

Señor

SUPERINTENDENTE DE INDUSTRIA Y COMERCIO
DIVISION DE NUEVAS CREACIONES

E. _____ S. _____ D. _____

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SUPERINDUSTRIA Y COMERCIO

Radicacion : 00025252 00010000

Fecha (AMD): 2004-08-31 18:26:59

Tramite : 002 PATENTES D 332 PRESENTAC 411 PRESENTA
Dependencia: 2020 DIVISION DE NUEVAS CREACIONES

Folios: 8

Re: P1.-**ABBOTT LABORATORIES**.-Expediente número
00-025.252.-

1. Me refiero al asunto de la referencia.
2. Por medio del presente, atentamente me permito manifestar a ese Despacho, que hubo un **cambio** de Representante Legal para todos los asuntos de la Propiedad Industrial en Bogotá de **ABBOTT LABORATORIES**, una sociedad organizada y existente de conformidad con las leyes del Estado de Illinois, Estados Unidos de América, domiciliada en Abbott Park, Estado de Illinois, Estados Unidos de América.
3. En consecuencia, atentamente solicito a ese Despacho reconocerme personería, en este asunto, de conformidad con el documento de Representación Legal para todos los asuntos de la Propiedad Industrial en Bogotá de la sociedad **ABBOTT LABORATORIES**, otorgado a favor de la **SUSCRITA (ALICIA LLOREDA)** y/o al doctor GUSTAVO TAMAYO y/o al doctor IGNACIO SANTAMARIA y/o ENRIQUE ALVAREZ de acuerdo con la copia debidamente autenticada ante Notario Público que adjunto al presente expediente (Artículos 26 y 39 de la Decisión 486 de la Comunidad Andina de Naciones).
4. Anexo al presente acompaño fotocopia, debidamente autenticada por Notario Público, de:
 - (a) Documento que acredita a la SUSCRITA y/o al doctor GUSTAVO TAMAYO y/o al doctor IGNACIO SANTAMARIA y/o ENRIQUE ALVAREZ en los términos del párrafo 1º. del Artículo 543 del Decreto-Ley 410 de 1971, como

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Representantes Legales en Bogotá para todos los asuntos relacionados con la propiedad industrial de la sociedad **ABBOTT LABORATORIES**, una sociedad organizada y existente de conformidad con las leyes del Estado de Illinois, Estados Unidos de América, domiciliada en Abbott Park, Estado de Illinois, Estados Unidos de América.

- (b) Certificación Notarial expedida el 12 de Julio de 2004; y
- (c) Traducción Oficial No. 2004-07-29-362 correspondiente a las partes pertinentes del documento anterior, también debidamente legalizada hasta por el Ministerio de Relaciones Exteriores bajo el número 246476 de 30 de Julio de 2004.

5. Ruego a usted tomar atenta nota de lo anterior y continuar con el trámite correspondiente.

Señor Superintendente,


ALICIA LLOREDA RICAURTE
T.P. 53.215
Código 231

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Los abajo firmados, **ABBOTT LABORATORIES**, una sociedad organizada y existente de conformidad con las leyes del Estado de Illinois, Estados Unidos de América,

con domicilio en 100 Abbott Park Road, Abbott Park, IL 60064 USA

nombramos por el presente a ALICIA LLOREDA y/o GUSTAVO TAMAYO y/o IGNACIO SANTAMARIA y/o ENRIQUE ALVAREZ, domiciliados en Bogotá, Colombia, con oficinas en dicha ciudad, Calle 72 No. 5-83, piso 6o., nuestros representantes legales y verdaderos en Bogotá, con facultades para recibir notificaciones y nombrar apoderados judiciales o extrajudiciales, con el fin de dar cumplimiento al parágrafo 1o. del artículo 543 del decreto 410 de 1971.

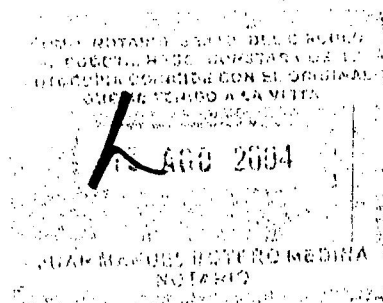
Los doctores ALICIA LLOREDA y/o GUSTAVO TAMAYO y/o IGNACIO SANTAMARIA y/o ENRIQUE ALVAREZ, o los apoderados que cualquiera de ellos designe, quedan especialmente facultados para representarnos ante las autoridades colombianas, administrativas, judiciales o de policía, en todos los trámites relativos a la propiedad industrial, a cuyo efecto les facultamos para dar ante dichas autoridades todos los pasos necesarios al objeto indicado; elevar solicitudes, declaraciones, reclamos, recursos y presentar desistimientos; formular descripciones, enmiendas, limitar el alcance de las solicitudes y los registros, presentar oposiciones y apelaciones; instaurar cancelaciones, renunciar total o parcialmente a los registros, abonar todos los impuestos y cuotas y efectuar todo otro pago determinado por la ley; recibir todos los documentos y valores, dando el descargo respectivo; llenar cualesquiera otros requisitos y tomar, en fin, todas las medidas que creyeren conducentes al resguardo de nuestros intereses; y adicionalmente quedan facultados para tomar intervención como demandantes o demandados ante los jueces que sean competentes, pudiendo transar, someter a árbitros, desistir, percibir, conciliar y apelar, con todas las demás facultades que resulten necesarias y por el presente declaramos desde ahora válido y bueno cuanto dichos representantes y/o los apoderados que cualquiera de ellos nombre hicieren en nuestro beneficio.

NOTARIO SEXTO (R) DEL CÍRCULO
DE BOGOTÁ, AGENTE QUE LA
FOTOCOPIA CONCORDA CON LA FOTOCOPIA
DE LA VISTA

27 AGO 2004

Asimismo, facultamos a los doctores ALICIA LLOREDA y/o GUSTAVO TAMAYO y/o IGNACIO SANTAMARIA y/o ENRIQUE ALVAREZ, para solicitar en la Oficina de Propiedad Industrial la protocolización de este documento y de cualquier poder que cualquiera de ellos otorgue a nombre nuestro.

Dado y firmado el 12 de Julio de 2004



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The undersigned, **ABBOTT LABORATORIES**, a corporation organized and existing under the laws of the State of Illinois, United States of America,

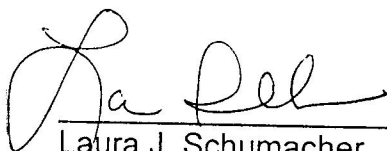
domiciled at 100 Abbott Park Road, Abbott Park, IL 60064 USA

hereby appoint, **ALICIA LLOREDA y/o GUSTAVO TAMAYO y/o IGNACIO SANTAMARIA y/o ENRIQUE ALVAREZ**, of Bogota, Colombia, with offices in said town, Calle 72 No. 5-83, Sixth Floor, our true and legal representatives in Bogotá, with power to receive notifications and to appoint judicial or extrajudicial agents, so as to comply with paragraph 1o. of article 543 of decree 410 of 1971.

Doctors **ALICIA LLOREDA y/o GUSTAVO TAMAYO y/o IGNACIO SANTAMARIA y/o ENRIQUE ALVAREZ**, or the agents by any one of them appointed, are especially empowered to represent us before the administrative, judicial or police authorities of Colombia, in all proceedings pertaining to industrial property, for which purpose we authorize them to take before the said authorities all the necessary steps for the said end; to file petitions, declarations, claims, recourses and withdrawals, to draw up specifications; to file amendments, to limit the scope of applications and registrations, file oppositions; file cancellations total or partially waive registrations, to pay all installments and effect all other payments prescribed by law; to receive proper receipts, to comply with all other requirements and, in short, to take all those measures which they may deem fit for the protection of our interests; and additionally we authorize said agents to act on our behalf, as complainants as well as defendants, before the competent judges, with full powers to make arrangements, to submit to arbitrators, to desist, to collect, to conciliate, to appeal and, in short, with all such further powers as may be required, and we hereby declare from now on as valid and good all that said representatives and/or the agents by any one of them appointed may do for our benefit.

We also authorize doctors **ALICIA LLOREDA y/o GUSTAVO TAMAYO y/o IGNACIO SANTAMARIA y/o ENRIQUE ALVAREZ**, to apply for protocolization of this document and of any power of attorney by any one of them conferred in our name, before the Office of Industrial Property.

Given and signed this 12th day of July, 2004



Laura J. Schumacher
Vice President, Secretary and Deputy General
Counsel

DE BOGOTÁ, HAGO CONSTAR QUE LA
FOTOCOPIA CONCIERDE CON LA FOTOCOPIA
AUTÉNTICA QUE HE TENIDO A LA VISTA

27 AGO 2004

PABLO MENDEZ BARAJAS
NOTARIO (E)

COMO NOTARIO HECHO DEL CIRCULO
DE BOGOTÁ, HAGO CONSTAR QUE LA
FOTOCOPIA CONCIERDE CON EL ORIGINAL
QUE HE TENIDO A LA VISTA

13 AGO 2004

JUAN MANUEL BINTERO MEDINA
NOTARIO



SPRINGFIELD, ILLINOIS

APOSTILLE

(Convention de La Haye du 5 Octobre 1961)

1. Country: United States of America

This public document

2. has been signed by TRINA LEE RUIZ

3. acting in the capacity of NOTARY PUBLIC, LAKE COUNTY

4. bears the seal/stamp of STATE OF ILLINOIS

Certified

5. Springfield, Illinois

6. JULY 20, 2004

7. by the Secretary of State, State of Illinois

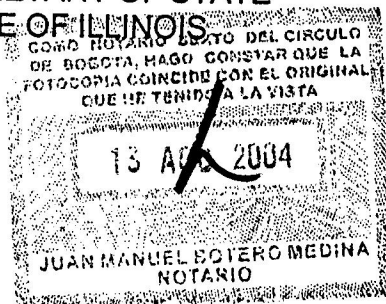
8. No. S04VB11001

9. Seal/Stamp:

10. Signature:



JESSE WHITE
SECRETARY OF STATE
STATE OF ILLINOIS



COMO NOTARIO SEXTO (E) DEL CIRCULO DE BOGOTA, HAGO CONSTAR QUE LA FOTOCOPIA COINCIDE CON LA FOTOCOPIA AUTENTICA QUE HE TENIDO A LA VISTA

27 AGO 2004

PABLO MENDEZ BARAJAL
NOTARIO (E)

CERTIFICADO NOTARIAL (SOCIEDAD)

Estados Unidos de América
Estado de {ss}
Condado de
Hoy 12 de Julio de 2004, compareció
Laura J. Schumacher, a quien conozco y
de quien me consta que firmó el anterior documento,
y quien debidamente juramentado declaró y dijo que
él es Vice Presidenta, Secretaria y Asesora
de ABBOTT

LABORATORIES, la compañía nombrada en el
documento que antecede, una sociedad
debidamente organizada y existente conforme a las
leyes del Estado de Illinois, Estados
Unidos de América, domiciliada en la ciudad de
Abbott Park, Condado de Lake
Estado de Illinois, Estados Unidos de
América, legalmente constituida para un período de
duración que aún no ha terminado, que ejerce su
objeto social conforme a las leyes del Estado de
Illinois, Estados Unidos de América;
que el declarante está autorizado por dicha
compañía para conferir este poder; que el sello
estampado por él al pie de tal poder, en nombre y en
representación de la expresada Compañía, es el
sello oficial de ella; y que el objeto para el cual se
confiere este instrumento está comprendido dentro
del de la sociedad.

El suscrito Notario ha visto los Estatutos de
incorporación firmados en Chicago
Estado de Illinois, con fecha Sep. 12, 2003,
y certifica que de conformidad con la legislación de
dicho Estado la anterior declaración juramentada es
prueba suficiente de que los hechos sobre que ella
versa son ciertos o verdaderos, de lo cual da fe.

Notary Public (Notario Público).

NOTARIAL CERTIFICATE (CORPORATION)

United States of America
State of {ss}
County of
On this 12th day of July, 2004,
personally
came

to me known, and known to me to be the person who
signed the foregoing instrument, who being by me
duly sworn did depose and say that she is the Vice President
Secretary and Deputy
General Counsel of ABBOTT

LABORATORIES, the company named within, a
Corporation organized and existing under the laws of
the State of Illinois, United
States of America, domiciled at the City of Abbott Park
County of Lake

State of Illinois, United States of America,
legally constituted for a period of tenure not yet
expired, which exercises its corporate purposes
according to the laws of the State of Illinois,
United States of America; that the deponent is
authorized by said Company to confer this power of
attorney; that the seal affixed hereunto by the
deponent in the name and on behalf of said
Corporation is the corporate seal thereof; and that the
purpose for which this instrument is granted is
included within the corporate purposes of the
Company.

The undersigned Notary Public has seen the articles
of Incorporation of said Corporation executed at
Chicago, State of Illinois, under date of
September 12, 2003, and hereby
certifies that under the laws of said State the
foregoing acknowledgment is sufficient proof that the
facts therein contained are true, which he attests.

Trina Lee Ruiz

OFFICIAL SEAL
TRINA LEE RUIZ
NOTARY PUBLIC, STATE OF ILLINOIS
MY COMMISSION EXPIRES 6-11-2007

27 AGO 2004

PABLO MENUEZ BARRA
NOTARIO (E)

COMO NOTARIO SEXTO DEL CIRCULO
DE BOGOTA, HAGO CONSTAR QUE LA
FOTOCOPIA COINCIDE CON EL ORIGINAL
QUE HE TENIDO A LA VISTA
13 AGO 2004
JUAN MANUEL BOTERO MEDINA
NOTARIO

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TRADUCCION OFICIAL No. 2004-07-29-362
DE UN DOCUMENTO PRESENTADO EN INGLES

PODER

Legalización de un Poder de Representación Legal, documento escrito en inglés y en español, dado y firmado el 12 de julio de 2004.

(firma: ilegible)

Laura J. Schumacher ✓

Vicepresidente, Secretaria y Asesora General Suplente ✓

Certificado Notarial (Sociedad), documento escrito en inglés y en español.

(firma: ilegible)

Notario Público

COMO NOTARIO SEXTO (E) DEL CIRCULO
DE BOGOTA, HAGO CONSTAR QUE LA
FOTOCOPIA COINCIDE CON LA ORIGINAL
AUTENTICA QUE HE TENIDO A LA VISTA

27 AGO 2004

PABLO MENDEZ BARAJAS
NOTARIO (E)

Sello Oficial

Trina Lee Ruiz ✓

Notario Público, Estado de Illinois

Mi Comisión Expira el 6-11-2007 ✓

COMO NOTARIO SEXTO DEL CIRCULO
DE BOGOTA, HAGO CONSTAR QUE LA
FOTOCOPIA COINCIDE CON EL ORIGINAL
QUE HE TENIDO A LA VISTA

13 AGO 2004

JUAN MANUEL POTERO MEDINA
NOTARIO

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Estado de Illinois
Secretario de Estado
APOSTILLA

(Convención de La Haya del 5 de octubre de 1961)

1. País: Estados Unidos de América
2. Este documento público
3. ha sido firmado por Trina Lee Ruiz
4. actuando como Notario Público, Condado de Lake
5. lleva el sello/estampilla del Estado de Illinois

Certificado

6. en Springfield, Illinois
7. el 20 de julio de 2004
8. por el Secretario de Estado, Estado de Illinois
9. No. S04VB11001
10. Firma: ilegible
11. Sello/Estampilla
12. Sello del Estado de Illinois
13. Jesse White

Secretario de Estado

Estado de Illinois

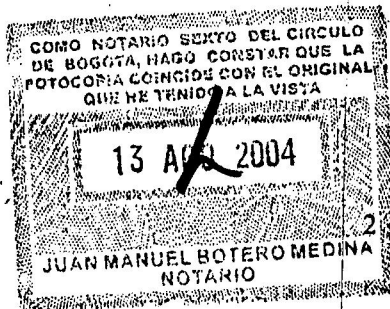
COMO NOTARIO SEXTO DEL CIRCULO
DE BOGOTA, HAGO CONSTAR QUE LA
FOTOCOPIA COINCIDE CON LA FOTOCOPIA
AUTENTICA QUE HE TENIDO A LA VISTA

27 AGO 2004

Traducido según mi mejor saber y entender, este día 29 de julio de 2004, en la ciudad de Bogotá, D.C. por Anita Escobar de Tamayo, Traductora Oficial. Res. 2177 de 1989, Ministerio de Justicia, República de Colombia.

TRADUCTOR OFICIAL
RESOLUCION 2177

Anita Escobar de Tamayo
ANITA ESCOBAR DE TAMAYO



MINISTERIO DE
RELACIONES EXTERIORES

NO SE ASUME
VERACIDAD DEL TEXTO

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JEFE DE LEGALIZACIONES
ECOTALE.

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Anita Escobar
CUYA FOTOGRAFIA APARECE EN EL
DOCUMENTO DESEMPENA
LAS FUNCIONES INDICADAS

27 AGO 2004

PABLO MENDOZ BARAJA
NOTARIO (E)

COMO NOTARIO SEÑTO DEL CIRCULO
DE BOGOTA, HAGO CONSTAR QUE LA
FOTOCOMIA COINCIDE CON EL ORIGINAL
QUE HE TENIDO A LA VISTA

13 AGO 2004

JUAN MANUEL BOTERO MEDINA
NOTARIO

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United States Patent [19]
Rubin

[11] **Patent Number:** **5,013,569**
[45] **Date of Patent:** **May 7, 1991**

[54] **INFANT FORMULA**

[75] **Inventor:** **David Rubin, San Diego, Calif.**

[73] **Assignee:** **Century Laboratories, Inc., Port Washington, N.Y.**

[21] **Appl. No.:** **526,096**

[22] **Filed:** **May 21, 1990**

[51] **Int. Cl.³** **A23C 9/20**

[52] **U.S. Cl.** **426/585; 426/801**

[58] **Field of Search** **426/801, 585, 580**

[56] **References Cited**

U.S. PATENT DOCUMENTS

3,542,560	11/1970	Tomarelli	426/585
3,558,323	1/1971	Cannalunga	426/98
3,649,295	3/1972	Bernhart	426/598
4,112,123	9/1978	Roberts	426/801
4,670,285	6/1987	Clandinin	426/585

FOREIGN PATENT DOCUMENTS

3512705	9/1986	Fed. Rep. of Germany	426/585
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3603000	8/1987	Fed. Rep. of Germany	426/801
64-80250	3/1989	Japan	426/801
1-196255	8/1989	Japan	426/585

OTHER PUBLICATIONS

21 CFR 105 Foods for Special Dietary Use.

Primary Examiner—Carolyn Paden

Attorney, Agent, or Firm—Browdy and Neimark

[57] **ABSTRACT**

An infant food formulation substantially approximating human milk in fatty acid composition comprising a mixture of DHA and EPA in a ratio of approximately 3:2 by weight, immunoglobulins to mimic the immunoglobulin content of mother's milk, a source of protein, a source of carbohydrate, a source of ash, and sufficient water to provide an easily assimilable infant formula, the DHA, the EPA, and the immunoglobulins being encapsulated in capsules having a diameter of less than 350 μ .

6 Claims, No Drawings

INFANT FORMULA

FIELD OF THE INVENTION

The present invention is directed to ready-to-feed and powdered infant formulas that can be used for pre-term and full-term infants.

BACKGROUND OF THE INVENTION

In the past, ready-to-feed infant formulas have been prepared by the appropriate blending of ingredients, including varying proportions of selected animal fats to yield a composition having a protein, mineral, carbohydrate, and fatty acid composition approximating that of human milk fat. However, the fatty acids of such artificial formulations have not been as well absorbed by the infant, or by experimental animals, e.g., the laboratory rat, as are the natural fatty acids in milk.

Canadian patent No. 927,187 discloses a dietary product intended to adapt cow's milk to the requirements of human infants, and to make the cow's milk similar to human milk. The lipid component of this dietary product is preferably a mixture of vegetable oils with soy lecithin and eventually with milk fats.

Canadian Patent No. 927,188 discloses an edible fat composition intended to resemble that of human milk fat. This composition includes various proportions of oleic oil; oleo oil; a seed oil comprising at least one or more of soybean oil, corn oil, peanut oil, sunflower seed oil, and cottonseed oil; coconut oil and/or babassu oil; and soy lecithin.

The dietary products and fatty acid compositions disclosed in these patents rely upon edible oils, soy lecithin, and/or milk fats to form the lipid component. However, these oils do not contain the C₂₀ and C₂₂ omega-6 and omega-3 fatty acids which are present in human milk. Accordingly, these preparations do not provide a balance of fatty acids that are similar in composition to that of human milk.

It is known that the composition of dietary fat is a major determinant of tissue composition during the formative stage in the growth and development of an organ. An analysis of human milk at day 16 of lactation was used to estimate infants' daily intake of C₂₀ and C₂₂ omega-3 and omega-6 fatty acids. The study indicated that significant amounts of these fatty acids are normally received by the infant fed human milk.

Past studies have not resolved the nutritional biochemical question of how much and which essential fatty acids should be provided in a dietary formula to premature infants to ensure normal synthesis of nerve tissues. Such tissues would normally contain high levels of long-chain metabolites of essential fatty acids as basic structural material. In particular, it is important that the quantities of the C₂₀ and C₂₂, omega-3 and omega-6 fatty acids be limited to appropriate ranges in a dietary formula. Insufficient supply of these fatty acids would interfere with brain development. Over-feeding of these fatty acid could distort normal prostaglandin metabolism and thus have adverse effects on the infant's physiology. For example, providing too much of these fatty acids could result in over-production of prostaglandins in the gut, which could lead to a hyperactive gut and diarrhea.

Studies on the composition of human milk have identified further substances not found in many cow's milk-based formulas. Recently, it has been shown that human milk contains physiologically active concentrations of

prostaglandins, specifically prostaglandin E₂, prostaglandin F_{2α}, and the metabolites of prostaglandin I₂, namely 6-keto-prostaglandin F_{1α}. These prostaglandins and their metabolites are present in human milk at all stages of lactation and change in concentration during lactation in a manner analogous to the development of the infant's capacity to absorb nutrients. For example, in approximately the first three weeks of infant life, the level of these prostaglandins and their metabolites increases in human milk, as does the infant's capacity to absorb nutrients.

It is known that prostaglandins affect functions related to nutrient absorption. Thus, in the human a variety of physiological functions are affected in the gut by prostaglandins, e.g., gastric acid and mucous secretion, smooth muscle contraction, local circulation, nutrient transport, and absorption.

However, providing the optimum ratio of the omega-3 and omega-6 C₂₀ and C₂₂ fatty acids in an infant formula is essential in order to provide early nutrition. For a growing infant, DHA is more important than EPA. For example, DHA is required for growth of the retina, and 70% of the lipid sheath of nerves is composed of DHA. DHA is also required for brain and nerve development. Therefore, it is important that an infant formula provide sufficient DHA to the infant. Naturally occurring sources, such as fish oil, are generally used as a source of EPA and DHA for infant formula. For example, in U.S. Pat. No. 4,670,285, Clandinin et al. disclose an edible fat formula for feeding infants wherein the omega- and omega-6 fatty acids are derived from fish oil. Unfortunately, the ratio of EPA to DHA in fish oil is the reverse of what is required by a growing infant, and an insufficient amount of DHA is present in the formula.

A number of other infant formulas have been commercialized in an attempt to duplicate the nutritional value of mother's milk. However, to date, none of these formulas has proven completely acceptable in terms of infant nutrition, particularly for premature infants.

Tomarelli et al., in U.S. Pat. No. 3,542,560, disclose an infant formula having a fat similar to the fat in human milk, including palmitic acid.

Cannalunga et al., in U.S. Pat. No. 3,558,323, disclose a vitamin-containing composition in beadlet form, the vitamins being generally fat-soluble vitamins, which can then be incorporated in milk. When these beadlets are dispersed in milk, they impart no off-flavor to the milk, and the beadlets can be mixed with spray-dried skim milk powder without affecting the stability of the powder.

Roberts, in U.S. Pat. No. 4,112,123, discloses a nutritionally balanced food composition for patients having abnormal catabolic states. These compositions include protein obtained from the ultra-filtration of sweet or acid wheys and contain β-lactoglobulin, α-lactalbumin, immunoglobulins, and serum albumin. This food made be prepared in dried powder form to be reconstituted with a liquid. The powder may include encapsulated and embedded minerals.

Durst, in U.S. Pat. No. 4,800,087, discloses pharmaceutical compositions comprising a pharmaceutical core comprising a pharmaceutically active dose of a compound and a microencapsulating polymer which coats the pharmaceutical core and is capable of masking the taste of the active compound. The polymer coating does not fracture or release active ingredients when

tabletted and/or chewed. These capsules may be included in a liquid formulation, although infant formula is not disclosed.

SUMMARY OF THE INVENTION

It is an object of the present invention to overcome the aforementioned deficiencies in the prior art.

It is another object of the present invention to provide a mixture of fatty acids for incorporation into an infant formula.

It is yet another object of the present invention to provide an infant formula for optimum growth.

According to the present invention, a fat composition is provided for use in infant formula comprising (all-Z)-4,7,10,13,16,19-docosahexaenoic acid, hereinafter referred to as DHA and (all-Z)-5,8,11,14,17-eicosapentaenoic acid, hereinafter referred to as EPA in an approximate ratio of from about 1:1 to about 2:1, and preferably about 3:2 by weight. These fatty acids are preferably in the form of free acids rather than as the naturally occurring triglycerides. The EPA and DHA can also be in the form of their pharmaceutically acceptable salts, esters, or amides. Additionally, these acids may be in their natural state as they are extracted from natural sources such as marine animals, daphnae, algae, and the like, although the weight ratios of the acids are different from that in the naturally occurring state. Lower esters and amides which can be converted in vivo to the acid and other pharmaceutically acceptable products may be used, the preferred ester being the ethyl ester. The preferred salts are the sodium, potassium, calcium, or magnesium salts, as well as any other pharmaceutically acceptable solid salts. Among the methods that can be used for obtaining EPA and DHA from these sources are those shown in Rubin et al., U.S. Pat. No. 4,792,418, which patent is hereby incorporated by reference.

According to another aspect of the present invention, an infant formula is provided which contains optimum amounts of DHA and EPA in a ratio of approximately 1:1 to about 2:1, and preferably about 3:2, by weight. The infant formula of the present invention also preferably includes immunoglobulins which are substantially identical to the immunoglobulins found in human milk. These immunoglobulins are included in the infant formula in the form of microcapsules which are stable to the processing conditions of the formula and are not detectable by the infant.

The infant formula of the present invention preferably contains from about 0.1 to about 5.0% by weight of the mixture of DHA and EPA which is a quantity substantially to mimic the relative quantity of fatty acid in human mother's milk. The DHA and EPA can be from synthetic sources, or can be obtained from natural sources in hydrolyzed form. As noted supra, the ratio of DHA to EPA in the present infant formula is different from the ratio found in naturally occurring sources. The DHA and EPA are preferably encapsulated in microcapsules having a diameter of less than 350 μ , so that they are not perceptible to the infant and so that they pass easily through the hole of the nipple used for feeding the infant.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

The mixture of DHA and EPA in a ratio of approximately 3:2 by weight can be incorporated into an infant formula in concentrated powder or liquid form, or in ready-to-use form.

The infant formula according to the present invention comprises a mixture of DHA and EPA in a ratio of approximately 3:2 by weight, a source of carbohydrate such as sucrose or dextrose, non-fat milk, water, and optional other edible fats. The optional edible fats may be any food-grade fat including, but not limited to, coconut oil, oleo oil, peanut oil, butterfat, soybean oil, olive oil, babassu oil, mutton tallow, and the like. Among the fatty acids that are provided by these fats are lauric acid, myristic acid, palmitic acid, stearic acid, oleic acid, and linoleic acid.

A typical ready-to-feed formulation for infants comprises, when diluted to feeding concentrations, from about 1-5% by weight fat; from about 0.01 to about 0.5% by weight immunoglobulins as appropriate, from about 4-10% by weight carbohydrate in a quantity substantially to mimic the carbohydrate content of human mother's milk, from about 0.5 to 4% by weight protein in a quantity substantially to mimic the protein content of human mother's milk, optional vitamins and minerals as required, a total solids content of from about 8 to 17% by weight, and the remainder water.

A typical protein source for use in infant formula is electrodialyzed whey or electrodialyzed skim milk or milk whey, although other protein sources are also available and may be used. Sugars include food grade substances such as glucose, dextrose, sucrose, or edible lactose. The following vitamins and minerals may also be incorporated in the infant formula: calcium, phosphorus, potassium, sodium, chloride, magnesium, manganese, iron, copper, zinc, selenium, iodine, and vitamins A, E, D, and B complex. These micronutrients are added in the form of commonly accepted nutritional compounds in amounts equivalent to those present in human milk on a per calories basis.

To prepare an infant formula according to the present invention, the fat soluble vitamins are dissolved in the mixture of fatty acids, and the remaining formula ingredients are dissolved in the water. The fat mixture with the dissolved vitamins and the water solution are then mixed and homogenized. Adequate amounts of other trace minerals are present in the electrodialyzed whey and non-fat milk.

The infant formula according to the present invention is sterilized and subsequently used on a ready-to-feed basis, or can be stored as a concentrate. The concentrate can be prepared by spray drying the formula prepared as above, and the formula can be reconstituted by rehydrating the concentrate. The infant formula is a stable liquid and has a suitable shelf life.

Preferably, both the fatty acids and the immunoglobulins are encapsulated in microcapsules. The choice of coating for the microencapsulation of the DHA and EPA and/or the globulin is determined by its lack of toxicity, desired particle size, and stability under the processing conditions for infant formulas, particularly sterilization. Any conventionally acceptable substantially oxygen-impermeable coating for pharmaceuticals can be used in the present invention. Examples of these coating compositions and methods for microencapsulation are given in U.S. Pat. No. 4,001,140 to Foris et al., which patent is hereby incorporated by reference. Other conventional microencapsulating methods and coating materials are well within the purview of one skilled in the art, and the specific microencapsulating method and coating are not peculiar to the present invention.

A particularly successful method for encapsulating the EPA and DHA and the globulins is by forming micelles in a water-in-oil emulsion, using a polymerizable surfactant such as acrylamide. The surfactant is polymerized in various ways, as by x-ray or gamma radiation. The particle sizes range from about 80 to about 300 nm. These particles are sufficiently small that the infant does not perceive their presence in the liquid formula, and there is no possibility of the capsules' interfering with liquid flow through the nipple.

Other methods of preparing microcapsules for use in the present invention include spray drying wherein the DHA and EPA are emulsified into a solution of a polymer, such as gum arabic, and spray-dried to make fine particles. Particles of 250 μ m are ideal for inclusion in the infant formulas according to the present invention. When the EPA and DHA or the globulins are incorporated into a meltable fat or wax, the process is called spray-chilling, since the emulsion need only be chilled below its melting point to form particles.

Another encapsulation process that can be used to encapsulate the DHA and EPA as well as the globulins is by suspending the EPA and DHA in a solution of the wall material. The wall polymer is then induced to separate as a liquid phase. By adding a nonsolvent for the polymer, decreasing the temperature, or by adding a phase inducer, another polymer that has higher solubility in the solvent. In the latter case, incompatibility between the two polymers causes the first polymer to separate as another phase. When the wall polymer separates as a polymer-rich liquid, this phase is called a coacervate and the process is called coacervation. As the coacervate forms, it must wet the suspended core particle and coalesce into a continuous coating. The final step is the hardening and isolation of the microcapsules.

Gelatin and gum arabic also for a pharmaceutically acceptable coating for the EPA and DHA and globulins for use in the present invention. In this process, gelatin having a high isoelectric point and gum arabic, which contains mainly carboxyl groups, are added to a core-containing suspension at pH 2-5 at a temperature above 35° C. to ensure that the coacervate is in the liquid phase. As the gelatin and gum arabic react, viscous liquid microdroplets of polymer-coacervate separate. This wall can be hardened by several means, including addition of formaldehyde. Finally, the mixture is cooled to 10° C., the pH is adjusted to about 9, and the microcapsule suspension is filtered.

In another coacervation process, two gelatins of differing isoelectric points are used as the reacting species. In this case, the coacervation is reversible before hardening, and any distorted capsules can be heated to restore their spherical shape. These microcapsules are hardened by the addition of glutaraldehyde.

Another technique for encapsulating the DHA and EPA and globulins for use in the present invention is based upon polymer-polymer incompatibility. A coacervate of the wall material is induced to form from solution by the presence or addition of a phase-inducer. The general phenomenon of polymer-polymer incompatibility is based on the fact that the free energy of mixing for polymers is positive owing to a positive entropy change and negligible entropy change.

Another method for microencapsulating the DHA and EPA and globulins for use in the present invention involves adding a nonsolvent for the wall polymers.

Another method for forming microcapsules of the EPA and DHA and globulins is based upon the observations that some cellulosic polymers are soluble in cold water but not in hot water, such as hydroxypropyl cellulose and ethyl hydroxyethyl cellulose. These materials precipitate from solution when the temperature exceeds a critical value of about 40°-70° C. To carry out microencapsulation of the compounds based upon this phenomenon, the compound to be encapsulated is dispersed in an aqueous solution of the cellulosic material at a low temperature where it is still soluble, in the presence of a surfactant. The dispersion is then heated until the cellulosic polymer gels or precipitates form solution, wetting the oil droplets. While the dispersion is hot, the cellulosic wall is solidified by reaction with a water-soluble agent such as dimethylolurea, urea-formaldehyde resin, or methoxymethylmelamine resin. Because this is typically a slow reaction, resulting in somewhat porous walls, a cross-linking agent is added before dispersion so as to produce microcapsules with tight walls.

Microcapsules for use in the present invention can also be prepared by interfacial polymerization. In interfacial polymerization, the two reactants in a polycondensation meet at an interface and react rapidly. The coatings may be polyesters, polyurea, polyurethane, or polycarbonates.

Another manner of microcapsule formation is based upon the fact that alginic acid anion forms an insoluble precipitate instantly upon contact with calcium ions. Hence, if droplets of an aqueous solution of sodium alginate are placed into a calcium chloride solution, a membrane quickly forms around the droplets. If the initial droplets contain enough alginate and are allowed to remain in the calcium-containing solution long enough, they gel completely.

Thus, any conventional microencapsulation technique can be used with an substantially oxygen-impermeable and heat-resistant coating material to form the microcapsules for use in the present invention.

Of course, since the microcapsules formed are to be used in an infant formula, only wall material approved by the FDA should be used. The GRAS list provides a listing of compounds that can be used for forming the capsule walls. Some materials, such as starches, cellulosic compounds, and gums, have been used for many years as food additives or as excipients in drug formulation.

Alternatively, the capsules can be formed by incorporating the EPA and DHA into an inclusion compound with a suitable host compound. The inclusion compound, which is in the form of a relatively free-flowable powder, is then microencapsulated with a substantially oxygen-impermeable coating material to form a protective microcapsule. The inclusion compound can be amyloses or cycloamyloses such as the cyclodextrins.

Typical ready-to-feed infant formulas contain the following ingredients, where the fat ingredient is a mixture of DHA and EPA in a ratio of approximately 3:2. These fats are in the form of the free fatty acids, and are encapsulated in microcapsules. The encapsulation of the free fatty acids prevents them from being oxidized by exposure to ambient air, and masks any unpleasant taste or odor they may impart to the formula. The immunoglobulins used are also encapsulated in microcapsules to preserve their activity.

Typical ready-to-feed formulations include the following ingredients, the fats being DHA and EPA in an approximately 3:2 weight ratio:

	Concentrated Liquid w/v	Powder w/w	Diluted Liquid w/v
Fat	2-10	8-40	1-5
Carbohydrate	8-20	32-80	4-10
Protein	1.8-6.6	8-28	0.9-3.4
Immunoglobulins	0.02-0.6	0.08-1	0.001-0.3
Total Solids	12-36	25-100	6-18
Water	88-64	0-5	93-82

The concentrated liquid and powder are easily reconstituted by adding sufficient water to make the desired concentration. The liquid and powder forms are shelf-stable in cans, as is the diluted formula. The microencapsulation of the fatty acids and of the immunoglobulins renders them stable upon exposure to the high temperatures and/or pressures used to sterilize the formula for packing.

The infant formulas of the present invention are particularly designed for feeding to premature infants. However, they are also suitable for feeding to full-term infants as well.

The foregoing description of the specific embodiments will so fully reveal the general nature of the invention that others can, by applying current knowledge, readily modify and/or adapt for various applications such specific embodiments without departing from the generic concept, and therefore such adaptations and modifications are intended to be comprehended within the meaning and range of equivalents of the disclosed embodiments. It is to be understood that the phraseology or terminology herein is for the purpose of description and not of limitation.

What I claim is:

1. An infant food formulation substantially approximating human milk in fatty acid composition, comprising:

a mixture of 4,7,10,13,16,19-docosahexaenoic acid (DHA) and 5,8,11,14,17-eicosapentaenoic acid (EPA) in a ratio of approximately from 1:1 to 2:1 by weight, the EPA and DHA being present in a

quantity substantially to mimic the relative quantity of fatty acid in human mother's milk;

immunoglobulins in a quantity substantially to mimic the immunoglobulin content of human mother's milk;

a source of protein in a quantity substantially to mimic the protein content of human mother's milk;

a source of carbohydrate in a quantity substantially to mimic the carbohydrate content of human mother's milk;

and sufficient water to provide an easily assimilable infant formula, said DHA and EPA and said immunoglobulins being microencapsulated.

2. The infant formula according to claim 1 wherein the DHA and EPA are in a ratio of approximately 3:2 by weight.

3. The infant formula according to claim 1 wherein the EPA and DHA are in the free acids form thereof or in the form of a pharmaceutically acceptable salt thereof.

4. The infant formula according to claim 1 comprising from about 1-5% by weight of fat, from about 0.01 to about 3.0% by weight immunoglobulins, from about 4-10% by weight carbohydrate, from about 0.5 to 4% by weight protein, from about 0.1 to 1% by weight ash, a total solids content of about 8-17% by weight, and the remainder water.

5. The infant formula according to claim 4 comprising from about 1-5% by weight of fat, from about 0.01 to about 3.0% by weight immunoglobulins, from about 4-10% by weight carbohydrate, from about 0.5 to 4% by weight protein, a total solids content of about 8-17% by weight, and the remainder water.

6. A concentrate for preparing an infant food formulation substantially approximating human milk in fatty acid composition, comprising:

a mixture of DHA and EPA in a ratio of approximately from 1:1 to 2:1 by weight, the EPA and DHA being present in a quantity substantially mimicking the relative quantity of fatty acid in human mother's milk;

immunoglobulins in a quantity substantially to mimic immunoglobulin content of human mother's milk; and

a source of protein in a quantity substantially to mimic the protein content of human mother's milk.

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US005340603A

United States Patent [19]

Neylan et al.

[11] **Patent Number:** 5,340,603[45] **Date of Patent:** Aug. 23, 1994[54] **NUTRITIONAL PRODUCT FOR HUMAN INFANTS HAVING CHRONIC LUNG DISEASE**

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[21] **Appl. No.:** 114,033

[22] **Filed:** Aug. 30, 1993

[51] **Int. Cl.⁵** A23C 11/10

[52] **U.S. Cl.** 426/73; 426/74; 426/580; 426/590; 426/601; 426/607; 426/656; 426/658; 426/801; 426/72

[58] **Field of Search** 426/801, 607, 658, 656, 426/74, 580, 590, 601

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[57]

ABSTRACT

A hypercaloric formula providing nutritional support for human infants having chronic lung disease, said formula having a caloric density of at least 800 kcalories per liter of formula and wherein not less than 56% of the total calories in said formula is derived from fat; not more than 15% of total calories is derived from a high quality protein source; and from about 20-27% of total calories is from a carbohydrate source; said formula having a calcium to phosphorous ratio in the range of 1.4 to 2.2, and having an m-inositol concentration of at least 50 milligrams per liter of formula.

13 Claims, No Drawings

C.) and add calcium carbonate and tricalcium phosphate.

Step 5: Adjust pH of the Slurry

Determine the pH of the slurry which was produced in STEP 4. The desired pH of the slurry is in the range of 6.50 to 6.70. If the pH of the slurry is less than 6.50 add a sufficient quantity of a 45% potassium hydroxide solution to adjust the pH of the slurry to about the middle of the desired range. Hold the slurry under agitation at a temperature in the range of 130° to 140° F. (54.4 °-60° C.) for at least fifteen minutes, preferably avoiding any excess agitation that would cause entrainment of air in the slurry.

Step 6: Processing

The slurry is processed continuously including homogenization and a high temperature-short time (HTST) heat treatment. The product is heated to 165°-175° F. (74°-79.4° C.) deaerated, emulsified, and homogenized. The product is then heated to a minimum of 165° F. (74° C.) and held for at least 18 seconds before cooling. The batch is held cooled while nutrient levels are measured. If needed, nutrient levels are adjusted to meet product specifications. The water soluble vitamin premix, the ferrous sulfate, choline chloride, L-carnitine, m-Inositol and ascorbic acid are dissolved in 140° F. (60° C.) water (approximately 200 lbs; 90.7 kg) and added to the product. Water is added to bring the product to the specified total solids level (approximately 1900 lbs; 862 kg). The product is then placed in suitable containers and sterilized.

A preferred embodiment of the present invention has: about 10.0% to about 15.0%, most preferably about 11% of the total calories in the product provided by protein; about 20% to about 27.0%, most preferably about 22% of the total calories in the product provided by carbohydrate; and about 60% to about 70%, most preferably about 67% of the total calories in the product provided by fat. Put another way, a liquid nutritional product for enteral feeding in accordance with a preferred embodiment of the present invention contains: about 26.0 g/liter (g/L) to about 34 g/L, most preferably about 28 g/L of protein; about 45 g/L to about 70 g/L, most preferably about 56 g/L of carbohydrate; and about 65 g/L to about 80 g/L, most preferably about 76 g/L provided by fat.

The source of fat in the liquid nutritional is a lipid blend wherein the oils may be selected from the group consisting of medium chain triglycerides, long chain triglycerides, soy oil, coconut oil, safflower oil, high oleic safflower oil, structured lipids, marine oil, phospholipids and lecithin. The preferred source of fat in the liquid nutritional product is a lipid blend comprising coconut and soy oils which has been described above in detail.

The preferred sources of protein in the liquid nutritional product of the present invention are non-fat dry milk powder and whey protein. The reason that this is the preferred source of protein is that they both are high quality proteins with high biological value. However, other suitable sources of protein that may be used in the practice of the present invention include milk and soy protein, and hydrolysates thereof.

The preferred sources of carbohydrate in the liquid nutritional product of the present invention are hydrolyzed corn starch and lactose. The reason that these are the preferred sources of carbohydrate is that both simple and complex carbohydrates are provided.

Other ingredients that may be advantageously used in the practice of the present Invention include oligosaccharides, dietary fiber, nucleotides and antioxidants such as beta-carotene.

The pulmonary function of a mammalian creature having respiratory insufficiency may be improved by feeding a liquid nutritional product in accordance with the present invention. The most preferred composition, by weight, of a liquid nutritional product for enteral feeding in accordance with the present invention is set forth in Table 11.

TABLE 11

PREFERRED NUTRITIONAL INFORMATION FOR NEW BPD30 PRODUCT (Invention) (Values given are per liter)		
NUTRIENT		Mass per liter
Nutrient	Protein, g	28.1
	Fat, g	74.7
Vitamins	Carbohydrate, g	56.2
	Vitamin A, IU	7060
	Vitamin D, IU	1611
	Vitamin E, IU	40.2
	Vitamin K ₁ , µg	135
	Thiamine (Vitamin B ₁), mg	3.9
	Riboflavin (Vitamin B ₂), mg	7.0
	Vitamin B ₆ , mg	3.2
	Vitamin B ₁₂ , mg	11.9
	Niacin, mg	52.4
	Folic Acid (Folacin), µg	424
	Pantothenic Acid, mg	25.8
	Biotin, µg	455
	Vitamin C (Ascorbic Acid), mg	455
Minerals	Choline, mg	287
	m-Inositol, mg	500
	L-Carnitine, mg	69
	Calcium, mg	1549
	Phosphorus, mg	769
	Magnesium, mg	155
	Iron, mg	7.2
	Zinc, mg	17.8
	Manganese, µg	215
	Copper, mg	2.8
	Iodine, µg	118
	Sodium, mg	356
	Potassium, g	1.45
	Chloride, mg	829
	Taurine, mg	50
	Selenium, µg	50
	Ca:P Ratio	1.4-2.2

The BPD30 formulation described in Tables 4, 10 & 11 is intended for ingestion by human infants with compromised lung function. The formulation may be fed by mouth or by tube and may be used as a supplement or as a complete diet. While the BPD30 infant formula and method of making said formula herein described constitute a preferred embodiment of this invention, it is to be understood that the invention is not limited to this precise form and that changes may be made therein without departing from the scope of the invention which is defined in the appended claims. The foregoing detailed description is given for the clearness of understanding only, and no unnecessary limitations should be understood therefrom, as aspects and advantages within the scope of the present invention will be apparent to those skilled in the art.

What is claimed is:

1. An infant formula comprising:

- a) protein at a concentration of between 25 and 35 grams per liter of formula;
- b) fat at a concentration of between 65 and 85 grams per liter of formula;

- c) carbohydrates at a concentration of between 40 and 75 grams per liter of formula;
- d) inositol;
- e) a calcium to phosphorous ratio in the range of 1.4 to 2.2;
- f) a caloric density of not less than 800 kilocalories/liter and not more than 1200 kilocalories/liter; and
- g) wherein at least 56% of said calories in said infant formula are derived from fat and the nutritional product is specially formulated for use in the management of human infants having compromised lung function.
2. The formula as claimed in claim 1 wherein said protein is at a concentration of between 26 and 32 grams per liter of formula, said fat is at a concentration of between 70 and 80 grams per liter of formula; said carbohydrate is at a concentration between 50 and 60 grams per liter of formula; said caloric density is between about 900 and 1100 kilocalories/liter; and wherein at least 60% of said calories are derived from fat.
3. The formula as claimed in claim 2 wherein said protein is provided by at least one material selected from the group consisting of non-fat milk and whey, said fat is provided by at least one material selected from the group consisting of medium chain triglycerides, long chain triglycerides, soy oil, coconut oil, safflower oil, high oleic safflower oil, structured lipids, marine oil, phospholipids and lecithin, and said carbohydrate is provided by at least one material selected from the group consisting of corn syrup, sucrose, glucose polymers, lactose, oligosaccharides.
4. The formula as claimed in claim 3 wherein said protein is provided by non-fat milk and whey, said fat is provided by soy oil and coconut oil, said carbohydrate is provided by corn syrup and lactose.
5. The formula as claimed in claim 1 wherein said protein is at a concentration of between 26 and 29 grams per liter of formula, said fat is at a concentration of between 75 and 78 grams per liter of formula, said carbohydrate is at a concentration of between 55 and 58 grams per liter of formula, said caloric density is between about 975 and 1050 kilocalories/liter; and

wherein at least 65% of said calories are derived from fat.

6. The formula as claimed in claim 1 wherein said protein is at a concentration of about 27.9 grams per liter of formula and is provided by a blend of non-fat milk and whey protein, said fat is at a concentration of about 76 grams per liter of formula and is provided by a blend of soy and coconut oils, and said carbohydrate is at a concentration of about 56.5 grams per liter of formula and is provided by a blend lactose and corn syrup, said caloric density being about 1000 kilocalories/liter; and wherein at least about 65% of said calories are derived from fat.

7. The formula as claimed in claim 1 wherein said fat provides not less than about 60% of the calories, said protein provides not more than about 15% of the calories, and said carbohydrate provides not more than about 25% of the calories.

8. The formula as claimed in claim 1 wherein said fat provides not less than about 67% of the calories, said protein provides about 11% of the calories, and said carbohydrate provides about 22% of the calories.

9. The formula as claimed in claim 1 wherein said inositol is at a concentration of between 50 and 800 milligrams per liter of formula.

10. The formula according to claim 9 wherein said inositol is at a concentration of between 400 and 700 milligrams per liter of formula.

11. The formula according to claim 10 wherein said inositol is at a concentration of about 600 milligrams per liter of formula.

12. The formula as claimed in claim 1 further comprising 4 to 7 grams of minerals per liter of formula, wherein said minerals are selected from the group consisting of calcium, phosphorous, magnesium, iron, zinc, manganese, copper, iodine, sodium, potassium, selenium and chloride.

13. The formula as claimed in claim 1 further comprising vitamins selected from the group consisting of vitamin A, C, B1, B2, B6, B12, D, E, K, niacin, folic acid, biotin, pantothenic acid, choline, carnitine, taurine and β -carotene.

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United States Patent [19]

Masor et al.

[11] Patent Number: **5,700,590**[45] Date of Patent: **Dec. 23, 1997**[54] **NUTRITIONAL FORMULA WITH RIBO-NUCLEOTIDES**

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[73] Assignee: **Abbott Laboratories**, Abbott Park, Ill.

[21] Appl. No.: **585,221**

[22] Filed: **Jan. 11, 1996**

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 178,687, Jan. 10, 1994, Pat. No. 5,492,899.

[51] Int. Cl.⁶ **A23L 1/305; A61K 31/70**

[52] U.S. Cl. **426/656; 426/69; 426/72; 426/73; 426/541; 426/601; 426/658; 426/801; 514/47; 514/45; 514/46; 514/50; 514/51**

[58] Field of Search **426/541, 801, 426/69, 72, 73, 658, 656, 601; 514/47, 45, 46, 49, 50, 51**

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[57] **ABSTRACT**

An improved enteral formula containing ribo-nucleotide equivalents (RNA, mono-, di- and triphosphate nucleotides, nucleosides and adducts such as activated sugars) at a level of at least 10 mg/100 Kcal (kilocalorie) of formula. More specifically, an infant formula containing at least 10 milligrams of nucleotide equivalents per 100 Kcal of formula where the nucleotide equivalents consist of RNA; mono-, di-, and triphosphate esters of adenosine, cytidine, guanosine, and uridine, and the d-ribose adducts thereof; and wherein the weight ratio of said cytidine nucleotide equivalents to said uridine nucleotide equivalents is 1.5:1 to 2.6:1; of said cytidine nucleotide equivalent to said adenosine nucleotide equivalents is 2:1 to 3.9:1; and of said cytidine nucleotide equivalents to said guanosine nucleotide equivalents is 1.75:1 to 2.8:1, is disclosed. The formula comprises carbohydrates, lipids, proteins, vitamins and minerals and four (4) ribo-nucleotide equivalents at specific levels and ratios. This invention also provides a dietary formula that enhances the immune system and alleviates diarrhea.

42 Claims, No Drawings

to 32 mcg per liter of formula. The selenium used in this aspect of the invention may be delivered in the form of selenate. The teachings of U.S. Pat. No. 5,221,545 are herein incorporated by reference.

In actual use, the formula of this invention may be consumed by any infant and should be in compliance with accepted levels of vitamins, minerals, micro-components and the like. The amount consumed does not differ from that associated with the normal consumption of commercially available infant formula.

A representative formula for the enteral nutritional product of the invention is set forth in Table I.

TABLE I

FORMULA ACCORDING TO THE INVENTION

Nutrient	Concentration per liter of formula
Protein	13.0-20 g
Protein Source	
CSM ¹	55-75%
WPC ²	7.15-15 g
	25-45%
	3.25-9.0 g
Lipid	13-21 g
H.O. Safflower Oil	35-55%
Soy Oil	20-40%
Coconut Oil	20-45%
Carbohydrate lactose	70-110 mg
Nucleotides	70-100 mg
CMP	29-39 mg
UMP	15-21 mg
AMP	10-16 mg
CMP	14-20 mg
Iron	8-16 mg
R,R,R, α tocopherol	10-30 IU
β Carotene	375-575 μ g
Selenium	14-32 mcg
Calcium	475-850 mg
Phosphorus	240-700 mg
Ca:P Ratio	1.4 to 2.4

¹CSM is Condensed Skim Milk

²WPC is Whey Protein Concentrate

The pediatric nutritional formula of this invention is generally prepared using the following method. An appropriate quantity of protein is dispersed in sufficient water or oil to solubilize or suspend it, thereby forming a protein solution/suspension. Typically this protein source would be intact milk proteins and/or hydrolyzed milk proteins. Vegetable proteins, such as soy protein, can also be used provided the high inherent levels of nucleotide equivalents have been removed. A carbohydrate source such as one or more of corn syrup solids, lactose maltodextrins and sucrose is dissolved in water, thereby forming a carbohydrate solution. A source of dietary fiber, such as soy polysaccharide, may also be added. Appropriate minerals are dissolved in water, the carbohydrate solution or oil, so as to form a mineral solution.

Once formed, the three solutions (protein, carbohydrate, and mineral) are combined in appropriate quantities with oils and oil soluble vitamins. This resulting solution is then heat processed and homogenized. Following processing, water soluble vitamins, iron, choline and other nutrients are added and then the nucleotides are added. The solution is then diluted with water to the appropriate caloric density, approximately 400-725 kcal per liter of formula. The formula is then dispensed into containers and retorted to obtain commercial sterility or packaged aseptically using commercially available techniques and equipment. As prepared, the formula contains appropriate nutrients in compliance with

the Infant Formula Act as of the date of this application. It should also be recognized that the unique formula of this invention could be prepared for use in powdered form or as a concentrated liquid.

The invention will be better understood in view of the following examples, which are illustrative only and should not be construed as limiting the invention.

DETAILED DESCRIPTION OF THE INVENTION

Analytical Techniques

One feature of the instant invention resides in the novel analytical technique used to identify and quantify the nucleotide equivalents useful in this invention. Analysis of certain starting materials, especially the protein, will determine the actual amount of nucleotides to be added. This analysis of the raw materials of the formula is critical to determine what nucleotides, if any, are contained in the starting materials. The analytical method is also critical to determine the proper ratios of the nucleotides to each other. The analytical method according to this invention will determine nucleotide equivalent levels in complex food matrices. The method in general exploits the enzymatic digestion of various forms of ribonucleic acids to the simple monomeric ribonucleosides and the ability of the cis-diol groups of ribonucleosides to form a pH dependent covalent complex with boronic acid. Boronate derivatized polyacrylamide gel is used to very selectively prefractionate ribonucleoside directly from complex matrices. The isolated ribonucleosides are subsequently separated via low pH reverse phase/ion-pairing HPLC using octanesulfonate as the ion-pairing agent. Ribonucleosides are detected via UV absorbance, and the corresponding levels are determined by comparison to external standards. The method can be used to quantitate inherent levels of ribonucleoside in foods. Because of the selective prefractionation, the method is essentially matrix independent. It should be understood that the novel analytical technique of this invention will not detect nucleosides from DNA or any form of nucleic acid that does not contain the cis-diol groups of ribose. It has been used to determine ribonucleic acid types and levels in infant and medical nutritional products, human milk, protein commodities, and clinical and commercial animal chows.

The following is an example of the analytical technique of this invention that can be used to determine the presence and ratios of the nucleotide equivalents.

EXAMPLE I

Analysis of Similac® with Iron

To a 10 ml Reacti-Therm vial with stir bar was placed 2.0 ml of Similac® with Iron (a non-fat milk protein infant formula produced by the Ross Products Division of Abbott Laboratories, ready to feed form, 676 Kcal per liter) 3.0 ml of 50 mM sodium acetate at pH 5.1, 50 μ l of 10 mM zinc sulfate and 50 μ l of the enzyme preparation nuclease P1 (Sigma Chemical). The enzyme preparation was 5 mg of dry enzyme powder, as received from Sigma, and 4 ml of 50 μ M sodium acetate at pH 5.1. The mixture was heated to 37° C. and stirred for 16 hours. This reaction converted the polymeric RNA to monomeric 5' mono-nucleotides.

To the same reaction vial was added 50 μ l of 30% ammonium hydroxide, 1 ml of 0.5M ammonium acetate (pH 8.75), 50 μ l of 1.0M magnesium chloride, 50 μ l of bacterial alkaline phosphatase (BAP) (Sigma Chemical as a suspension) and 50 μ l of a nucleotide pyrophosphatase

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enzyme preparation (Sigma Chemical). The pyrophosphatase enzyme preparation was 5 mg of dry powder in 4 ml of 0.5M ammonium acetate buffer. The mixture was incubated at 37° C. for three hours. This reaction converted the nucleoside containing adducts and the nucleotides to the ribonucleosides.

The reaction mixture was transferred to a 50 ml volumetric flask using 25 ml of 0.5M sodium phosphate, pH 10.5. Water was added to a final volume of 50 ml. The sample mixture was shaken and may be filtered to remove insoluble protein.

5 grams of dried Affi-Gel-601, boronate derivatized (from Bio-Rad) was hydrated in 50 ml of 100 mM phosphate buffer at pH 6.5. To a 10 ml open column was added the hydrated Affi-Gel-601 to obtain a packed volume of about 1 ml. The gel was converted to the basic form by washing with 5 ml aliquots of 0.25M sodium phosphate buffer, pH 10.5, until the gel no longer swelled. The gel was now about 2 ml in volume. The gel was resuspended in the buffer to maintain adequate flow.

To the prepared gel was added 10 ml of the sample that was previously treated with the enzymes and the eluant was discarded. At this point, the nucleosides are covalently attached, through the cis-diol groups, to the boronic acid gel. The gel was washed with 20 ml of 0.25M sodium phosphate, pH 10.5 and the eluant was discarded. The nucleosides were eluted and collected in a 10 ml volumetric flask by adding 2 ml of 1.0M phosphoric acid to the column followed by 5 ml of 0.1M phosphoric acid. At this point the nucleosides have been isolated from the sample and are now ready to be characterized.

The volumetric flask was brought to a final volume of 10 ml with water. The sample was then placed on a HPLC for separation and quantification of nucleosides using external standards. The nucleosides were separated via low pH, reverse phase, ion pairing chromatography using an acetonitrile gradient. The nucleosides were detected by U.V. absorbance at 260 nm and 280 nm. Nucleosides were quantified by reference to external standards and the results were converted to the corresponding monophosphate nucleotide value by multiplying the nucleoside value by the molecular weight ratio of the monophosphate nucleotide over the nucleoside. The results were expressed as mg/L, of mononucleotide.

NUCLEOTIDES IN SIMILAC ® WITH IRON

uridine - 3-5	guanosine - trace	adenosine - trace
inosine - trace	cytidine - 1-3	

It should be noted that some samples have been found to be active with respect to nucleic acid degradation. Of particular concern is the enzymatic conversion of AMP to IMP. Heat inactivation has proven to be effective in rendering the sample inactive. The procedure for heat inactivation is to heat the sample to over 100° C. for at least 15 minutes. After the sample has cooled, buffer, enzyme, and zinc are added and the first hydrolysis is carried out.

This analytical technique was used on raw materials to determine base line nucleotide content and on final clinical product to confirm the presence and concentration of the four nucleotides used in the invention.

EXAMPLE II

Preparation of Enteral Formula

On a commercial scale, a control and an experimental formula according to the invention were prepared having the

compositions set forth in Table II. The two formula are as close as possible to being identical except for the nucleotide components.

TABLE II

COMPOSITION OF STUDY FEEDINGS

Nutrient	CON (Control)	NUC (Formula of the Invention) per liter
Protein, g	14.0	14.4
Fat, g	36.5	38.3
Carbohydrate, g	77.1	75.5
Calcium, mg	544.4	532.5
Phosphorus, mg	295.0	316.2
Magnesium, mg	73.5	77.7
Sodium, mg	170.1	179.2
Potassium, mg	931	948.6
Chloride, mg	487.7	493.2
Iron, mg	14.0	14.0
Zinc, mg	5.1	5.1
Copper, mcg	608	608
Iodine, mcg	61	61
Manganese, mcg	34	34
Vitamin A, IU	2930	2970
Vitamin D, IU	405	405
Vitamin E, IU	24.6	24.8
Vitamin K, mcg	54	54
Vitamin C, mg	170	172
β-Carotene, mcg	450	450
Selenium, mcg	23	23
Thiamin, mcg	1350	1360
Riboflavin, mcg	1014	1014
Pyridoxine, mcg	480	480
Vitamin B ₁₂ , mcg	1.7	1.7
Niacin, mcg	7095	7095
Folic acid, mcg	101	101
Pantothenic acid, mcg	3041	3041
Biotin, mcg	30	30
Taurine, mg	45	45
Choline, mg	108	108
Inositol, mg	32	32
Energy, Kcal	676	676
CMP, mg	2.72*	31.2
UMP, mg	4.19*	17.7
AMP, mg	0.57*	9.8
GMP, mg	0.45*	14.4

*-inherent levels from raw materials

In this example, a 7711 Kg batch of the formula according to the invention was prepared (NUC). The control formula (CON) was prepared in a similar fashion except the addition of the nucleotides was omitted. The list of ingredients and amounts are found in Table III.

TABLE III

Ingredients and Amounts for NUC Formula

Ingredient	Amount
High Oleic Safflower Oil	120.2 Kg
Coconut Oil	85.7 Kg
Soy Oil	80.3 Kg
Lecithin	2.92 Kg
Mono- and diglyceride	2.92 Kg
Oil Soluble Vit. Premix	0.365 Kg
βCarotene	0.0137 Kg
Carrageenan	1.43 Kg
Whey Protein Concentrate	61.2 Kg
Lactose	476.3 Kg
Potassium Citrate	4.6 Kg
Magnesium Chloride	0.735 Kg
Low Heat Condensed Skim Milk	821 Kg
Calcium Carbonate	3.36 Kg

TABLE III-continued

Ingredients and Amounts for NUC Formula	
Ingredient	Amount
Ferrous sulfate	0.450 Kg
Water Soluble Vitamin	1.11 Kg
Premix Trace Minerals/	
Taurine	
Choline Chloride	0.600 Kg
Adenosine 5'monophosphate	0.113 Kg
Guanosine 5'monophosphate-Na2	0.197 Kg
Cytidine 5' monophosphate	0.259 Kg
Uridine 5'monophosphate-Na2	0.216 Kg
Ascorbic Acid	1.78 Kg
45% KOH	2.36 Kg

Total Yield 7711 Kg

The first step is the preparation of the oil blend. To an appropriately sized blend tank with agitation and heating soy oil, coconut oil and high oleic safflower oil were added. The mixture was heated to 73.8°-79.4° C. The lecithin and mono- and diglycerides (Myverol 18-06) were added to the blend tank with agitation. The oil soluble vitamin premix was added with agitation. The premix container was rinsed with the oil blend and transferred back to the blend tank to ensure complete delivery of the vitamin premix. The beta-carotene was added to the oil blend and the mixture agitated until the components were well dispersed. The beta-carotene container was rinsed with the oil blend and the contents returned to the blend tank to ensure complete delivery of the beta-carotene solution. Lastly, the carrageenan was added to the oil blend and the mixture was agitated and held at 54.4°-60° C. until used.

The carbohydrate, mineral and CSM (condensed skim milk) protein slurry was prepared next. To water heated to 68.3°-73.8° C. the lactose was added and the mixture agitated until the lactose was well dissolved. Potassium citrate was then added followed by potassium chloride, sodium chloride and magnesium chloride. The condensed skim milk (CSM) was then added. Tri-calcium phosphate was added, the mixture agitated and held at 54.5°-60° C. until used.

The protein-in-water (PIW) slurry was then prepared. The whey protein concentrate was added to water at 54.5°-60° C. under mild agitation. The PIW slurry was held under mild agitation until needed. Also contemplated in this invention is the use of protein-in-fat (PIF) slurries, wherein an appropriate amount of protein is admixed with all or a portion of the oil component.

The PIW slurry was then added to the prepared oil blend. The required amount of the carbohydrate, mineral and CSM slurry was then added to the oil blend. The pH of the mixture was then determined and if below specification it was adjusted using KOH to a pH of 6.75 to 6.85. The mixture was then held at 54.4°-60° C. under agitation for at least 15 minutes.

The mixture was then heated to 68.3°-73.8° C. and deaerated under vacuum. The mixture was then emulsified through a single stage homogenizer at 6.21 to 7.58 MPa.

After emulsification, the mixture was heated to 120°-122° C. for 10 seconds and then 149°-150° C. for 5 seconds. The mixture was then passed through a flash cooler to reduce the temperature to 120°-122° C. and then through a plate cooler to reduce the temperature to 71.1°-79.4° C. The mixture was then passed through a two stage homogenizer at 26.89 to 28.27 MPa and 2.76 to 4.14 MPa. The mixture was held at

73.9° to 83.2° C. for 16 seconds and then cooled to 1.1° to 6.7° C. At this point, samples are taken for microbiological and analytical testing. The mixture was held under agitation.

A calcium carbonate solution may be prepared for use in adjusting the calcium level of the mixture if outside of specification.

A vitamin stock solution was prepared. To water heated to 37.8° to 65.6° C. was added potassium citrate and ferrous sulfate. The vitamin premix was then added and the mixture agitated. The choline chloride was added and then the required amount of this vitamin mixture was added to the batch.

The nucleotide solution was then prepared. The following nucleotides were added to water with mild agitation in the following order: AMP, GMP, CMP, UMP. Agitation was continued for about 10 minutes to dissolve the nucleotides. The nucleotide solution was then added to the batch. This is one critical aspect of the invention. It is extremely important that the nucleotides be added after the homogenizations and heat treatments. Numerous experiments have been conducted that have shown the addition of the nucleotides at any other point will result in degradation of the nucleotides and thereby change the specific levels and ratios as claimed. It is believed that AMP is converted to IMP through the presence of adenosine deaminase in the raw materials, especially the protein components.

Lastly, an ascorbic acid solution was prepared and added slowly to the batch with agitation for at least 10 minutes. Final dilution with water to meet specified levels of solids and caloric density was completed. The batch was then packaged in 32 ounce metal cans and sterilized using conventional technology.

EXAMPLE III

Clinical Study of Enteral Formula

The purpose of the clinical investigation was to determine the effect of a nucleotide-fortified formula according to the present invention on the development of the neonatal immune system in infants as measured by the antibody response to childhood vaccines.

This was a 12-month, randomized, controlled, blinded, multi-site trial of term infants. Infants enrolled into the study received human milk (HM) or one of two clinically labelled formulas: 1) control formula (CON) or 2) CON formula supplemented with nucleotides (NUC). The analyzed composition of each formula is set forth in Table II. A total of 311 infants completed the study (107 CON, 101 NUC, 103 HM). Infants followed the immunization schedule recommended by the American Academy of Pediatrics with single lots of Hib TITER® Hemophilus influenzae type b conjugate vaccine (Diphtheria CRM 197 and tetanus protein conjugate sold by Lederle, Inc.) and Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed, sold by Lederle, Inc. Infants were full-term with a gestational age of 38-42 weeks, at or above the 5th percentile for weight, length, and head circumference and were enrolled between 2 and 10 days of age. All subjects were healthy with no indication of systemic disease and did not receive any medications, mineral, or vitamin supplements.

The primary outcome variable investigated was vaccine response at 6, 7, and 12 months of age. Also investigated were differential white blood cell count, lymphocyte subset analysis, NK activity, and lymphoblast transformation in response to specific and non-specific stimuli at 2, 6, 7, and 12 months of age. Secondary outcome variables included

enhance the immune system. In this example and in commercial production of enteral formulas according to the invention, background levels of nucleotide equivalents are determined and then the formula would be supplemented with appropriate commodities, such as CMP, AMP, UMP and GMP, to the claimed levels and ratios. It should be remembered that by nucleotide equivalents is meant ribonucleotides, ribo-nucleosides, RNA, and ribo-nucleotide adjuncts, such as activated sugars. The sum of all these elements determine the total potentially available ribonucleotides equivalents.

Two additional pieces of data strongly support that the formula according to this invention provides an unexpected result. The number of subjects who have achieved protective levels of anti-Hib immunoglobulin as shown in Table VII is consistently 10% higher in the NUC group. The three-way comparison does not show a statistical difference. However, a two-way comparison between the NUC and CON formula groups at 7 months is significant ($P < 0.05$).

An additional piece of data comes from two of the clinical sites which chose to collect morbidity data. As part of the study the incidence of diarrhea was determined at the two clinical study sites. Of 26 infants fed the NUC formula, only two reported diarrhea while 10 of 29 reported diarrhea in the CON formula. The X^2 analysis comparing the incidence of diarrhea in infants fed the two formulas is significant ($P < 0.05$). In summary, the improved response to vaccination, the higher percent of subjects who have protective levels of antibodies, and the reduced incidence of diarrhea show that infants consuming the nucleotide-fortified formula according to this invention achieve enhanced immunological development as compared to those consuming the control formula.

INDUSTRIAL APPLICABILITY

The results from these experiments demonstrate that the enteral formula of this invention is effective in enhancing the immune system and treating diarrhea. The medical community is constantly searching for nutritional formulas that will benefit the infant. The present invention can clearly fill that need. The nucleotide equivalent level of the formula in the study is about the minimum for efficacious effect. Additionally, the formula is nutritionally complete as an infant formula. The manufacture of the formula utilizes conventional equipment and may be readily accomplished.

While the infant formula and method of making said formula herein described constitute a preferred embodiment of this invention, it is to be understood that the invention is not limited to this precise formulation or method and that changes may be made therein without departing from the scope of the invention which is defined in the appended claims.

What is claimed is:

1. An enteral formula, said formula comprising:

- 1) protein, said protein being of a concentration of between 10 and 35 grams per liter of formula;
- 2) fat, said fat being of a concentration of between 20 and 45 grams per liter of formula;
- 3) carbohydrates, said carbohydrates being of a concentration of between 60 and 110 grams per liter of formula; and
- 4) at least 70 mg of nucleotide equivalents per liter of formula, and wherein said nucleotide equivalents are nucleotide equivalents of each of adenosine, cytidine, guanosine and uridine; and wherein the weight ratio of CMP:UMP is from about 1.5:1 to about 2.6:1; of

CMP:AMP is from about 2:1 to about 3.9:1; and of CMP:GMP is from about 1.75:1 to about 2.8:1.

2. An enteral formula according to claim 1 wherein the source of protein is selected from the group consisting of condensed skim milk, non-fat milk, acid whey, milk protein concentrate, nucleotide equivalent reduced soy protein and cheese whey.

3. An enteral formula according to claim 1 wherein said protein is of a concentration of between 13 and 20 grams per liter of formula and consists of 50-70% by weight condensed skim milk and 30-50% by weight cheese whey.

4. An enteral formula according to claim 1 wherein said fat is selected from the group consisting of soy oil, coconut oil, corn oil, safflower oils, fish oils, egg yolk oils, sunflower oils, microbial oils, fungal oils and blends thereof.

5. An enteral formula according to claim 4 wherein said fat is of a concentration of between 24 and 38 grams per liter of formula and consists of a blend of high oleic safflower oil, soy oil and coconut oil.

6. An enteral formula according to claim 1 which additionally comprises an antioxidant system, said antioxidant system consisting of R.R.R. α -tocopherol at a concentration of 10 to 30 IU per liter of formula, β -carotene at a concentration of 375 to 575 μ g per liter of formula and selenium at a concentration of 14 to 32 mcg per liter of formula.

7. An enteral formula according to claim 1 wherein said nucleotide equivalents are present in the following ranges per liter of formula: CMP 29-39 mg; UMP 15-20 mg; AMP 10-15 mg and GMP 14-20 mg.

8. An enteral formula according to claim 1 wherein said protein is of a concentration of between 13 and 16 grams per liter of formula, said fat is a blend of soy oil, high oleic safflower oil and coconut oil and said carbohydrate is of a concentration of between 65 and 85 grams per liter of formula and consists of lactose.

9. An infant formula, said formula comprising:

- 1) protein, said protein being of a concentration of between 10 and 35 grams per liter of formula;
- 2) fat, said fat being of a concentration of between 20 and 45 grams per liter of formula;
- 3) carbohydrates, said carbohydrates including those from total dietary fiber being of a concentration of between 60 and 110 grams per liter of formula; and
- 4) at least 70 mg of nucleotide equivalents per liter of formula and said nucleotide equivalents are selected from the group consisting of RNA; mono-, di- and triphosphate esters of adenosine, cytidine, guanosine and uridine; and wherein the weight ratio of said cytidine nucleotide equivalents to said uridine nucleotide equivalents is from about 1.5:1 to about 2.6:1; of said cytidine nucleotide equivalents to said adenosine nucleotide equivalents is from about 2:1 to about 3.9:1; and of cytidine nucleotide equivalents to said guanosine equivalents is from about 1.75:1 to about 2.8:1.

10. A method of improving the immune response sensitivity of the immune system of a human, wherein said method comprises feeding a human in need of treatment a formula, the improvement comprising feeding said human a formula consisting essentially of:

- 1) protein, said protein being of a concentration of between 10 and 35 grams per liter of formula;
- 2) fat, said fat being of a concentration of between 20 and 45 grams per liter of formula;
- 3) carbohydrates, said carbohydrates being of a concentration of between 60 and 110 grams per liter of formula; and

4) at least 70 mg of nucleotide equivalents per liter of formula, and wherein said nucleotide equivalents are nucleotide equivalents of each of adenosine, cytidine, guanosine and uridine; and wherein the weight ratio of CMP:UMP is from about 1.5:1 to about 2.6:1; of CMP:AMP is from about 2:1 to about 3.9:1; and of CMP:GMP is from about 1.75:1 to about 2.8:1.

11. A method according to claim 10 wherein the source of said protein is supplied in a form selected from the group consisting of condensed skim milk, non-fat milk, cheese whey, milk protein concentrate, nucleotide reduced vegetable protein, protein hydrolyzates and mixtures thereof.

12. A method according to claim 10 wherein said protein is of a concentration of between 13 and 20 grams per liter of formula and consists of 50-70% by weight condensed skim milk and 30-50% by weight cheese whey.

13. A method according to claim 10 wherein said fat is supplied in a form selected from the group consisting of soy oil, coconut oil, corn oil, safflower oils, fish oils, egg yolk oils, sunflower oils, fungal oils and blends thereof.

14. A method according to claim 10 wherein said fat is of a concentration of between 24 and 38 grams per liter of formula and consists of a blend of high oleic safflower oil, soy oil and coconut oil.

15. A method according to claim 10 which said protein is of a concentration of 13 to 15 grams per liter of formula, said fat is of a concentration of 30 to 40 grams per liter of formula and has as its source a blend of soy oils, coconut oils and high oleic safflower oil, and said carbohydrates are of a concentration of 70 to 80 grams per liter of formula, and dietary fiber, said dietary fiber is soy polysaccharide derived from soy beans.

16. A method according to claim 10 wherein said nucleotide equivalents are in the form of CMP, AMP, GMP and UMP, and are present at a level of up to 1.0 gram per liter of formula.

17. A method according to claim 10 wherein the formula additionally contains 10 to 30 IU of R.R.R. α -tocophenol per liter of formula, 400-575 μ g of β -carotene per liter of formula and 14-32 mcg of selenium per liter of formula.

18. A method according to claim 10 wherein said nucleotide equivalents are present in the following ranges per liter of formula as fed: cytosine equivalents 30-33 mg; uridine equivalents 16-19 mg; adenosine equivalents 11-14 mg and guanosine equivalents 15-18 mg.

19. A method of improving the immune response sensitivity of the immune system of a human infant, said method comprising feeding a human infant in need of treatment a nutritional formula, the improvement comprising feeding a human infant a nutritionally complete formula comprising:

- 1) protein;
- 2) fat;
- 3) carbohydrates; and

4) at least 70 mg nucleotide equivalents per liter of formula, said nucleotides comprising the monophosphate esters of adenosine, cytidine, guanosine and uridine and wherein the weight ratio of CMP:UMP is from about 1.5:1 to about 2.6:1; of CMP:AMP is from about 2:1 to about 3.9:1; and of CMP:GMP is from about 1.75:1 to about 2.8:1.

20. A method according to claim 19 wherein said monophosphate esters are present in the following ranges per liter of formula as fed: CMP 30-33 mg; UMP 16-19 mg; AMP 11-14 mg and GMP 15-18 mg.

21. A method according to claim 19 wherein said protein is of a concentration of between 13 and 16 grams per liter of formula, said fat is a blend of soy oil, high oleic safflower oil

and coconut oil, and said carbohydrate is of a concentration of between 65 and 85 grams per liter of formula and consists of lactose.

22. A method according to claim 19 wherein the formula additionally contains 10 to 30 IU of R.R.R. α -tocophenol per liter of formula, 400-500 μ g of β -carotene per liter of formula and 14-32 mcg of selenate per liter of formula.

23. A method of improving the immune response sensitivity of the immune system of a human infant to an antigen, said method comprising feeding a human infant in need of treatment a nutritional formula, the improvement comprising feeding said human infant an infant formula that contains: 29-39 mg of CMP per liter of formula; 15-21 mg of UMP per liter of formula; 10-16 mg of AMP per liter of formula and 14-20 mg of GMP per liter of formula or their nucleotide equivalents and wherein the weight ratio of CMP:UMP is from about 1.5:1 to about 2.6:1; of CMP:AMP is from about 2:1 to about 3.9:1; and of CMP:GMP is from about 1.75:1 to about 2.8:1.

24. The method according to claim 23 wherein said human infant formula comprises per liter of formula:

CMP, 30-33 mg

UMP, 16-19 mg

AMP, 11-14 mg

GMP, 15-18 mg.

25. An enteral formula comprising per 100 Kcal of formula:

- a) from about 1.5 to about 5 grams of protein;
- b) from about 3 to about 6.5 grams of fat;
- c) from about 8.7 to about 16 grams of carbohydrate; and
- d) about 10 milligrams of nucleotide equivalents, wherein the nucleotide equivalents are nucleotide equivalents of adenosine, cytidine, guanosine and uridine and wherein the weight ratio of CMP:UMP is greater than about 1.5:1, the weight ratio of CMP:AMP is greater than about 2:1 and the weight ratio of CMP:GMP is greater than about 1.75:1.

26. An enteral formula comprising per 100 Kcal of formula:

- a) from about 1.5 to about 5 grams of protein;
- b) from about 3 to about 6.5 grams of fat;
- c) from about 8.7 to about 16 grams of carbohydrate; and
- d) nucleotide equivalents of adenosine, cytidine, guanosine and uridine and wherein the weight ratio of CMP:UMP is greater than about 1.5:1, the weight ratio of CMP:AMP is greater than about 2:1 and the weight ratio of CMP:GMP is greater than about 1.75:1.

27. An enteral formula according to claim 26, wherein the weight ratio of CMP:UMP is from about 1.5:1 to about 2.6:1; the weight ratio of CMP:AMP is from about 2:1 to about 3.9:1; and the weight ratio of CMP:GMP is from about 1.75:1 to about 2.8:1; and wherein at least some of the nucleotide equivalents are added as nucleotide monophosphates.

28. A nutritionally complete infant formula comprising: protein; fat; carbohydrate; and nucleotide equivalents of adenosine, cytidine, guanosine and uridine, wherein the weight ratio of CMP:UMP is greater than about 1.5:1, the weight ratio of CMP:AMP is greater than about 2:1 and the weight ratio of CMP:GMP is greater than about 1.75:1 and wherein the level of nucleotide equivalents is about 10 milligrams per 100 Kcal of formula.

29. An enteral formula comprising:

- a) from about 1.5 to about 5 grams of protein per 100 Kcal of formula;

- b) from about 3 to about 6.5 grams of fat per 100 Kcal of formula;
- c) from about 8.7 to about 16 grams of carbohydrate per 100 Kcal of formula; and
- d) from about 2 to about 7 mg of nucleotide equivalents per gram of protein, wherein the nucleotide equivalents are adenosine, cytidine, guanosine and uridine nucleotide equivalents and wherein the weight ratio of CMP:UMP is greater than about 1.5:1, the weight ratio of CMP:AMP is greater than about 2:1 and the weight ratio of CMP:GMP is greater than about 1.75:1 the weight.

30. An enteral formula comprising:

- a) from about 1.5 to about 5 grams of protein per 100 Kcal of formula;
- b) from about 3 to about 6.5 grams of fat per 100 Kcal of formula;
- c) from about 8.7 to about 16 grams of carbohydrate per 100 Kcal of formula; and
- d) from about 1.5 to about 3.5 mg of nucleotide equivalents per gram of fat, wherein the nucleotide equivalents are adenosine, cytidine, guanosine and uridine nucleotide equivalents and wherein the weight ratio of CMP:UMP is greater than about 1.5:1, the weight ratio of CMP:AMP is greater than about 2:1 and the weight ratio of CMP:GMP is greater than about 1.75:1.

31. An enteral formula comprising:

- a) from about 1.5 to about 5 grams of protein per 100 Kcal of formula;
- b) from about 3 to about 6.5 grams of fat per 100 Kcal of formula;
- c) from about 8.7 to about 16 grams of carbohydrate per 100 Kcal of formula; and
- d) from about 0.6 to about 1.2 mg of nucleotide equivalents per gram of carbohydrate, wherein the nucleotide equivalents are adenosine, cytidine, guanosine and uridine nucleotide equivalents and wherein the weight ratio of CMP:UMP is greater than about 1.5:1, the weight ratio of CMP:AMP is greater than about 2:1 and the weight ratio of CMP:GMP is greater than about 1.75:1.

32. An enteral formula comprising:

- a) from about 1.5 to about 5 grams of protein per 100 Kcal of formula;
- b) from about 3 to about 6.5 grams of fat per 100 Kcal of formula;
- c) from about 8.7 to about 16 grams of carbohydrate per 100 Kcal of formula; and
- d) nucleotide equivalents of adenosine, cytidine, guanosine and uridine, wherein the level of cytidine equivalent is from about 0.8 to about 4 mg of CMP per gram of protein and wherein the weight ratio of CMP:UMP is greater than about 1.5:1, the weight ratio of CMP:AMP is greater than about 2:1 and the weight ratio of CMP:GMP is greater than about 1.75:1.

33. An enteral formula comprising:

- a) from about 1.5 to about 5 grams of protein per 100 Kcal of formula;
- b) from about 3 to about 6.5 grams of fat per 100 Kcal of formula;
- c) from about 8.7 to about 16 grams of carbohydrate per 100 Kcal of formula; and
- d) nucleotide equivalents of adenosine, cytidine, guanosine and uridine, wherein the level of cytidine

equivalent is from about 0.6 to about 1.9 mg of CMP per gram of fat and wherein the weight ratio of CMP:UMP is greater than about 1.5:1, the weight ratio of CMP:AMP is greater than about 2:1 and the weight ratio of CMP:GMP is greater than about 1.75:1.

34. An enteral formula comprising:

- a) from about 1.5 to about 5 grams of protein per 100 Kcal of formula;
- b) from about 3 to about 6.5 grams of fat per 100 Kcal of formula;
- c) from about 8.7 to about 16 grams of carbohydrate per 100 Kcal of formula; and
- d) nucleotide equivalents of adenosine, cytidine, guanosine and uridine, wherein the level of cytidine equivalent is from about 0.2 to about 0.7 mg of CMP per gram of carbohydrate and wherein the weight ratio of CMP:UMP is greater than about 1.5:1, the weight ratio of CMP:AMP is greater than about 2:1 and the weight ratio of CMP:GMP is greater than about 1.75:1.

35. An enteral formula comprising:

- a) from about 1.5 to about 5 grams of protein per 100 Kcal of formula;
- b) from about 3 to about 6.5 grams of fat per 100 Kcal of formula;
- c) from about 8.7 to about 16 grams of carbohydrate per 100 Kcal of formula; and
- d) nucleotide equivalents of adenosine, cytidine, guanosine and uridine, wherein the level of cytidine equivalent is about 2 mg of CMP per 100 Kcal of formula and wherein the weight ratio of CMP:UMP is greater than about 1.5:1, the weight ratio of CMP:AMP is greater than about 2:1 and the weight ratio of CMP:GMP is greater than about 1.75:1.

36. An enteral formula comprising per 100 Kcal of formula:

- a) from about 1.5 to about 5 grams of protein;
- b) from about 3 to about 6.5 grams of fat;
- c) from about 8.7 to about 16 grams of carbohydrate; and
- d) from about 1.5 to about 15 milligrams of nucleotide equivalents, wherein the nucleotide equivalents are nucleotide equivalents of adenosine, cytidine, guanosine and uridine and wherein the weight ratio of CMP:UMP is greater than about 1.5:1, the weight ratio of CMP:AMP is greater than about 2:1 and the weight ratio of CMP:GMP is greater than about 1.75:1.

37. An enteral formula according to claim 36, wherein the weight ratio of CMP:UMP is from about 1.5:1 to about 2.6:1; the weight ratio of CMP:AMP is from about 2:1 to about 3.9:1; and the weight ratio of CMP:GMP is from about 1.75:1 to about 2.8:1; and wherein at least some of the nucleotide equivalents are added as nucleotide monophosphates.

38. An enteral formula comprising:

- a) from about 1.5 to about 5 grams of protein per 100 Kcal of formula;
- b) from about 3 to about 6.5 grams of fat per 100 Kcal of formula;
- c) from about 8.7 to about 16 grams of carbohydrate per 100 Kcal of formula; and
- d) nucleotide equivalents of adenosine, cytidine, guanosine and uridine, wherein the level of adenosine equivalent is about 1 mg of AMP per 100 Kcal of formula and wherein the weight ratio of CMP:UMP is greater than about 1.5:1, the weight ratio of CMP:AMP

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is greater than about 2:1 and the weight ratio of CMP:GMP is greater than about 1.75:1.

39. An enteral formula comprising:

- a) from about 1.5 to about 5 grams of non-fat milk protein per 100 Kcal of formula;
- b) from about 3 to about 6.5 grams of fat per 100 Kcal of formula;
- c) from about 8.7 to about 16 grams of carbohydrate per 100 Kcal of formula; and
- d) nucleotide equivalents of adenosine, cytidine, guanosine and uridine, wherein the level of cytidine equivalent is from about 0.8 to about 4 mg of CMP per gram of non-fat milk protein and wherein the weight ratio of CMP:UMP is greater than about 1.5:1, the weight ratio of CMP:AMP is greater than about 2:1 and the weight ratio of CMP:GMP is greater than about 1.75:1.

40. An enteral formula comprising per liter of formula:

- a) from about 10 to about 35 grams of protein;
- b) from about 20 to about 45 grams of fat;
- c) from about 60 to about 110 grams of carbohydrate; and
- d) about 40 milligrams of nucleotide equivalents, wherein the nucleotide equivalents are nucleotide equivalents of adenosine, cytidine, guanosine and uridine and wherein the weight ratio of CMP:UMP is greater than about 1.5:1, the weight ratio of CMP:AMP is greater than about 2:1 and the weight ratio of CMP:GMP is greater than about 1.75:1.

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41. An enteral formula supplemented with nucleotide mono-phosphates, comprising per 100 Kcal of formula:

- a) from about 1.5 to about 5 grams of protein;
- b) from about 3 to about 6.5 grams of fat;
- c) from about 8.7 to about 16 grams of carbohydrate; and
- d) nucleotide equivalents of adenosine, cytidine, guanosine and uridine and wherein the weight ratio of CMP:UMP is from about 1.5:1 to about 2.6:1, the weight ratio of CMP:AMP is from about 2:1 to about 3.9:1, and the weight ratio of CMP:GMP is from about 1.75:1 to about 2.8:1.

42. An enteral formula supplemented with nucleotide mono-phosphates, comprising per 100 Kcal of formula:

- a) from about 1.5 to about 5 grams of protein;
- b) from about 3 to about 6.5 grams of fat;
- c) from about 8.7 to about 16 grams of carbohydrate; and
- d) from about 1.5 to about 15 milligrams of nucleotide equivalents, wherein the nucleotide equivalents are nucleotide equivalents of adenosine, cytidine, guanosine and uridine and wherein the weight ratio of CMP:UMP is from about 1.5:1 to about 2.6:1, the weight ratio of CMP:AMP is from about 2:1 to about 3.9:1, and the weight ratio of CMP:GMP is from about 1.75:1 to about 2.8:1.

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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIVISION DE NUEVAS CREACIONES

2020
Bogotá, D.C., Abril 7 de 2005

Doctor
ALICIA LLOREDA RICAURTE

ASUNTO	Radicación No.	00 025 252
	Trámite	002
	Evento	001
	Actuación	430
	Oficio No.	12528
	Folios	0

Como resultado del examen de patentabilidad de la solicitud de patente de invención, realizado según lo establece el artículo 45 de la Decisión 486 de la Comisión de la Comunidad Andina, se notifica el siguiente concepto técnico:

1. Documentos estudiados

Para el presente estudio se tuvieron en cuenta el capítulo descriptivo comprendido en los folios 5 - 72 y el nuevo capítulo reivindicatorio de los folios 73, 74 133 - 138 de la solicitud en estudio.

2. Objeto de la Invención

El objeto de la presente solicitud de patente de invención consiste en:

Las reivindicaciones 1 a 4, 19, 25 a 28 se refieren a un fortalecedor en polvo para leche humana que comprende: componente de proteína, componente graso, componente carbohidrato. Opcionalmente vitaminas (A, B1, B2, B6, B12, C, D, E, K, biotina, ácido fólico, ácido pantoténico, niacina), m-inositol, minerales (calcio, fósforo, magnesio, zinc, manganeso, cobre, sodio, potasio, cloruro, hierro, selenio, cromo, molibdeno), camitina (¿?) (¿carnitina?), taurina y un emulsionante.

Las reivindicaciones 5 a 9, 15 a 18, 20 a 21, 23 a 24 se refieren al uso del fortalecedor para fabricar leche humana fortalecida que además contiene emulsor, vitaminas, minerales y calcio insoluble. Y se administra diariamente.

Las reivindicaciones 10 a 14, 22 se refieren a una unidad de dosis que contiene un fortalecedor en polvo que comprende: componente de proteína, componente graso, componente carbohidrato. Opcionalmente vitaminas (A, B1, B2, B6, B12, C, D, E, K, biotina, ácido fólico, ácido pantoténico, niacina), m-inositol, minerales (calcio, fósforo, magnesio, zinc, manganeso, cobre, sodio, potasio, cloruro, hierro, selenio, cromo, molibdeno), camitina, taurina y un emulsionante.

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El problema planteado en esta solicitud es la necesidad de proporcionar un fortalecedor en polvo para leche humana para alimentación de infantes prematuros.

Para resolver este problema técnico la solicitud en estudio proporciona un fortalecedor en polvo para leche humana que comprende: componente de proteína, componente graso, componente carbohidrato. Opcionalmente vitaminas (A, B1, B2, B6, B12, C, D, E, K, biotina, ácido fólico, ácido pantoténico, niacina), m-inositol, minerales (calcio, fósforo, magnesio, zinc, manganeso, cobre, sodio, potasio, cloruro, hierro, selenio, cromo, molibdeno), camitina (¿?) (¿carnitina?), taurina y un emulsionante.

El objeto de la invención definido anteriormente se clasificó de acuerdo con la IPC: A 23 C 9/158 // 9/20C // 11/04 // 9/00.

También se reivindica prioridad de la Solicitud de Patente de los Estados Unidos US 60 128 575 de abril 9 de 1999, con respecto a la cual la fecha de presentación de la actual solicitud cumple el plazo máximo permitido.

3. Reivindicaciones de Uso

El artículo 14 de la Decisión 486 de la Comisión de la Comunidad Andina establece: *"Los Países Miembros otorgarán patentes para las invenciones, sean de producto o procedimiento, en todos los campos de la tecnología, siempre que sean nuevas, tengan nivel inventivo y sean susceptibles de aplicación industrial"*.

El artículo 14 de la Decisión 486 de la Comisión de la Comunidad Andina establece: *"Los productos o procedimientos ya patentados, comprendidos en el estado de la técnica, de conformidad con el Artículo 16 de la presente Decisión, no serán objeto de nueva patente, por el simple hecho de atribuirse un uso distinto al originalmente comprendido por la patente inicial"*.

Las reivindicaciones 5 a 9, 15 a 18, 20 a 21, 23 a 24 se refieren al uso del fortalecedor para fabricar leche humana fortalecida que además contiene emulsor, vitaminas, minerales y calcio insoluble. Y se administra diariamente.

Se observa que el uso de un fortalecedor para fabricar y administrar diariamente leche humana fortalecida, de las reivindicaciones 5 a 9, 15 a 18, 20 a 21, 23 a 24, que no es una invención de producto ni de procedimiento, no es patentable de acuerdo con las normas citadas, que especifican que los usos no son patentables.

4. Determinación del Estado de la Técnica

El artículo 16 de la decisión 486 de la comisión de la Comunidad Andina que establece que *"El estado de la técnica comprenderá todo lo que haya sido accesible al público por una descripción escrita u oral, utilización, comercialización o cualquier otro medio antes de la fecha de presentación de la solicitud de patente o, en su caso, de la prioridad reconocida"*.

Solo para el efecto de la determinación de la novedad, también se considerará dentro del estado de la técnica, el contenido de una solicitud de patente en trámite ante la oficina nacional competente, cuya fecha de presentación o de prioridad fuese anterior a la fecha de presentación o de prioridad de la solicitud

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de patente que se estuviese examinando, siempre que dicho contenido esté incluido en la solicitud de fecha anterior cuando ella se publique o hubiese transcurrido el plazo previsto en el artículo 40”.

Considerando que la fecha de presentación de la primera solicitud de patente de la cual se reivindica prioridad es abril 9 de 1999, se consultaron las bases de datos y los archivos con que cuenta la entidad con fecha de publicación anterior y se encontraron los siguientes documentos que anticipan el objeto de esta solicitud:

No.	Documento	Título	Fecha de Publicación
D1	US 5 013 569	Fórmula Infantil	May 7, 1991
D2	US 5 340 603	Producto Nutricional para Infantes humanos que tienen enfermedad pulmonar crónica	Ago 23, 1994
D3	US 5 700 590	Fórmula Nutricional con Ribonucleótidos	Dic 23, 1997

5. Evaluación de los requisitos de Patentabilidad

El artículo 14 de la Decisión 486 de la Comisión de la Comunidad Andina establece que *“Los Países Miembros otorgarán patentes para las invenciones, sean de producto o de procedimiento, en todos los campos de la tecnología, siempre que sean nuevas, tengan nivel inventivo y sean susceptibles de aplicación industrial”*.

En cumplimiento del artículo 14 de la Decisión 486, se procedió a evaluar el cumplimiento de los requisitos de novedad, nivel inventivo y aplicación industrial, con el fin de establecer la patentabilidad de la invención reivindicada en la solicitud en estudio.

Evaluación de la Novedad

El Art. 16 de la Decisión 486 de la Comisión de la Comunidad Andina establece: *“Una invención se considerará nueva cuando no está comprendida en el estado de la técnica. El estado de la técnica comprenderá todo lo que haya sido accesible al público por una descripción escrita u oral, utilización comercialización o cualquier otro medio antes de la fecha de presentación de la solicitud de patente, o, en su caso, de la prioridad reconocida.*

Solo para el efecto de la determinación de la novedad, también se considerará dentro del estado de la técnica, el contenido de una solicitud de patente en trámite ante la oficina nacional competente, cuya fecha de presentación o de prioridad fuese anterior a la fecha de presentación o de prioridad de la solicitud de patente que se estuviese examinando, siempre que dicho contenido esté incluido en la solicitud de fecha anterior cuando ella se publique o hubiese transcurrido el plazo previsto en el Art 40”.

Las reivindicaciones 1 a 4, 19, 25 a 28 se refieren a un fortalecedor en polvo para leche humana que comprende: componente de proteína, componente graso, componente carbohidrato. Opcionalmente vitaminas (A, B1, B2, B6, B12, C, D, E, K, biotina, ácido fólico, ácido pantoténico, niacina), m-inositol, minerales (calcio, fósforo, magnesio, zinc, manganeso, cobre, sodio, potasio, cloruro, hierro, selenio, cromo, molibdeno), camitina, taurina y un emulsionante.

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Las reivindicaciones 10 a 14, 22 se refieren a una unidad de dosis que contiene un fortalecedor en polvo que comprende: componente de proteína, componente graso, componente carbohidrato. Opcionalmente vitaminas (A, B1, B2, B6, B12, C, D, E, K, biotina, ácido fólico, ácido pantoténico, niacina), m-inositol, minerales (calcio, fósforo, magnesio, zinc, manganeso, cobre, sodio, potasio, cloruro, hierro, selenio, cromo, molibdeno), camitina, taurina y un emulsionante.

D1 enseña una fórmula infantil que comprende: componente de proteína, componente graso, componente carbohidrato. Opcionalmente vitaminas (A, complejo B, minerales (calcio, fósforo, magnesio, zinc, manganeso, cobre, sodio, potasio, cloruro, hierro, selenio), (ver columnas 4, 7 y 8). En la columna 7 enseña la composición que contiene 8 - 28 de proteína, 8 - 40 de grasa y 32 - 80 de carbohidratos.

D2 enseña una fórmula infantil que comprende: componente de proteína 25 - 35, componente graso 65 - 85, componente carbohidrato 40 - 75. Opcionalmente vitaminas (A, B1, B2, B6, B12, C, D, E, K, biotina, ácido fólico, ácido pantoténico, niacina), m-inositol, minerales (calcio, fósforo, magnesio, zinc, manganeso, cobre, sodio, potasio, cloruro, hierro, selenio), carnitina, taurina y un emulsionante (ver columnas 22 y 23).

D3 enseña una fórmula nutricional hipercalórica para infantes que comprende: componente de proteína 10 - 35, componente graso 20 - 45, componente carbohidrato 60 - 110. Y vitaminas (A, B1, B2, B6, B12, C, D, E, K, biotina, ácido fólico, ácido pantoténico, niacina), m-inositol, minerales (calcio, fósforo, magnesio, zinc, manganeso, cobre, sodio, potasio, cloruro, hierro, selenio), taurina y un emulsionante (ver columnas 7, 10, 11, 19).

Se observa que los elementos que conforman el fortalecedor en polvo objeto de las reivindicaciones 1 a 4, 19, 25 a 28, 10 a 14, 22 de esta solicitud, es decir: componente de proteína, componente graso, componente carbohidrato, vitaminas, minerales y emulsionante, habían sido enseñados en las fórmulas de D1: que contiene componente de proteína, componente graso, componente carbohidrato, vitaminas, minerales, D2: que contiene componente de proteína, componente graso, componente carbohidrato, vitaminas, minerales y emulsionante, D3: que contiene componente de proteína, componente graso, componente carbohidrato, vitaminas, minerales y emulsionante, por lo cual no puede ser considerado nuevo.

Evaluación del Nivel Inventivo

El artículo 18 de la Decisión 486 de la Comisión de la Comunidad Andina establece que *Se considerará que una invención tiene nivel inventivo, si para una persona del oficio normalmente versada en la materia técnica correspondiente, esa invención no hubiese resultado obvia ni se hubiese derivado de manera evidente del estado de la técnica.*

Las reivindicaciones 1 a 4, 19, 25 a 28 se refieren a un fortalecedor en polvo para leche humana que comprende: componente de proteína, componente graso, componente carbohidrato. Opcionalmente vitaminas (A, B1, B2, B6, B12, C, D, E, K, biotina, ácido fólico, ácido pantoténico, niacina), m-inositol, minerales (calcio, fósforo, magnesio, zinc, manganeso, cobre, sodio, potasio, cloruro, hierro, selenio, cromo, molibdeno), camitina, taurina y un emulsionante.

Las reivindicaciones 10 a 14, 22 se refieren a una unidad de dosis que contiene

un fortalecedor en polvo que comprende: componente de proteína, componente graso, componente carbohidrato. Opcionalmente vitaminas (A, B1, B2, B6, B12, C, D, E, K, biotina, ácido fólico, ácido pantoténico, niacina), m-inositol, minerales (calcio, fósforo, magnesio, zinc, manganeso, cobre, sodio, potasio, cloruro, hierro, selenio, cromo, molibdeno), camitina, taurina y un emulsionante.

D1 enseña una fórmula infantil que comprende: componente de proteína, componente graso, componente carbohidrato. Opcionalmente vitaminas (A, complejo B, minerales (calcio, fósforo, magnesio, zinc, manganeso, cobre, sodio, potasio, cloruro, hierro, selenio), (ver columnas 4, 7 y 8). En la columna 7 enseña la composición que contiene 8 - 28 de proteína, 8 - 40 de grasa y 32 - 80 de carbohidratos.

D2 enseña una fórmula infantil que comprende: componente de proteína 25 - 35, componente graso 65 - 85, componente carbohidrato 40 - 75. Opcionalmente vitaminas (A, B1, B2, B6, B12, C, D, E, K, biotina, ácido fólico, ácido pantoténico, niacina), m-inositol, minerales (calcio, fósforo, magnesio, zinc, manganeso, cobre, sodio, potasio, cloruro, hierro, selenio), carnitina, taurina y un emulsionante (ver columnas 22 y 23).

D3 enseña una fórmula nutricional hipercalórica para infantes que comprende: componente de proteína 10 - 35, componente graso 20 - 45, componente carbohidrato 60 - 110. Y vitaminas (A, B1, B2, B6, B12, C, D, E, K, biotina, ácido fólico, ácido pantoténico, niacina), m-inositol, minerales (calcio, fósforo, magnesio, zinc, manganeso, cobre, sodio, potasio, cloruro, hierro, selenio), taurina y un emulsionante (ver columnas 7, 10, 11, 19).

Se observa que la combinación de las enseñanzas de estas anterioridades: D1 que enseña una fórmula que contiene componente de proteína, componente graso, componente carbohidrato, vitaminas, minerales, D2 que enseña una fórmula que contiene componente de proteína, componente graso, componente carbohidrato, vitaminas, minerales y emulsionante, D2 que enseña una fórmula que contiene componente de proteína, componente graso, componente carbohidrato, vitaminas, minerales y emulsionante; sugiere la fórmula que contiene componente de proteína, componente graso, componente carbohidrato, vitaminas, minerales y emulsionante; que es objeto de esta solicitud. Las reivindicaciones no mencionan una característica que conceda un efecto diferente o especial a la composición, así que esta es obvia y evidente para una persona versada en la materia. Entonces debido a que: (a) la conformación de las composiciones de esta solicitud, a partir de las anterioridades, es evidente para una persona conocedora de la materia; porque siendo bien conocidas las fórmulas que contienen componente de proteína, componente graso, componente carbohidrato, vitaminas, minerales y emulsionante, para una persona conocedora de la materia era evidente el elaborar las composiciones de esta solicitud de manera similar, teniendo en cuenta estos compuestos; (b) las reivindicaciones de esta solicitud no mencionan una característica que conceda un efecto diferente o especial a las composiciones, que pueda considerarse como un aporte a la técnica, porque las anterioridades ya enseñaban las fórmulas que contienen componente de proteína, componente graso, componente carbohidrato, vitaminas, minerales y emulsionante requeridas por estas, así que estas son obvias para una persona versada en la materia y (c) el problema planteado en esta solicitud era la necesidad de proporcionar un fortalecedor en polvo para leche humana para alimentación de infantes prematuros y puesto que para resolver este problema técnico la solicitud proporciona fórmulas que contienen componente de

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proteína, componente graso, componente carbohidrato, vitaminas, minerales y emulsionante, es decir de manera similar a como se resolvía en las anterioridades D1, D2 y D3; entonces el objeto de las reivindicaciones 1 a 4, 19, 25 a 28, 10 a 14, 22 de esta solicitud no tiene **nivel inventivo**.

Se dice en la solicitud que (1) esta fórmula contiene más proteína: 24 - 55, grasa: 1 - 30 y carbohidrato: 15 - 75 que las fórmulas del estado del arte. Es claro de acuerdo con la tabla siguiente:

Componente	Solicitud	D1	D2	D3
Proteína	24 - 55	8 - 28	25 - 35	10 - 35
Grasa	1 - 30	8 - 40	65 - 85	20 - 45
Carbohidrato	15 - 75	32 - 80	40 - 75	60 - 110
Cobre	si	no	si	Si
Zinc	si	no	si	Si
Calcio insoluble	si	no	si	Si
Emulsificante	si	no	si	si

que los contenidos de grasa y carbohidratos ya habían sido considerados en las anterioridades, y aunque el contenido de proteína es más alto, no es un hecho sorprendente porque estaba al alcance de cualquier persona conocedora de la materia. (2) esta fórmula contiene opcionalmente, calcio insoluble que evita que la proteína precipite: se observa que también D2 y D3 contienen calcio insoluble. (3) esta fórmula contiene opcionalmente emulsificante con el fin de aumentar la estabilidad de la emulsión: se observa que también D2 y D3 emulsificante con el fin de aumentar la estabilidad de la emulsión (4) se dice que esta fórmula tiene la ventaja de agregar Zinc y Cobre a la dieta infantil: se observa que igualmente, D2 y D3 son fórmulas que contiene Zinc y Cobre. De manera que el objeto de las reivindicaciones 1 a 4, 19, 25 a 28, 10 a 14, 22 de esta solicitud no tiene **nivel inventivo**.

6. Conclusión

En conclusión, los requisitos de patentabilidad de la presente solicitud están afectados así:

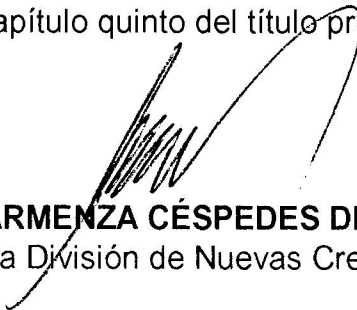
Item	Documento	Reivindicaciones afectadas	Requisito que afecta
D1	US 5 013 569	1 a 4, 19, 25 a 28, 10 a 14, 22	Novedad y Nivel inventivo
D2	US 5 340 603	1 a 4, 19, 25 a 28, 10 a 14, 22	Novedad y Nivel inventivo
D3	US 5 700 590	1 a 4, 19, 25 a 28, 10 a 14, 22	Novedad y Nivel inventivo

En cumplimiento del artículo 45 de la Decisión 486 de la Comisión de la Comunidad Andina, se le indica que debe dar respuesta dentro del término de sesenta días contados a partir de la fecha de la notificación de la presente comunicación. En caso de no dar respuesta al presente requerimiento o si a pesar de la respuesta subsistieran los impedimentos para la concesión, se denegará la patente.

Notifíquese el presente oficio conforme a lo dispuesto en el numeral 5.2, literal

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e), del capítulo quinto del título primero de la Circular Unica No. 10 de 2001.


ALIX CARMENZA CÉSPEDES DE VERGEL
Jefe de la División de Nuevas Creaciones.

El anterior requerimiento fue notificado por fijación en lista, de fecha
21 ABR. 2005.

CONCEPTO TÉCNICO No. 507	EXAMINADOR TÉCNICO Código 202007
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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

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RADICACIÓN: 0-25252

EDICTO No. 11304

LA SECRETARÍA GENERAL AD-HOC HACE SABER:

Que esta Superintendencia profirió Resolución No. 20138 de 22-AGO-2005. Que el contenido de la parte resolutive es como sigue: El Superintendente de Industria y Comercio.

RESUELVE

ARTICULO PRIMERO: Negar el privilegio de patente de invención para la solicitud correspondiente a "FORTALECEDOR EN POLVO PARA LECHE HUMANA".

ARTICULO SEGUNDO: Notificar personalmente el contenido de la presente resolución

a la doctora Alicia Lloreda Ricaurte, o a quien haga sus veces, en su calidad de apoderada de Abbott Laboratories., entregándole copia de la misma, advirtiéndole que contra ella procede el recurso de reposición interpuesto ante el Superintendente de Industria y Comercio, al momento de la notificación o dentro de los 5 días hábiles siguientes a ella.

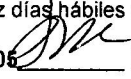
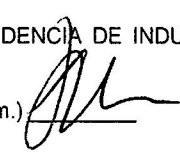
NOTIFÍQUESE Y CUMPLASE

Dada en Bogotá, D.C., a los 22 AGO. 2005

EL SUPERINTENDENTE DE INDUSTRIA Y COMERCIO,


JAIME RUBIO ESCOBAR

Para notificar a los interesados, se fija el presente EDICTO en lugar visible al público en la SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO, por el término de (10) diez días hábiles contados a partir de las 8:30 a.m. de hoy.

Secretaría General Ad-Hoc 06-SEP-2005  Este edicto se desfija hoy 19-SEP-2005 a las cinco (5:00 p.m.) 
Secretaría General Ad-Hoc
EDICTO No. 11304