

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
29 April 2010 (29.04.2010)

PCT

(10) International Publication Number
WO 2010/046321 A1

(51) International Patent Classification:

A23L 1/0522 (2006.01) A23L 1/29 (2006.01)
A23L 1/305 (2006.01) A61P 1/04 (2006.01)
A61K 31/718 (2006.01) A61K 38/01 (2006.01)

(21) International Application Number:

PCT/EP2009/063612

(22) International Filing Date:

16 October 2009 (16.10.2009)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

08167053.1 20 October 2008 (20.10.2008) EP

(71) Applicant (for all designated States except US):
NESTEC S.A. [CH/CH]; Ave. Nestlé 55, CH-1800
Vevey (CH).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **BERGONZELLI
DEGONDA, Gabriela** [CH/CH]; Ch. de Grandvignes 44,
CH-1030 Bussigny (CH). **FAURE, Magali** [FR/CH];
Chemin des Crocus 2, CH-1074 Mollie-margot (CH).
FINK, Reinhold [DE/CH]; Obstgartenweg 38, CH-3672
Oberdiessbach (CH). **GARCIA-RODENAS, Clara Lu-
cia** [ES/CH]; Les Vergers de Lavaux A, CH-1072 Forel
(CH). **HUBER-HAAG, Karl-Josef** [DE/CH]; Avenue de
Rochettaz 36, CH-1009 Pully (CH). **NEUMAYER,
Christoph Alexander** [DE/CH]; Brunnmattstrasse 17,
CH-3007 Bern (CH).

(74) Agent: **CORTICCHIATO, Olivier**; Ave. Nestlé 55,
CH-1800 Vevey (CH).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,

AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ,
CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO,
DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,
KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD,
ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI,
NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD,
SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT,
TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ,
TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV,
MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM,
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted
a patent (Rule 4.17(ii))
- as to the applicant's entitlement to claim the priority of
the earlier application (Rule 4.17(iii))
- of inventorship (Rule 4.17(iv))

Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments (Rule 48.2(h))

(54) Title: NUTRITIONAL COMPOSITION WITH ANTI-REGURGITATION PROPERTIES

(57) Abstract: A nutritional composition for the management of regurgitation in infants which composition includes which composition includes a protein source consisting essentially of partially hydrolysed proteins, a lipid source and a carbohydrate source comprising a starch selected from cereal starch or potato starch wherein the starch amounts to between 18 to 25% of the nutritional composition on a dry weight basis.



WO 2010/046321 A1

Nutritional Composition with anti-regurgitation properties.

This invention relates to a nutritional composition, more specifically to a nutritional composition designed to prevent or reduce regurgitation in infants suffering from post-
5 prandial gastro-oesophageal reflux.

Post-prandial gastro-oesophageal reflux which is more commonly referred to as regurgitation or spitting-up is a common problem in infants up to the age of about six months. Typically, the infant will regurgitate some stomach contents after a feed, the
10 amount varying from a teaspoonful to rather larger amounts in severe cases. The condition may have several different causes including a loose cardiac sphincter, an overly tight pyloric sphincter, air bubbles ingested with the feed or simply feeding too fast or too much. Generally, the condition resolves itself as the baby gets older without the need for medical intervention.

15

Mother's milk is recommended for all infants. However, in some cases breast feeding is inadequate or unsuccessful or inadvisable for medical reasons or the mother chooses not to breast feed either at all or for a period of more than a few weeks. Infant formulas have been developed for these situations.

20

As noted above, regurgitation generally diminishes as the baby gets older, usually ceasing altogether by 7 or 8 months of age. However, some mothers and other care-givers find the condition distressing and specialised anti-regurgitation formulas have been developed to try to alleviate it. For example, it has been proposed to add
25 thickening agents such as rice cereal or carob bean or locust gums to regular infant formula to reduce the incidence and/or severity of regurgitation. These prior art approaches have various disadvantages. For example, the addition of rice cereal to infant formula renders the formula hyper-caloric thus exposing the infant to a risk of gaining weight too quickly. Approaches based on the use of gums have tended to suffer
30 from the disadvantage that it is difficult to control the viscosity of the reconstituted formula.

More recently in EP 745330 it was proposed to manage regurgitation by feeding a formula thickened with a food starch such as potato starch or waxy grain starch. However, there remains a need for nutritional composition specifically designed to manage the problem of regurgitation in infants aged up to about eight months.

5

Summary of the Invention

The present inventors have realised that, in designing a nutritional composition for the management of regurgitation or spitting up in infants, it is advantageous to address the possible physiological cause of the problem at the same time as providing a thickened composition as advocated in the prior art.

10

Surprisingly, the inventors have observed that nutritional compositions containing partially hydrolyzed proteins can bind to the human CCK1 receptor and, by this mean, contribute to accelerate gastric emptying and to reduce regurgitation in infants.

15

Accordingly, the present invention provides a nutritional composition for the management of regurgitation in infants which composition includes a protein source consisting essentially of partially hydrolysed proteins, a lipid source and a carbohydrate source comprising a starch selected from cereal starch or potato starch wherein the starch amounts to between 18 to 25% of the nutritional composition on a dry weight basis.

20

The invention also extends to the use of a protein source consisting essentially of partially hydrolysed proteins, a lipid source and a carbohydrate source comprising from a starch selected from cereal starch or potato starch for the preparation of a nutritional composition for the management of regurgitation in infants wherein the starch amounts to between 18 to 25% of the nutritional composition on a dry weight basis.

25

The invention further extends to a method for the management of regurgitation in infants comprising feeding a therapeutic amount of a nutritional composition including a protein source consisting essentially of partially hydrolysed proteins, a lipid source

30

and a carbohydrate source comprising a starch selected from cereal starch or potato starch wherein the starch amounts to between 18 to 25% of the nutritional composition on a dry weight basis to an infant in need thereof.

5 Colecystokinin (CCK) is a peptide hormone which is found both in the gastrointestinal tract throughout the human small intestine and nerves in the myenteric plexus of the enteric nervous system and in the central nervous system. CCK regulates the motor functions in the gastrointestinal tract and is responsible for a postprandial reduction in the cardiac sphincter pressure, an increase in the frequency of transient cardiac sphincter
10 relaxations and an inhibition of gastric emptying. CCK1 receptor specifically mediates these CCK effects. Recent clinical studies show that pharmacological antagonist of CCK1 receptor accelerate gastric emptying and reduce the frequency of regurgitation in gastroesophageal reflux disease patients and have been suggested as an effective therapy for this condition (Peter SA, D'Amato M, Beglinger C., CCK1 antagonists: are they ready for clinical use? Dig Dis. 2006;24(1-2):70-82.)
15

Without wishing to be bound by theory, the inventors believe that both frequent cardiac relaxations and increased pressure in the stomach after a meal are important factors contributing to the frequency and severity of regurgitation in infants who tend to suffer
20 from this condition and that inhibition of CCK1 may decrease cardiac relaxation frequency and reduce the time take for the stomach to empty such as is provided by the use of partially hydrolysed proteins may significantly ameliorate these risk factors. At the same time, the use of a higher than usual proportion of starch in the composition provides both an increased viscosity compared with conventional infant formulas and an
25 improved mouthfeel compared to unthickened infant formulas based on partially hydrolysed proteins.

As such the invention is believed to encompass effects extended beyond the mere thickening of the composition (that is conventionally believed to have a positive impact
30 on regurgitation). It is further hypothesized that the thickening effect and the effect on

receptors as explained above (“physiological effect”) synergize together to provide an improved anti-regurgitation benefit.

5 In one embodiment the invention relates to the use of a selected composition (of the invention) for the manufacture of a composition or of an infant formula in infants suffering from regurgitation.

10 In one embodiment the patient target group are infants between 0 and 4 months or between 0 and 6 months or between 4 and 12 months. In one embodiment the infants suffer from high frequency regurgitation and may be at risk of dehydration or malnutrition.

Detailed Description of the Invention

15 In this specification, the following expressions have the meanings assigned to them below:-

20 “protein source consisting essentially of partially hydrolysed proteins” means a source of amino nitrogen comprising a mixture of peptides of various sizes according to the degree of hydrolysis with a small quantity of free amino acids resulting from the hydrolysis process and containing no intact protein molecules;

“infant” means a child under the age of 12 months;

25 “management of regurgitation” means prevention of, or reduction in severity or frequency of, postprandial regurgitation.

All percentages and ratios are by weight unless otherwise specified.

30 A nutritional composition according to the present invention includes a protein source which consists essentially of partially hydrolysed proteins. The degree of hydrolysis of

the proteins may be between 5 and 40 % or between 5% and 50% but is more preferably between 15 and 25% or between 15% and 20% .

The energy density of a nutritional composition according to the invention is less than 680 kcal/l, preferably between 620 and 670 kcal/l. The protein source may be present in
5 an amount of not more than 3 or no more than 2.7 g/100kcal, preferably 1.7 to 2.6 or 1.7 to 2.1 g/100kcal. Provided that the protein is partially hydrolysed, the type of protein is not believed to be critical to the present invention provided that the minimum requirements for essential amino acid content are met and satisfactory growth is ensured. Thus, protein sources including rice, casein and soy and mixtures thereof may
10 be used although whey proteins are preferred either alone or mixed with casein proteins in a ratio between 60:40 and 70:30 whey:casein. The whey protein may be a whey protein isolate, acid whey, sweet whey or sweet whey from which the caseino-glycomacropeptide has been removed (modified sweet whey). Preferably, however, the whey protein is modified sweet whey. Sweet whey is a readily available by-product of
15 cheese making and is frequently used in the manufacture of nutritional compositions based on cows' milk. However, sweet whey includes a component which is undesirably rich in threonine and poor in tryptophan called caseino-glycomacropeptide (CGMP). Removal of the CGMP from sweet whey results in a protein with a threonine content closer to that of human milk. A process for removing CGMP from sweet whey is
20 described in EP 880902.

The protein source may additionally be supplemented with free amino acids if this is necessary to meet the minimum requirements for essential amino acid content. These requirements are published for example in EC Directive 2006/141/EC.

25

If modified sweet whey is used as the whey protein in a mixture of 60% whey and 40% casein, the protein source is preferably supplemented by free histidine in an amount of up to 0.19% of total protein content.

30

The protein source may be hydrolysed as desired and as is known in the art. For example, a whey protein hydrolysate may be prepared by enzymatically hydrolysing the

whey fraction in one or more steps. If the whey fraction used as the starting material is substantially lactose free, it is found that the protein suffers much less lysine blockage during the hydrolysis process. This enables the extent of lysine blockage to be reduced from about 15% by weight of total lysine to less than about 10% by weight of lysine; for example about 7% by weight of lysine which greatly improves the nutritional quality of the protein source.

The nutritional composition of the present invention contains a source of carbohydrate comprising a starch selected from cereal starch or potato starch wherein the starch amounts to between 18 to 25% of the nutritional composition on a dry weight basis. Preferably the starch or starches comprise between 18 and 23% of the composition on a dry weight basis. Suitable cereal starches include corn starch and rice starch. Preferably, however, the starch is potato starch, more preferably pre-cooked potato starch. This is because unlike cereal starches, potato starch is commercially available in a form which is not contaminated with intact proteins. A suitable commercially available potato starch for use in the present invention is Quemina 21.216 Potato Starch sold by Agrana, A-1220 Vienna. The remainder of the carbohydrate source is preferably lactose although other carbohydrates such as saccharose and maltodextrin may also be added. Preferably, the carbohydrate content of the nutritional composition is between 9 and 14 g/100 kcal.

Preferably, the nutritional composition of the present invention is nutritionally complete, that is, it contains adequate nutrients to sustain healthy human life for extended periods. As such, the nutritional composition of the present invention preferably contains a source of lipids. The lipid source may be any lipid or fat which is suitable for use in nutritional compositions to be fed to infants. Preferred fat sources include coconut oil, low erucic rapeseed oil (canola oil), soy lecithin, palm olein, and sunflower oil. The essential polyunsaturated fatty acids linoleic acid and α -linolenic acid will also be added as may small amounts of oils containing high quantities of preformed long chain polyunsaturated fatty acids arachidonic acid and docosahexaenoic

acid such as fish oils or single cell oils. In total, the lipid content may be between 4.4 and 6 g/100 kcal.

5 The nutritional composition may also contain all vitamins and minerals understood to be essential in the daily diet in nutritionally significant amounts. Minimum requirements have been established for certain vitamins and minerals. Examples of minerals, vitamins and other nutrients optionally present in the nutritional composition include vitamin A, vitamin B₁, vitamin B₂, vitamin B₆, vitamin B₁₂, vitamin E, vitamin K, vitamin C, vitamin D, folic acid, inositol, niacin, biotin, pantothenic acid, choline, 10 calcium, phosphorous, iodine, iron, magnesium, copper, zinc, manganese, chloride, potassium, sodium, selenium, chromium, molybdenum, taurine, and L-carnitine. Minerals are usually added in salt form.

15 If necessary, the nutritional composition may contain emulsifiers and stabilisers such as soy lecithin, citric acid esters of mono- and di-glycerides, and the like. The nutritional composition may optionally contain other substances which may have a beneficial effect such as probiotic bacteria, fibres, nucleotides, nucleosides, and the like in the amounts customarily found in nutritional compositions to be fed to infants.

20 The nutritional composition may be prepared in any suitable manner. For example, a nutritional composition may be prepared by blending together the protein source, the carbohydrate source, and the lipid source in appropriate proportions. If used, emulsifiers may be included in the blend at this stage. The vitamins and minerals may be added at this point but are usually added later to avoid thermal degradation. Any lipophilic 25 vitamins, emulsifiers and the like may be dissolved into the fat source prior to blending. Water, preferably water which has been subjected to reverse osmosis, may then be mixed in to form a liquid mixture.

30 The liquid mixture may then be thermally treated to reduce bacterial loads. For example, the liquid mixture may be rapidly heated to a temperature in the range of about

80°C to about 110°C for about 5 seconds to about 5 minutes. This may be carried out by steam injection or by heat exchanger; for example a plate heat exchanger.

5 The liquid mixture may then be cooled to about 60°C to about 85°C; for example by flash cooling. The liquid mixture may then be homogenised; for example in two stages at about 7 MPa to about 40 MPa in the first stage and about 2 MPa to about 14 MPa in the second stage. The homogenised mixture may then be further cooled and any heat sensitive components; such as vitamins and minerals may be added. The pH and solids content of the homogenised mixture is conveniently standardised at this point.

10

The homogenised mixture is transferred to a suitable drying apparatus such as a spray drier or freeze drier and converted to powder. The powder should have a moisture content of less than about 5% by weight.

15

A nutritional composition according to the invention may be fed to an infant suffering from regurgitation as the sole source of nutrition until the age of four to six months and subsequently as part of a mixed diet during the introduction of solid foods as required to manage the regurgitation. In one embodiment the composition according to the invention is intended for infants between 0 and 4 weeks, between 0 and 2 months, 20 between 0 and 4 months or between 0 and 6 months. In one embodiment the composition is intended for infants between 4 and 12 months, or between 6 and 24 months.

25

Example 1

An example of a nutritional composition according to the present invention is given below.

Nutrient	per 100kcal	per litre
Energy (kcal)	100	670
Protein (g) 100% hydrolysed whey protein	1.90	12.8

Degree of hydrolysis 18%		
Fat (g)	5.08	34.1
Linoleic acid (g)	0.78	5.2
α -Linolenic acid (mg)	94	630
Carbohydrate (g)	11.66	78.1
of which:		
Lactose	7.63	51.1
Potato starch	4.03	27.0
Minerals (g)	0.41	2.8
Na (mg)	30	200
K (mg)	108	720
Cl (mg)	93	620
Ca (mg)	69	470
P (mg)	37	240
Mg (mg)	8.8	59
Mn (μ g)	23	150
Se (μ g)	1.8	12
Vitamin A (μ g RE)	100	670
Vitamin D (μ g)	1.3	8.8
Vitamin E (mg TE)	1.0	6.9
Vitamin K1 (μ g)	8.6	58
Vitamin C (mg)	14	91
Vitamin B1 (mg)	0.098	0.66
Vitamin B2 (mg)	0.18	1.2
Niacin (mg)	1.0	6.9
Vitamin B6 (mg)	0.068	0.46
Folic acid (μ g)	17	120
Pantothenic acid (mg)	1.0	6.9
Vitamin B12 (μ g)	0.2	1.3
Biotin (μ g)	2.5	17
Choline (mg)	10	69
Fe (mg)	1.1	7.3
I (μ g)	14	96
Cu (mg)	0.074	0.5
Zn (mg)	0.74	4.9

Example 2

An example of a nutritional composition (infant formula) according to the present invention is given below :

Nutrient	per 100kcal	per litre
Energy (kcal)	100	670
Protein (g) 100% hydrolysed whey protein Degree of hydrolysis 18%	2.43	16.2
Fat (g)	4.65	31.05
Linoleic acid (g)	0.77	5.13
α -Linolenic acid (mg)	97	650
Carbohydrate (g) of which:	12.11	80.9
Lactose	7.77	51.9
Potato starch	4.34	29
Minerals (g)	0.53	3.5
Na (mg)	47	310
K (mg)	117	780
Cl (mg)	99	660
Ca (mg)	115	770
P (mg)	72	480
Mg (mg)	8.5	57
Mn (μ g)	16	110
Se (μ g)	2.7	18
Vitamin A (μ g RE)	110	730
Vitamin D (μ g)	1.8	12
Vitamin E (mg TE)	0.87	5.8
Vitamin K1 (μ g)	7.5	50
Vitamin C (mg)	20	140
Vitamin B1 (mg)	0.11	0.72
Vitamin B2 (mg)	0.26	1.8
Niacin (mg)	0.93	6.2
Vitamin B6 (mg)	0.07	0.49
Folic acid (μ g)	19	130
Pantothenic acid (mg)	0.59	3.9
Vitamin B12 (μ g)	0.2	1.4
Biotin (μ g)	2.3	15
Choline (mg)	17	110
Fe (mg)	1.1	7.3
I (μ g)	16	110
Cu (mg)	0.074	0.5
Zn (mg)	0.74	4.9

Example 3: In vitro CCK1 binding assays:

Three infant formulae (WPH1, WPH2 and RPH) were tested for their ability to inhibit the binding of a ligand to the human CCK1 receptor. WPH1 and WPH2 are commercial infant formulae based on and comprising whey protein hydrolysates. RPH is a commercial infant formula based on and comprising a rice protein hydrolysate. The formulae comprise starch between 18 and 25% (w/w of dry composition).

WPH1 contains 11.5% mildly hydrolyzed whey proteins at 18% hydrolysis degree; WPH2 contains 14.8% extensively hydrolyzed whey proteins at 42% hydrolysis degree; RPH contained 14% mildly hydrolyzed rice proteins at 21% hydrolysis degree.

The three formulas were tested at 13 mg/ml protein-equivalent concentration. Briefly, they were dissolved in an aqueous media and incubated for 60 min at 22°C with human recombinant CHO cells transfected to express the CCK1 receptor on their membrane. The ability of the formulas to compete with, and inhibit the binding of a radioactive ligand ($[^{125}\text{I}]\text{CCK-8s}$, 0.08 nM) to the human CCK1 receptor was measured by scintillation counting. A percentage of inhibition of binding was calculated. A high percentage of inhibition indicates a high binding activity of the formulas. Antagonists of the CCK receptors have been shown to accelerate gastric emptying and reduce the regurgitation episodes in patients. It is hypothesized that the formulae of the invention have a similar effect on the receptors and on the regurgitation /gastric emptying in general.

Results are displayed in Figure 1. Both WPH1 and RPH2, containing mild hydrolyzate whey and rice protein respectively show a substantial binding activity to CCK1 receptor. In contrast, WPH2, containing extensively hydrolyzed whey protein, displayed a mild binding activity.

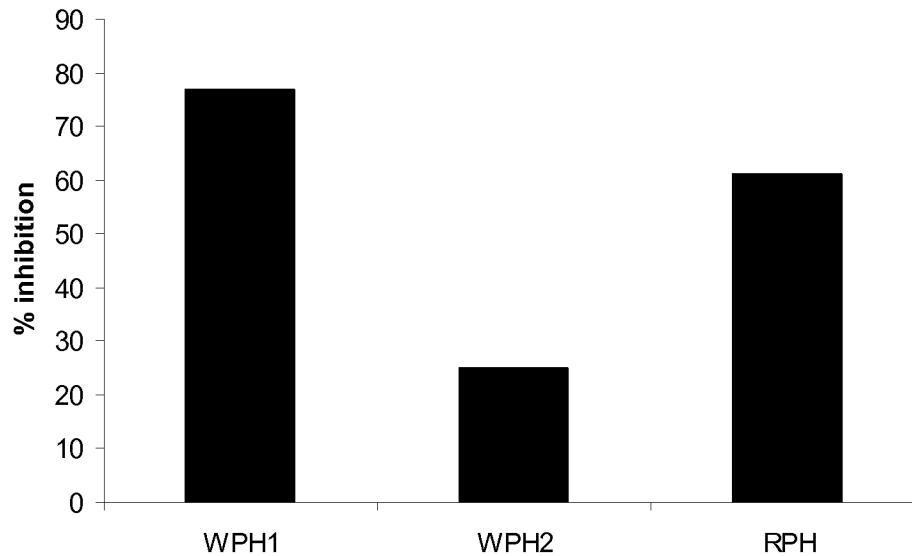
Claims

1. A nutritional composition for the management of regurgitation in infants which composition includes which composition includes a protein source consisting essentially of partially hydrolysed proteins, a lipid source and a carbohydrate source comprising a starch selected from cereal starch or potato starch wherein the starch amounts to between 18 to 25% of the nutritional composition on a dry weight basis.
5
- 10 2. A nutritional composition according to Claim 1, wherein the degree of hydrolysis of the partially hydrolysed proteins is between 15 and 25%.
- 15 3. A nutritional composition according to Claim 1 or 2, wherein the partially hydrolysed proteins are whey proteins.
4. A nutritional composition according to Claim 1 or 2, wherein the partially hydrolysed proteins comprise rice proteins.
- 20 5. A nutritional composition as claimed in any preceding claim, wherein the starch comprises from 18 to 23% by weight of the nutritional composition.
6. A nutritional composition as claimed in any preceding claim, wherein the starch is potato starch.
- 25 7. A nutritional composition as claimed in any preceding claim wherein the remainder of the carbohydrate source is lactose.
- 30 8. Use of a protein source consisting essentially of partially hydrolysed proteins, a lipid source and a carbohydrate source comprising from a starch selected from cereal starch or potato starch for the preparation of a nutritional composition for

the management of regurgitation in infants wherein the starch amounts to between 18 to 25% of the nutritional composition on a dry weight basis.

- 5
9. The use of Claim 8, wherein the degree of hydrolysis of the partially hydrolysed proteins is between 15 and 25%.
10. The use of Claim 8 or 9, wherein the partially hydrolysed proteins are whey proteins.
- 10
11. The use of Claim 8 or 9, wherein the partially hydrolysed proteins comprise rice proteins.
12. The use of any of claims 8 to 11, wherein the starch comprises from 18 to 23% by weight of the nutritional composition.
- 15
13. The use of any of Claims 8 to 12, wherein the starch is potato starch.
14. The use of any of Claims 8 to 13, wherein the remainder of the carbohydrate source is lactose.

Figure 1



Capacity of 3 infant formulas comprising mild whey (WPH1) and rice (RPH) or
5 extensive whey (WPH2) protein hydrolyzates to inhibit the binding of a radioactive
ligand ($[^{125}\text{I}]\text{CCK-8s}$, 0.08 nM) to the human CCK1 receptor. Results are expressed as
percentage of binding inhibition. A high percentage of inhibition indicates a high
binding activity of the formulas.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2009/063612

A. CLASSIFICATION OF SUBJECT MATTER

INV. A23L1/0522 A23L1/305 A61K31/718 A23L1/29 A61P1/04
A61K38/01

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 A61K A61P

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 practical, search terms used)

EPO-Internal, WPI Data, BIOSIS, FSTA, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 745 330 A (SQUIBB BRISTOL MYERS CO [US]) 4 December 1996 (1996-12-04) cited in the application	1-14
Y	page 2, lines 4-30 page 3, lines 37-47 page 4 - page 8; examples 1,2 page 11; claims 1,5,19,20	1-14
	-/--	

Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

3 February 2010

Date of mailing of the international search report

18/02/2010

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Stiegler, Petra

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2009/063612

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SAVINO F ET AL: "Minor feeding problems during the first month of life: effect of a partially hydrolysed milk formula containing fructo- and galacto-oligosaccharides" ACTA PAEDIATRICA, UNIVERSITETSFORLAGET, OSLO, NO, vol. 91, no. SUPPLEMENT 441, 1 September 2003 (2003-09-01), pages 86-90, XP009056971 ISSN: 0803-5253	1-14
Y	page 86, column 1 - column 2 page 87, column 1, paragraph 3; table 1 page 89, column 2, paragraph 2	1-14
X	STAELENS S ET AL: "Gastric emptying in healthy newborns fed an intact protein formula, a partially and an extensively hydrolysed formula" CLINICAL NUTRITION, CHURCHILL LIVINGSTONE, LONDON, GB, vol. 27, no. 2, 1 April 2008 (2008-04-01), pages 264-268, XP022584800 ISSN: 0261-5614 [retrieved on 2008-02-15]	1-14
Y	page 265, column 1, paragraph 1 page 266; table 1 page 267, column 2, paragraph 5	1-14
X	WO 01/56406 A (ABBOTT LAB [US]) 9 August 2001 (2001-08-09)	1-14
Y	page 1, line 29 page 2, lines 7-21 page 6, line 25 - page 7, line 18 page 14 - page 15; example 5	1-14
X	WO 01/41581 A (NUTRICIA NV [NL]; BINDELS JACOB GEERT [NL]; BAALEN ANTONIE VAN [NL]; H) 14 June 2001 (2001-06-14)	1-14
Y	sentences 1-15,27-32 page 3, line 30 - page 4, line 4 page 4, line 25 - page 5, line 3 page 10, line 16 - page 11, line 19	1-14
	-/--	

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2009/063612

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FRANCESCO SAVINO, STEFANO MACCARIO, EMANUELE CATAGNO, FRANCESCO CRESI, FRANCO CAVALLO, PAOLA DALMASSO, SILVIA FANARO: "Advances in the management of digestive problems during the first months of life" ACTA PAEDIATRICA, vol. 94, no. S449, 2005, pages 120-124, XP002511772	1-14
Y	page 120, column 1, paragraph 1 page 120, column 2, paragraph 3 page 121, column 1, paragraph 2; table 1 page 122, column 2, paragraph 1 page 123, paragraph 3	1-14
A	ANONYMOUS: "Hydrolyzed Whey Protein"[Online] 2007, XP002511773 Retrieved from the Internet: URL:http://daviscofoods.com/HWP/> [retrieved on 2009-01-23] paragraph [0006]	1-4,9-11

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2009/063612

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 0745330	A	04-12-1996	AR 002113 A1	07-01-1998
			AT 171846 T	15-10-1998
			AT 238690 T	15-05-2003
			BR 9602558 A	22-04-1998
			CZ 9601497 A3	11-12-1996
			DE 69600745 D1	12-11-1998
			DE 69600745 T2	06-05-1999
			DE 69627867 D1	05-06-2003
			DE 69627867 T2	26-02-2004
			DE 745330 T1	15-05-1997
			DK 745330 T3	15-02-1999
			DK 0846422 T3	11-08-2003
			ES 2094716 T1	01-02-1997
			ES 2197297 T3	01-01-2004
			GR 97300004 T1	28-02-1997
			PL 314546 A1	09-12-1996
			PT 846422 E	29-08-2003
US 6099871 A	08-08-2000			
WO 0156406	A	09-08-2001	AT 321462 T	15-04-2006
			AU 780438 B2	24-03-2005
			AU 2949001 A	14-08-2001
			BG 107019 A	30-04-2003
			BR 0106681 A	30-04-2002
			CA 2396148 A1	09-08-2001
			CN 1400870 A	05-03-2003
			CZ 20022743 A3	13-11-2002
			DE 60118387 T2	07-12-2006
			DK 1251750 T3	07-08-2006
			EP 1251750 A1	30-10-2002
			ES 2261432 T3	16-11-2006
			HK 1050983 A1	27-10-2006
			HU 0204382 A2	28-04-2003
			IL 150326 A	19-06-2005
			JP 2003521501 T	15-07-2003
			MX PA02006938 A	28-01-2003
			NO 20023684 A	02-10-2002
			NZ 519695 A	29-10-2004
			PL 357134 A1	12-07-2004
			PT 1251750 E	31-08-2006
			SI 21018 A	30-04-2003
			SK 12562002 A3	03-12-2002
			TR 200201921 T2	21-01-2003
			TW 241167 B	11-10-2005
US 2002176911 A1	28-11-2002			
US 6365218 B1	02-04-2002			
WO 0141581	A	14-06-2001	AR 027193 A1	19-03-2003
			AT 290320 T	15-03-2005
			AU 771010 B2	11-03-2004
			AU 3242001 A	18-06-2001
			BR 0016341 A	27-08-2002
			CA 2393269 A1	14-06-2001
			CN 1409603 A	09-04-2003
			CN 1788615 A	21-06-2006
			CZ 20022012 A3	16-10-2002
			DE 60018604 D1	14-04-2005
			DE 60018604 T2	09-03-2006

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2009/063612

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0141581	A	EP 1062873 A1	27-12-2000
		ES 2238339 T3	01-09-2005
		HK 1049429 A1	20-05-2005
		HU 0203736 A2	28-03-2003
		JP 4242589 B2	25-03-2009
		JP 2003515354 T	07-05-2003
		MX PA02005851 A	14-10-2003
		NO 20022751 A	12-08-2002
		NZ 519513 A	30-07-2004
		PL 355943 A1	31-05-2004
		PT 1237419 E	29-07-2005
		RU 2243698 C2	10-01-2005
		SK 8512002 A3	03-12-2002
		TW 250848 B	11-03-2006
		US 2003072865 A1	17-04-2003
ZA 200204504 A	05-06-2003		
