étant le composant (b).

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3. Composition selon la revendication 1, constituée de 20,0 à 24,4 %, de préférence d'environ 22,2 % en poids de composant (a), le complément à 100 % étant le composant (b).

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4. Composition selon l'une quelconque des revendications précédentes, dans laquelle lesdits dérivés de l'acide linoléique et lesdits dérivés de l'acide linoléique sont des sels, des esters et des amides des acides respectifs.

5. Formulation pharmaceutique qui comprend les composants (a) et (b) tels que définis selon l'une quelconque des revendications précédentes, et dans les pourcentages relatifs définis dans ces revendications, en association avec au moins une substance pharmaceutiquement acceptable, choisie parmi les diluants, véhicules et adjuvants, excepté un véhicule ou diluant huileux comprenant un acide gras saturé en C₈₋₁₈, l'acide oléique ou un dérivé de ces acides.

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6. Formulation pharmaceutique selon la revendication 5, et qui est adaptée à l'administration par voie orale, parentérale ou rectale.

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7. Formulation pharmaceutique selon l'une quelconque des revendications 5 ou 6, qui est sous la forme de doses unitaires.

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8. Formulation pharmaceutique selon la revendication 5, qui est sous la forme d'une réserve qui va libérer dans le corps les composants actifs (a) et (b) lentement, en une durée présélectionnée.

9. Composition alimentaire, adaptée à la consommation par les mammifères, qui est caractérisée par la présence: (i) d'un diluant ou véhicule ingérable oralement, excepté un véhicule ou diluant huileux comprenant un acide gras saturé en C₈₋₁₈, l'acide oléique ou un dérivé de ces acides, (ii) de l'acide linoléique et/ou un de ses dérivés physiologiquement non toxiques et hydrolysables et (iii) de l'acide linoléique et/ou un de ses dérivés physiologiquement non toxiques et hydrolysables, telle que la proportion du composant (ii), calculée en pourcentage en poids par rapport aux composants (ii) et (iii) combinés, est dans la gamme de 13,0 à 27,5 % les pourcentages de (ii) et de (iii) étant calculés sous forme d'acide libre.

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10. Composition alimentaire selon la revendication 9 et dans laquelle ladite proportion est de 14,3 à 25,0 %, de préférence de 16,3 à 24,4 %, en particulier de 18,2 à 22,2 %, et de façon particulièrement préférée d'environ 20,0 %.

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11. Composition alimentaire selon la revendication 9 et dans laquelle ladite proportion est de 20,0 à 24,4 %, de préférence d'environ 22,2 %.



12. Composition alimentaire selon l'une quelconque des revendications 9 à 11, dans laquelle lesdits dérivés de l'acide linoléique et lesdits dérivés de l'acide linoléique sont des sels, des esters et des amides des acides respectifs.

5 13. Composition alimentaire selon l'une quelconque des revendications 9 à 12, dans laquelle ledit diluant ou véhicule ingérable oralement comprend une confiserie à base de sucre, une céréale, un produit à base de fruits ou de légumes, une boisson ou un concentré de boisson, un produit à base de viande hachée ou un analogue végétal de celui-ci, ou tout diluant, véhicule ou excipient inerte connu dans la technique pharmaceutique.

10 14. Composition alimentaire selon l'une quelconque des revendications 9 à 13, qui comprend au moins une des vitamines hydrosolubles choisie parmi la thiamine, la riboflavine, la niacine, la pyridoxine, l'acide panthothénique, la biotine, l'acide folique, la cobalamine et l'acide ascorbique ; une des vitamines oléosolubles choisie parmi le rétinol, le calciférol, le tocophérol et la ménadione ; sous forme combinée,
15 des éléments sodium, potassium, calcium, phosphore, magnésium, chlore et soufre, fer, cuivre, iode, manganèse, cobalt, zinc, molybdène, fluor, sélénium et chrome ; un des acides gras insaturés qui sont connus pour être métabolisés en prostaglandines, et les dérivés physiologiquement acceptables desdits acides gras (tels que les sels, les esters et les amides) ; et les antioxydants, agents de mise en suspension et agents dispersants acceptables, et l'eau.

20 15. Composition alimentaire selon l'une quelconque des revendications 9 à 14, qui est sous la forme d'une poudre, d'un comprimé, d'une capsule, d'une solution, d'un concentré, d'un sirop, d'une suspension, d'un gel ou d'une dispersion.

25 16. Composition alimentaire selon l'une quelconque des revendications 1 à 4, formulation pharmaceutique selon l'une quelconque des revendications 5 à 8, ou composition alimentaire selon l'une quelconque des revendications 9 à 15, destinée à être utilisée dans un procédé de traitement chez l'homme pour induire chez celui-ci une action physiologique bénéfique choisie parmi le renforcement de la mémoire, l'analgésie, la régulation du sommeil et l'inhibition des symptômes de la sénilité.

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Revendications pour les Etats contractants suivants : GR, ES

1. Procédé pour la préparation d'une composition qui consiste à mélanger les composants (a) et (b) tels que définis ci-après, et en les proportions indiquées, à savoir (a) de 13,0 à 27,5 % en poids, par
35 rapport aux poids total de (a) plus (b), d'acide linoléique et/ou de ses dérivés, calculé sous forme d'acide libre, lesdits dérivés de l'acide linoléique étant à la fois physiologiquement hydrolysables et pharmacologiquement acceptables, et (b) le complément à 100 % d'acide linoléique et/ou de ses dérivés, calculé sous forme d'acide libre, lesdits dérivés de l'acide linoléique étant à la fois physiologiquement hydrolysables et pharmacologiquement acceptables, étant entendu que ladite opération de
40 mélange est réalisée en l'absence d'un véhicule ou diluant huileux qui comprend un acide gras saturé en C₈₋₁₈, l'acide oléique ou un dérivé de ces acides.

2. Procédé selon la revendication 1, dans lequel on mélange de 14,3 à 25,0 %, de préférence de 16,3 à 24,4 %, en particulier de 18,2 à 22,2 %, et de façon particulièrement préférée, d'environ 20,0 % en
45 poids de composant (a), et le complément à 100 % de composant (b).

3. Procédé selon la revendication 1, dans lequel on mélange de 20,0 à 24,4 % de composant (a), de préférence d'environ 22,2 % en poids de composant (a), et le complément à 100 % de composant (b).

50 4. Procédé selon l'une quelconque des revendications précédentes, dans lequel lesdits dérivés de l'acide linoléique et lesdits dérivés de l'acide linoléique sont des sels, des esters et des amides des acides respectifs.

5. Procédé pour la préparation d'une formulation pharmaceutique, qui consiste à mélanger les composants (a), (b) et (c) suivants.

55 (a) de 13,0 à 27,5 % en poids, par rapport au poids total de (a) plus (b), d'acide linoléique et/ou de ses dérivés, calculé sous forme d'acide libre, lesdits dérivés de l'acide linoléique étant à la fois physiologiquement hydrolysables et pharmacologiquement acceptables ;



(b) de 87,0 à 72,5 % en poids, par rapport au poids total de (a) plus (b), d'acide linoléique et/ou de ses dérivés, calculé sous forme d'acide libre, lesdits dérivés de l'acide linoléique étant à la fois physiologiquement hydrolysables et pharmacologiquement acceptables; et

(c) au moins une substance pharmaceutiquement acceptable, choisie parmi les diluants, véhicules et adjuvants, excepté un véhicule ou diluant huileux comprenant un acide gras saturé en C_{8-18} , l'acide oléique ou un dérivé de ces acides.

6. Procédé selon la revendication 5, dans lequel le mélange est sous une forme adaptée à l'administration par voie orale, parentérale ou rectale, ou/et sous la forme de doses unitaires, ou sous la forme d'une réserve qui libère dans le corps les composants actifs (a) et (b) lentement, en une durée prédéterminée.

7. Procédé selon la revendication 6, dans lequel les proportions requises des composants (a) et (b) sont mélangés pour obtenir une composition préformée qui est ensuite mélangée avec le composant (c).

8. Procédé selon l'une quelconque des revendications 5 à 7, dans lequel le composant (a) représente de 14,3 à 25,0 %, de préférence de 16,3 à 24,4 %, en particulier de 18,2 à 22,2 %, et de façon particulièrement préférée, d'environ 20,0 % en poids, par rapport au poids total de (a) plus (b) combiné, calculés sous forme d'acide libre.

9. Procédé selon l'une quelconque des revendications 5 à 7, dans lequel le composant (a) représente de 20,0 à 24,4 %, de préférence d'environ 22,2 % en poids, par rapport au poids total de (a) plus (b) combiné, calculés sous forme d'acide libre.

10. Procédé pour la préparation d'une composition alimentaire, qui consiste à mélanger les composants comprenant (i) un diluant ou véhicule ingérable oralement, excepté un véhicule ou diluant huileux comprenant un acide gras saturé en C_{8-18} , l'acide oléique ou un dérivé de ces acides, (ii) l'acide linoléique et/ou de ses dérivés physiologiquement non toxiques et hydrolysables et (iii) l'acide linoléique et/ou de ses dérivés physiologiquement non toxiques et hydrolysables, tels que la proportion du composant (ii), calculée en pourcentage en poids par rapport aux composants (ii) et (iii) combinés, est dans la gamme de 13,0 à 27,5 %, les pourcentages de (ii) et de (iii) étant calculés sous forme d'acide libre.

11. Procédé selon la revendication 10, dans lequel le composant (a) représente de 14,3 à 25,0 %, de préférence de 16,3 à 24,4 %, en particulier de 18,2 à 22,2 %, et de façon particulièrement préférée, d'environ 20,0 % en poids, par rapport au poids total de (a) plus (b) combiné, calculés sous forme d'acide libre.

12. Procédé selon la revendication 10, dans lequel le composant (a) représente de 20,0 à 24,4 %, de préférence d'environ 22,2 % en poids, par rapport au poids total combiné de (a) plus (b), calculés sous forme d'acide libre.

13. Procédé selon l'une quelconque des revendications 10 à 12, dans lequel lesdits dérivés de l'acide linoléique et lesdits dérivés de l'acide linoléique sont des sels, des esters et des amides des acides respectifs.

14. Procédé selon l'une quelconque des revendications 10 à 13, dans lequel ledit diluant ou véhicule ingérable oralement comprend une confiserie à base de sucre, une céréale, un produit à base de fruits ou de légumes, une boisson ou un concentré de boisson, un produit à base de viande hachée ou un analogue végétal de celui-ci, ou tout diluant, véhicule ou excipient inerte connu dans la technique pharmaceutique.

15. Procédé selon l'une quelconque des revendications 10 à 14, dans lequel on mélange également au moins un composant supplémentaire choisi parmi les vitamines hydrosolubles telles que la thiamine, la riboflavine, la niacine, la pyridoxine, l'acide panthothénique, la biotine, l'acide folique, la cobalamine et l'acide ascorbique; les vitamines oléosolubles telles que le rétinol, le calciférol, le tocophérol et la ménadione; sous forme combinée, des éléments sodium, potassium, calcium, phosphore, magnésium, chlore et soufre, fer, cuivre, iode, manganèse, cobalt, zinc, molybdène, fluor, sélénium et chrome; un

des acides gras insaturés qui sont connus pour être métabolisés en prostaglandines, et les dérivés physiologiquement acceptables (tels que les sels, esters et amides) desdits acides gras ; et les antioxydants, agents de mise en suspension et agents dispersants acceptables, et l'eau.

- 5 16. Procédé selon l'une quelconque des revendications 10 à 15, dans lequel le mélange est sous la forme d'une poudre, d'un comprimé, d'une capsule, d'une solution, d'un concentré, d'un sirop, d'une suspension, d'un gel ou d'une dispersion.

10 Ansprüche

1. Zusammensetzung aus (a) 13,0 bis 27,5 Gewichtsprozent Linolensäure und/oder ihren Derivaten, bezogen auf die freie Säure, wobei die Derivate der Linolensäure sowohl physiologisch hydrolysierbar als auch pharmakologisch akzeptabel sind, und (b) 87,0 bis 72,5 Gewichtsprozent Linolsäure und/oder
15 ihren Derivaten, bezogen auf die freie Säure, wobei die Derivate der Linolsäure sowohl physiologisch hydrolysierbar als auch pharmakologisch akzeptabel sind.
2. Zusammensetzung nach Anspruch 1 aus 14,3 bis 25,0 Gew.%, vorzugsweise 16,3 bis 24,4 Gew.%,
20 möglichst 18,2 bis 22,2 Gew.% und insbesondere etwa 20,0 Gewichtsprozent des Bestandteils (a) und dem auf 100% zu ergänzenden Rest an dem Bestandteil (b).
3. Zusammensetzung nach Anspruch 1 aus 20,0 bis 24,4 Gew.%, vorzugsweise etwa 22,2 Gew.% des Bestandteils (a) und dem auf 100% zu ergänzenden Rest an dem Bestandteil (b).
- 25 4. Zusammensetzung nach einem der vorhergehenden Ansprüche, wobei die Derivate der Linolensäure und die Derivate der Linolsäure Salze, Ester und Amide der jeweiligen Säuren sind.
5. Pharmazeutische Zusammensetzung aus den Bestandteilen (a) und (b) in den betreffenden prozentualen Anteilen nach einem der vorhergehenden Ansprüche, zusammen mit mindestens einer pharmazeutisch akzeptablen Substanz aus der Gruppe: Verdünnungsmittel, Träger und Adjuvantien, mit Ausnahme eines öligen Trägers oder Verdünnungsmittels mit einer C₈₋₁₈ gesättigten Fettsäure, von Ölsäure oder einem Derivat dieser Säuren.
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6. Pharmazeutische Zusammensetzung nach Anspruch 5 für die orale, parenterale oder rektale Verabreichung.
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7. Pharmazeutische Zusammensetzung nach Anspruch 5 oder 6 in Form von Dosiereinheiten.
8. Pharmazeutische Zusammensetzung nach Anspruch 5 in Form eines Depots, das die aktiven Bestandteile (a) und (b) langsam über eine vorher ausgewählte Zeitspanne in den Körper freigibt.
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9. Nährende Zusammensetzung für den Verzehr durch Säuger, gekennzeichnet durch Anwesenheit von (i) einem oral einnehmbaren Verdünnungsmittel oder Träger, mit Ausnahme eines öligen Trägers oder Verdünnungsmittels mit einer C₈₋₁₈ gesättigten Fettsäure, von Ölsäure oder einem Derivat dieser Säuren, (ii) Linolensäure und/oder ihren physiologisch unschädlichen und hydrolysierbaren Derivaten und (iii) Linolsäure und/oder ihren physiologisch unschädlichen und hydrolysierbaren Derivaten, so daß der Anteil des Bestandteils (ii), berechnet als prozentualer Gewichtsanteil der kombinierten Bestandteile (ii) und (iii), zwischen 13,0 und 27,5% liegt, wobei (ii) und (iii) jeweils auf freie Säuren bezogen sind.
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- 50 10. Nährende Zusammensetzung nach Anspruch 9, wobei der Anteil 14,3 bis 25,0 % ,vorzugsweise 16,3 bis 24,4 %, möglichst 18,2 bis 22,2% und insbesondere etwa 20,0% beträgt.
11. Nährende Zusammensetzung nach Anspruch 9, wobei der Anteil 20,0 bis 24,4%, vorzugsweise etwa 22,2% beträgt.
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12. Nährende Zusammensetzung nach einem der Ansprüche 9 bis 11, wobei die Derivate der Linolensäure und die Derivate der Linolsäure Salze, Ester und Amide der jeweiligen Säuren sind.



13. Nährende Zusammensetzung nach einem der Ansprüche 9 bis 12, wobei das oral einnehmbare Verdünnungsmittel oder der Träger ein Konfekt auf Zuckerbasis, ein Fertiggetreideprodukt, ein Frucht- oder ein Gemüseprodukt, ein Getränk oder Getränkekonzentrat, ein zerkleinertes Fleischprodukt oder analoges Gemüseprodukt ein inertes Verdünnungsmittel, Träger oder in der Pharmazie bekannter Exzipient ist.
14. Nährende Zusammensetzung nach einem der Ansprüche 9 bis 13, die mindestens enthält eines der wasserlöslichen Vitamine: Thiamin, Riboflavin, Niacin, Pyridoxin, Pantothenensäure, Biotin, Folsäure, Cobalamin und Ascorbinsäure; eines der fettlöslichen Vitamine: Retinol, Calciferol, Tocopherol und Menadion; in kombinierter Form die Elemente Natrium, Kalium, Calcium, Phosphor, Magnesium, Chlor und Schwefel, Eisen, Kupfer, Jod, Mangan, Kobalt, Zink, Molybdän, Fluor, Selen und Chrom; ungesättigte Fettsäuren, von denen bekannt ist, daß sie im Körper zu Prostaglandinen metabolisieren, und physiologisch verträgliche Derivate (wie Salze, Ester und Amide) dieser Fettsäuren; und akzeptable Antioxidantien, Dispersions- und Suspensionsmittel und Wasser.
15. Nährende Zusammensetzung nach einem der Ansprüche 9 bis 14 in Form eines Puders, einer Tablette, einer Kapsel, einer Lösung, eines Konzentrats, eines Sirups, einer Suspension, eines Gels oder einer Dispersion.
16. Zusammensetzung nach einem der Ansprüche 1 bis 4, pharmazeutische Formulierung nach einem der Ansprüche 5 bis 8 oder nährende Zusammensetzung nach einem der Ansprüche 9 bis 15 zur Verwendung bei einer Methode zur Behandlung des Menschen, um vorteilhafte physiologische Effekte wie Gedächtnisverbesserung, Analgesie, Schlafregulation und Unterdrückung von Alterserscheinungen zu erzielen.

Patentansprüche für folgende Vertragsstaaten: GR, ES

1. Verfahren zur Herstellung einer Zusammensetzung durch Vermischen der wie nachstehend definierten Bestandteile (a) und (b) und in den angegebenen Mengenverhältnissen, nämlich 13,0 bis 27,5 Gew.% von (a), bezogen auf das Gesamtgewicht (a) plus (b), wobei (a) Linolensäure und/oder ihre Derivate bedeutet, bezogen auf die freie Säure, und die Derivate der Linolensäure sowohl physiologisch hydrolysierbar als auch pharmakologisch akzeptabel sind, und (b) als auf 100% zu ergänzender Rest an Linolensäure und/oder ihre Derivate, bezogen auf die freie Säure, wobei die Derivate der Linolensäure sowohl physiologisch hydrolysierbar als auch pharmakologisch akzeptabel sind, mit der Maßgabe, daß das Vermischen in Abwesenheit eines öligen Trägers oder Verdünnungsmittels mit einer C₈₋₁₈ gesättigten Fettsäure, von Ölsäure oder Derivaten dieser Säuren durchgeführt wird.
2. Verfahren nach Anspruch 1, wobei 14,3 bis 25,0 Gew.%, vorzugsweise 16,3 bis 24,4 Gew.%, möglichst 18,2 bis 22,2 Gew.% und insbesondere etwa 20,0 Gew.% Bestandteil (a) und der auf 100% zu ergänzende Rest an dem Bestandteil (b) vermischt werden.
3. Verfahren nach Anspruch 1, wobei 20,0 bis 24,2 Gew.% Bestandteil (a), vorzugsweise etwa 22,2 Gew.% Bestandteil (a) und der auf 100% zu ergänzende Rest an dem Bestandteil (b) vermischt werden.
4. Verfahren nach einem der vorhergehenden Ansprüche, wobei die Derivate der Linolensäure und die Derivate der Linolensäure Salze, Ester und Amide der jeweiligen Säuren sind.
5. Verfahren zur Herstellung einer pharmazeutischen Zusammensetzung durch Vermischen der folgenden Bestandteile (a), (b) und (c), nämlich:
 - (a) hiervon 13,0 bis 27,5 Gew.%, bezogen auf das Gesamtgewicht (a) plus (b), wobei (a) Linolensäure und/oder ihre Derivate bedeutet, bezogen auf die freie Säure, und die Derivate der Linolensäure sowohl physiologisch hydrolysierbar als auch pharmakologisch akzeptabel sind;
 - (b) hiervon 87,0 bis 72,5 Gew.% bezogen auf das Gesamtgewicht (a) plus (b), wobei (b) Linolensäure und/oder ihre Derivate bedeutet, bezogen auf die freie Säure, und die Derivate der Linolensäure sowohl physiologisch hydrolysierbar als auch pharmakologisch akzeptabel sind; und
 - (c) mindestens eine pharmazeutisch akzeptable Substanz aus der Gruppe: Verdünnungsmittel, Träger und Adjuvantien, mit Ausnahme eines öligen Trägers oder Verdünnungsmittels mit einer

