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(54) **Title**: COMPOSITION FOR THE PREVENTION OR TREATMENT OF NEURODEGENERATIVE DISEASES.

(57) **Abstract**: The invention is in the field of the prevention, amelioration or treatment of neurodegenerative diseases, in particular of dementia including Alzheimer's disease, Huntington's Disease, Parkinson's disease, Multiple Sclerosis and Amyotrophic Lateral Sclerosis. The invention provides new compositions that allow an improved prevention, amelioration and treatment of such diseases. More in particular, the invention provides a composition comprisingaxanthophyll anda hydrolysate of a protein, comprising di- and tripeptides.

COMPOSITION FOR THE PREVENTION OR TREATMENT OF NEURODEGENERATIVE DISEASES.

Field of the invention

The invention is in the field of the prevention, amelioration and treatment of neurodegenerative diseases, in particular of dementia, including the vascular form of dementia and Alzheimer's disease, Huntington's Disease, Parkinson's disease, Multiple Sclerosis and Amyotrophic lateral sclerosis. The invention provides new compositions that allow an improved prevention, amelioration and treatment of such diseases.

Background of the invention

Neurodegeneration is a term for a range of overlapping conditions that primarily affect neurons in the human brain. These conditions are currently incurable and lead to the progressive loss of structure and/or function of neurons, which includes death of these cells. They result from failure in brain connectivity, which is formed by neuronal-neuronal, neuronal-glial, and glial-glial contacts. Neurons are the building blocks of the nervous system, which includes the brain and spinal cord. Neurons do not reproduce or replace themselves, so when they become damaged or die they cannot be replaced by the body. Neurodegenerative diseases (ND) cause problems with movement (ataxia) or mental functioning (dementia). Examples of neurodegenerative diseases are amyotrophic lateral sclerosis (ALS), Parkinson's disease, Huntington's disease, and dementia, which is most commonly known as Alzheimer's disease (AD). Dementias are responsible for the greatest burden of disease with Alzheimer's representing approximately 60-70% of cases. Generally, the risk of developing a neurodegenerative disease increases with aging.

The WHO has estimated that there are worldwide about 35 million AD patients; these numbers are expected to double by 2030 and triple by 2050 (1), which makes AD the most common neurodegenerative disease. Additionally, the impact of neurodegenerative diseases, such as AD, on health, quality of life, and health care costs shows the importance of finding preventive interventions that slow down the progression of ND. If prevention of cognitive decline –in the case of AD- is possible, we will be able to lower the risk of future disease and concomitant secondary damage at later ages.

The process of neurodegeneration has several aspects, which are not well-understood. Examples of these aspects are genetic mutations, protein

misfolding, protein degradation and mitochondrial dysfunction. Although the understanding of neurodegenerative diseases has noticeable advanced in the past decades, well-established treatment and prevention measures are not available.

WO2014/187942 describes the treatment or prevention of neurodegenerative disorders using menthol, linalool and/or icilin. Currently, several drugs are marketed for the treatment of ND. These drugs claim to help delaying or preventing symptoms from becoming worse, but only for a limited time. Additionally, they may help control some behavioral symptoms. However, these drugs present themselves with various side effects such as nausea, vomiting, diarrhea, muscle cramps, fatigue, weight loss, dizziness, decreased appetite, constipation and headache. This shows the clear need for treatments that may intervene with multiple mechanisms of the development of neurodegeneration.

There are a number of animal models available to study the mechanisms and causes of neurodegenerative diseases. These animal models are widely used to study the efficacy of drugs for the treatment and prevention of neurodegenerative diseases. One of the best known models is the burrowing test, wherein the behavior of mice is observed in order to assess brain damage or malfunction as well as the progression of neurodegenerative diseases. The test seems particularly useful to detect early signs of beginning dysfunction and for the monitoring of the disease progression [30]. The model has been shown to be sensitive to hippocampus damage and the progression of neurodegenerative diseases (2). In at least one Alzheimer`s disease model, neuropathological changes found in, amongst others, hippocampus regions, could be correlated with a significant reduction in burrowing performance (3).

Summary of the invention.

Employing a mouse model for neurodegenerative diseases, we found that a composition, preferably an aqueous composition comprising a xanthophyll in combination with a hydrolysate of a protein comprising di- and tripeptides may advantageously be used to treat, prevent, or ameliorate neurodegenerative diseases.

Detailed description of the invention.

The results described herein show that a composition comprising a xanthophyll and a hydrolysate of a protein, comprising di- and tripeptides provides a therapeutic effect on burrowing performance when administered to a test animal.

As used herein, the term “a xanthophyll” encompasses one or more species of xanthophylls and is equivalent to the term “at least one xanthophyll”. Examples of suitable xanthophylls are lutein and zeaxanthin.

As used herein, the term “may” encompasses the word “can,” and the term “may be” encompasses the words “is” or “are,” depending on context. Furthermore, presence of the word “may” is intended to explain options for practicing or implementing the disclosure, without limitation.

As used herein, the term “a hydrolysate of a protein comprising di- and tripeptides” refers to a hydrolysate of a protein wherein the hydrolysate comprises a certain amount of di- and tripeptides that are derived from the protein as a consequence of hydrolysis.

As used herein, the term “hydrolysis” refers to the process in which a molecule of water is added to a substance. Such a reaction is preferably performed in the presence of an enzyme.

The composition showed a pronounced increase in 2h burrowing performance of LDLr-/- Leiden mice, and the effect of the composition was found to be synergistic, i.e. more than the sum of the effects of the xanthophyll and the hydrolysate separately.

There is ample evidence that xanthophylls have a beneficial effect on inflammatory processes in brain (4), skin (5), eye (6) and liver (7, 8). Xanthophylls may be conveniently administered to a subject in need of such a treatment.

In a preferred embodiment, the xantophyll may be contained in egg yolk. When chickens are fed with a diet enriched with xanthophylls, the yolk contains increased amounts of these natural substances, which are found in the micelles. However, the amounts of xanthophylls that can be safely administered are on the one hand limited by the amount of xanthophylls contained in the egg yolk and on the other hand by the maximum amount of egg yolk that can be safely administered to a subject. In order to maximize the amount of xanthophylls that can be effectively delivered in the blood stream, strategies have been deployed to maximize the absorption of xanthophylls in the gut.

It has previously been described that the absorption in the gut may be greatly enhanced by mixing the xanthophylls-containing egg yolk with polar lipids (21). For example certain dairy products are good sources of suitable polar lipids or phospholipids.

The egg yolk may be formulated as an aqueous dispersion, such as a dairy dispersion. The absorption in the gut of xanthophylls such as lutein and

zeaxanthin is greatly enhanced by this formulation (9, 10). Without wanting to be bound by theory, it is thought that this improved absorption is due to the formation of micelles that are present in the mixtures (11).

An aqueous dispersion comprising dairy products, such as buttermilk and egg yolk containing lutein and zeaxanthin, has been used to treat individuals with early signs of age-related macular degeneration, and has shown a positive effect on visual acuity (21).

Protein hydrolysates containing di- and tripeptides have been used to treat diseases as well. A salmon protein hydrolysate has been shown to decrease the expression of ICAM-1, VCAM-1 and MCP-1 in the aortic arch of apoE-/- mice (12). *In vitro* research showed the ability of an almond protein hydrolysate to modulate levels of IL-6, IL-1β and TNF-α in macrophages (13).

EP 1685764 A1 describes the use of a food product comprising a protein hydrolysate selected from ovomucin, lysozyme and ovotransferrin for treating high blood pressure.

In Zucker Diabetic Fatty rats, a dose of 1-3 gram per day of a hydrolysate of lysozyme from egg white showed effects on inflammatory markers (14). It has also been shown that a hydrolysate of lysozyme from egg white reduced renal interleukin (Il)-1b/Il-13 mRNA expression, renal tumor necrosis factor (TNF)-α, mRNA and P22phox protein expression and glomerulosclerosis. The same composition additionally reduced albuminuria, and restored aortic endothelium-dependent relaxation (EDR). Indomethacin added to the organ bath instantly improved aortic EDR, indicating a role for cyclo-oxygenase (COX)-derived contractile prostanoids in opposing relaxation in ZDF rats. This indomethacin effect was reduced by a hydrolysate of lysozyme from egg white, and coincided with decreased renal COX-1/2 protein expression. Thus, protein hydrolysates comprising di- and tripeptides were shown to have anti-inflammatory effects. Effects on neurodegeneration have not been shown so far.

We have now found that a composition comprising a xanthophyll and a hydrolysate of a protein comprising di- and tripeptides may be advantageously used in the treatment, amelioration or prevention of neurodegenerative diseases.

The hydrolysate comprising di- and tripeptides is preferably obtained by digesting a protein with a hydrolyzing enzyme. The protein is preferably selected from the group consisting of lysozyme, ovomucin and ovotransferrin. The hydrolyzing enzyme is preferably an endopeptidase, such as a serine protease. In a particularly advantageous embodiment, the serine protease is a subtilase, preferably subtilisin,

more preferably Alcalase™.

The composition according to the invention may further comprise an additional pharmacologically active or nutritionally beneficial compound, such as a compound selected from the group consisting of an omega-3 fatty acid, docosahexaenoic acid, eicosapentaenoic acid, Uridin, vitamin D, Folic acid, Vitamin E, xanthophylls, iodine, selenium and zinc. In one embodiment, the composition according to the invention is an aqueous composition.

It is particularly preferred that the content of di- and tripeptides is above 5% of the total protein content of the composition according to the invention. In a preferred embodiment, the di- and tri-peptides may make up at least 10% of the total protein content of the composition.

It is even more preferred that at least 30%, such as 40% or 45%, such as at least 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95% or even at least 98% of the peptides in the composition, such as the aqueous composition have a molecular weight below 500 Da. This fraction contains the di- and tripeptides.

There are a large number of methods available for determining the total protein content in a food product. The skilled person is well aware of the pros and cons of each of these methods and will be able to choose an appropriate method depending on the choice of the food product. Just by way of example, the well-known Kjeldahl method may be used with ovalbumin as the standard.

The composition according to the invention may be a ready-for-use solution, as a stock solution from which the daily dose may be obtained or prepared by dilution or it may be a dry composition from which a daily dose may be obtained by adding a fluid. The composition may also be used as dry matter and mixed with a food stuff, The skilled person is well aware of these and other ways of administering a composition to a subject in need of the composition.

The di-and tripeptide content may also be expressed as a percentage of the total protein content of the composition. The composition according to the invention may therefore also be characterized by the feature that at least 30% of the peptides in the hydrolysate comprising di- and tripeptides have a molecular weight of less than 0.5 kD.

In a preferred embodiment, the composition comprises at least 10 gram of di- and tripeptides per kg of composition, such as at least 20, 40, 60, 80 or 100 gram per kg of composition. In a further preferred embodiment, the composition comprises at least 200, 400, 800, or added up to 1000 gram of di- and tripeptides per kg of composition.

A suitable daily dose of the composition for a human is between 5 and 250 gram, preferably between 10 and 200 gram, such as between 20 and 100 gram, such as 25 gram, or 50 gram. A skilled person is well aware of the recommended daily dose suitable for other subjects such as non-human animals.

One daily dose should preferably contain about at least 500 mg of di- and tripeptides, such as at least 1000 mg, 2000 mg or 5000 mg (Table 1).

Table 1: Preferred compositions according to the invention

Ingredient:	**Preferred ready for use [mg/kg composition]**	**Recommended daily dose [mg]**	**Preferred minimum conc. [mg/kg composition]**	**Preferred maximum conc. [mg/kg composition]**
Dairy polar lipids	500	12	20	10.000
Xanthophyll	50	1	5	500
Omega-3 fatty acid	9.000	200	1.000	50.000
Di- and tripeptides	100.000	2.000	10.000	900.000

The xanthophyll may be contained in an aqueous or non-aqueous solution or in a dry form. It is however preferred that the xanthophyll is contained in an aqueous dispersion. Such a dispersion is contained in the term “aqueous composition” and may be selected from the group consisting of skimmed milk, semi-skimmed milk, buttermilk, a buttermilk fraction, fermented milk, yoghurt, soy drink, soy milk, fermented soy milk, fruit juices, fruit purees, syrups, vegetable juices and vegetable purees. Preferably, the aqueous dispersion is buttermilk or a buttermilk fraction.

In a preferred embodiment, a composition according to the invention comprises at least 20 mg of dairy polar lipids per kg of composition, such as at least 40, 60, 80, or 100 mg/kg. In a preferred embodiment, the composition comprises at least 200 mg of dairy polar lipids, such as 300, 400, 500, 600, 700, 800 or 900 mg per kg of composition. Whereas there is hardly any upper limit for the dairy polar lipid content of the composition, for practical purposes the dairy polar lipid content may be kept below 10.000 mg per kg of the composition.

A xanthophyll content of at least 2 mg per kg of composition is preferred, preferably the composition comprises at least 3, 4, 5, 6, 8, 10, 15, 20, 30 or

even at least 50 mg per kg. Preferred xanthophylls are lutein and zeaxanthin. In a further preferred embodiment, the composition comprises at least 10 mg lutein per kg composition, such as 12, 14, 16, 18 or at least 20 mg per kg, such as 25, 30, 35 or at least 40 mg per kg.

In a further preferred embodiment, the invention relates to a composition comprising at least 1000 mg of omega-3 fatty acids such as DHA per kg composition, such as at least 2000. 3000. 4000, 5000, 6000, 7000, 8000, 9000 or even 10000 mg per kg composition or more. Although there is no maximum for the DHA content of the composition, for practical purposes the composition may not contain more than 50000 mg of DHA per kg of composition.

A preferred daily dose of the omega-3 fatty acid is about 50 mg, such as 100 mg, such as 150 mg, 200, 400 or 500 mg.

It should be noted that the term 'buttermilk' as used herein refers to a dairy product obtained in a fermentation of a dairy product, such as whole milk. The use of what may be called 'synthetic buttermilk', such as acidified low fat milk or fat free milk is less preferred, although it is often labelled as buttermilk by dairy manufacturers. The fermentation process enriches buttermilk with the desirable polar lipids, which are present at only low levels or entirely absent in the synthetic buttermilk products. Generally, dairy products such as buttermilk, containing at least 80 mg of polar lipids per liter are suitable for use in the manufacture of the composition of the present invention. Preferred is the use of dairy products with an even higher dairy polar lipid content, such as at least 100 mg per liter, such as 120, 140, 180. 220, 260, 300, 340, 380 or even at least 420 mg per liter.

The xanthophyll is preferably selected from the group consisting of zeaxanthin, lutein and meso-zeaxanthin and may be comprised in egg yolk. So the composition according to the invention may comprise egg yolk or an egg yolk fraction containing the xanthophyll component of the egg yolk.

It is particularly preferred that the egg yolk and the aqueous dispersion are present in a weight ratio between 1:2 to 1:7, particularly preferred are ratios between 1:2 and 1:3.

The compositions as described herein may also be in a concentrated, dehydrated or dry form, obtainable by dehydrating the aqueous compositions as described herein.

The composition according to the invention may advantageously be employed as a food product, as a food supplement, or as a medicament for the treatment of a disease. More in particular, it may be used in the treatment, prevention

or amelioration of a neurodegenerative disease, such as for example a disease selected from the group consisting of dementia including Alzheimer's disease, Huntington's Disease, Parkinson's disease, Multiple Sclerosis and Amyotrophic Lateral Sclerosis.

Examples

Example 1: production of a composition comprising a xanthophyll.

A composition comprising a xanthophyll was produced from eggs obtained by feeding lutein and zeaxanthin to chickens and collecting the yolks from eggs produced by these chickens (WO 2009/078716). These eggs are referred to as enriched eggs herein.

Feeds for producing the enriched eggs were formulated and produced within the legal requirements for animal feed. The use of lutein and zeaxanthin is regulated under EU regulation 1831/2003. The dosage of lutein and zeaxanthin in feed did not exceed the legal limit of 80 ppm in animal feed.

Enriched eggs produced by poultry that were fed the lutein and zeaxanthin enriched feed contained 45 – 80 mg lutein per kg egg yolk and 10-30 mg zeaxanthin per kg egg yolk.

The animals were also fed a diet rich in omega-3 fatty acids; the eggs contained approximately 200 mg omega-3 fatty acids per kg egg yolk, with a standard deviation of 10 mg.

Example 2 : Manufacturing of an aqueous dispersion comprising xanthophylls.

Eggs enriched with xanthophylls and DHA were produced under an ISO 22000/HACCP certified quality scheme as described in example 1. Eggs were separated in yolk and albumen in an automated facility in an ISO 22000:2005 certified plant. Egg yolk from 165,000 enriched eggs was mixed (15 min., 4°C) with 5,500 liters of buttermilk containing 80 mg polar lipids per liter, and 170 kg of sugar. The liquid was pasteurized for 3 minutes at 65°C and cooled to 4°C. This composition is herein referred to as NWT-02 or NWT-02 liquid formulation.

For storage, the composition was dried to a powder with 4(±1)% moisture content and mixed with free flowing agent (SiO_2, Sipernat 22S).

Example 3: Preparation of a protein hydrolysate comprising di- and tripeptides.

A 5% (w/v) solution of lysozyme in water (100% protein content,

Belovo SA, Bastogne, Belgium) was prepared and adjusted to a pH between 7.5 and 8.5 with 3M KOH. Hydrolysis was started by adding Alcalase(Tm) (Novozymes) to a final concentration of 4% on protein basis. The solution was incubated for a total of 5-6 hours at 60°C, under continuous stirring. Alcalase was then inactivated by increasing the temperature to 90°C for 15 minutes. The solution was then cooled down to 2°C and stored overnight under continuous stirring.

The resulting hydrolysate solution was filtered through a 10µm filter and subsequently through a 1µm filter. Thereafter, the filtrate was heat treated for 15s at 135°C and concentrated to a dry matter of 57°Brix (approximately dry matter of 45%) by a NIRO evaporator at a flow of 3300L/h at 90°C. After evaporation, the product was spray dried to obtain a powder with very good flowability properties, as evidenced by visual observation.

The final product had the following characteristics: white powder, good solubility, degree of hydrolysis of 21% (15) and a maximum molecular weight of less than 10 kDa. Peptide size distribution was as follows: 46% <500Da, 23% 500-1000 Da, 32% >1000 Da. This product is herein further referred to as NWT-03.

Example 4: Preparation of alternative protein hydrolysates.

Ovomucin, ovotransferrin, ovalbumin and casein were each individually hydrolysed by a mixture of four different commercially available proteases (protease mixtures, Newlase F, Promod 278P, Alcalase and Umamizyme).

The proteins were dissolved in water and incubated with the enzyme mix according to the manufacturer's instructions. The enzymes were then inactivated by increasing the temperature to 90°C for 15 minutes. The solution was then cooled down to 2°C and stored overnight under continuous stirring.

The hydrolysate solution was filtered through a 10 µm filter and subsequently through a 1µm filter. Thereafter, the filtrate was heat treated for 15s at 135°C and concentrated to a dry matter of 57°Brix by a NIRO evaporator at a flow of 3300L/h at 90°C. After evaporation, the product was spray dried to obtain a powder with very good flowability properties, as evidenced by visual observation.

The final product had the following characteristics: white powder, good solubility, degree of hydrolysis of 24% and a maximum molecular weight of less than 10 kDa. Peptide size distribution was as follows: 98% <500Da, 1% 500-1000 Da, 1% >1000 Da.

Example 5: Preparation of NWT-02 for mice diets.

NWT-02 was fed to mice as ad-mix through a high-fat diet, comprising 59 g NWT02/kg high fat diet containing 24% (w/w) lard fat (Research Diets, D12541, USA). This amounts to an intake of 0.16 g NWT-02/mouse/day which equals an intake of between 7 and 9 micrograms lutein/mouse/day.

Example 6: Preparation of NWT-03 for mice diets.

NWT-03 was fed to mice as ad-mix through a high-fat diet, comprising 35.7 g NWT03/kg high fat diet containing 24% (w/w) lard fat (Research Diets, D12541, USA). This amounts to an intake of 0.1 g NWT03/mouse/day.

Example 7: Preparation of NWT-02 and NWT-03 in mice diets.

NWT-02 plus NWT-03 was fed to mice as ad-mix through a high-fat diet, comprising 59 g NWT02/kg high fat diet and 35.7 g NWT03/kg high fat diet containing 24% (w/w) lard fat (Research Diets, D12541, USA). This amounts to an intake of 0.16 g NWT-02 plus 0.1 g NWT-03/mouse/day.

Example 8: In vivo animal experiments.

The study was performed using 48 male, approx. 12 weeks old, LDLr-/- Leiden mice. Mice were fed a high fat diet (HFD) containing 24% lard, as described and used earlier (16) with or without the NWT-02 and/or NWT-03 preparations as described above. All mice were fed a HFD from t=0 until t=9 weeks. Mice were matched at t=9 weeks into 4 groups of 12 mice based on body weight and plasma glucose levels. The groups formed were:

1) HFD control (n=12)
2) HFD + NWT-02 (n=12)
3) HFD + NWT-03 (n=12)
4) HFD + NWT-02 +NWT-03 (n=12)

Example 9: Functional tests

At t=9 and t=21 weeks, the mice were tested in a burrowing test as follows (according to Deacon, J Vis Exp. 2012 Jan 5; (59):e2607).

Mice were habituated to the procedure a week prior to the test by placement of the burrow tube into the home cage. After two baseline measurements (overnight, 48 h apart), the burrow test was performed. The mouse was placed in a cage with the burrow tube containing 200 g of food pellets. The tube was weighed after 2 hours.

The difference between the burrowing behaviour at the start (t = 9 weeks) and the end (t = 21 weeks) of the treatment was determined. It was found that the mice fed with a high fat diet (group 1) and those fed with a high fat diet in combination with NWT-02 burrowed substantially the same amount of material (-2,1 gram and -2,5 gram respectively) at the beginning and the end of the test (figure 1).

Mice fed with a high fat diet containing NWT-03 burrowed 12,7 gram on average, whereas the mice fed with a high fat diet comprising both NWT-02 and NWT-03 burrowed 25,2 grams on average.

It is concluded that NWT-03 has a positive effect on cognition and may be used for the treatment of neurodegenerative diseases. This effect is synergistically enhanced by the addition of NWT-02.

Example 10; testing of equivalent NWT03 preparations

The functional tests as described in example 9 were repeated with alternative sources of di- and tripeptides obtained by enzymatic digestion of Ovomucin, ovotransferrin, ovalbumin and casein, as described in example 4. The difference observed in the burrowing behaviour were marginal; all preparations tested showed that the protein hydrolysates had a positive effect on cognition and may therefore be used for the treatment of neurodegenerative diseases. This effect was again synergistically enhanced by the addition of NWT-02.

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CLAIMS

1. An aqueous composition comprising:
   a. at least one xanthophyll and
   b. a hydrolysate of a protein, comprising di- and tripeptides
   for use in the treatment, prevention or amelioration of a neurodegenerative disease, wherein the neurodegenerative disease is selected from the group consisting of dementia, Alzheimer's disease, Huntington's Disease, Parkinson's disease, Multiple Sclerosis and Amyotrophic Lateral Sclerosis, wherein the protein is selected from the group consisting of lysozyme, ovomucin, ovotransferrin, ovalbumin and casein.

2. The composition for use according to claim 1, wherein the hydrolysate is obtainable by treating the protein with an enzyme.

3. The composition for use according to claim 2, wherein the enzyme is an endopeptidase.

4. The composition for use according to claim 2 wherein the enzyme is selected from the group of enzymes consisting of a serine protease, subtilase, subtilisin, and Alcalase™.

5. The composition for use according to any one of claims 1 - 4, wherein the composition additionally comprises a pharmacologically active compound selected from the group consisting of an omega-3 fatty acid, docosahexaenoic acid, eicosapentaenoic acid, vitamin D, Uridin, Folic acid, Vitamin E, iodine, selenium and zinc.

6. The composition for use according to any one of claims 1 – 5 wherein the di- and tri-peptides make up at least 10% of the total protein content of the composition.

7. The composition for use according to any one of claims 1 – 6 wherein the di- and tripeptides have a molecular weight of less than 0.5 kD.

8. The composition for use according to any one of claims 1 – 7 wherein the at least one xanthophyll is contained in an aqueous dispersion.

9. The composition for use according to claim 8 wherein the aqueous dispersion is selected from the group consisting of skimmed milk, semi-skimmed milk,

buttermilk, a buttermilk fraction, fermented milk, yoghurt, soy drink, soy milk, fermented soy milk, fruit juices, fruit purees, syrups, vegetable juices and vegetable purees.

10. The composition for use according to claim 9 wherein the aqueous dispersion is buttermilk or a buttermilk fraction.

11. The composition for use according to any one of claims 1 – 10 wherein the at least one xanthophyll is selected from the group consisting of zeaxanthin, lutein and meso-zeaxanthin.

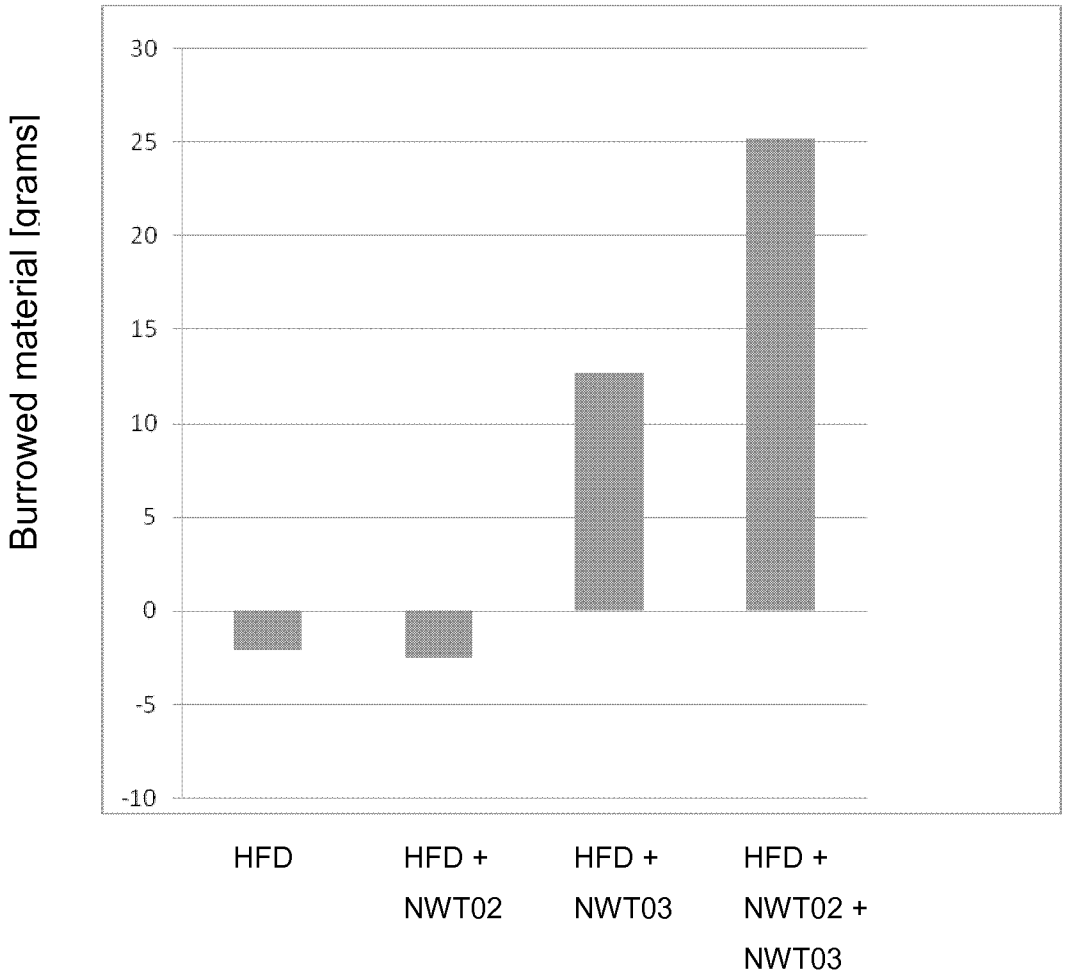
12. The composition for use according to any one of claims 1 - 11 additionally comprising egg yolk.

13. The composition for use according to claim 12 wherein the egg yolk and the aqueous dispersion are present in a weight ratio between 1:2 to 1:7, preferably between 1:2 and 1:3.

14. A composition for use according to any one of claims 1 – 13 wherein the aqueous composition is dehydrated.

15. A composition for use according to any one of claims 1 – 14 wherein the aqueous composition is contained in a food product.

Figure 1


Burrowed material [grams]
30
25
20
15
10
5
0
-5
-10
HFD
HFD + NWT02
HFD + NWT03
HFD + NWT02 + NWT03

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2017/053891

A. CLASSIFICATION OF SUBJECT MATTER
INV. A23L33/18 A23L33/155 A23L15/00
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A23L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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A	EP 1 685 764 A1 (GLOBUS EGG SCIENCES B V [NL]) 2 August 2006 (2006-08-02) cited in the application paragraphs [0026], [0031], [0032], [0038] - [0040]; claims 1-11	1-15
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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
20 April 2017	28/04/2017

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	De Jong, Ellen

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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