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Señor

SUPERINTENDENTE DE INDUSTRIA Y COMERCIO
DIVISION DE NUEVAS CREACIONES

E. _____ S. _____



Re: P1.-NESTEC S.A.-Solicitud de Patente de Invención en Fase Nacional
PCT para "FRACCIONES DE LECHE Y PREPARACIONES DE
LECHE PARA EL TRATAMIENTO Y/O PREVENCION DE LAS
ENFERMEDADES MEDIADAS POR COX-2".-Clase A23L 1/305.-
Expediente número 06-018.273.-

1. Me refiero a mi memorial de 13 de Junio de 2006.
2. De conformidad con lo dispuesto en el Artículo 5.2.12 de la Circular Externa No. 03 de 28 de Abril de 2003, y estando dentro del plazo de seis meses contados desde la fecha de la publicación de la solicitud en la Gaceta de la Propiedad Industrial número **579** de 31 de Agosto de 2007, solicito a ese Despacho proceder a realizar el examen de patentabilidad de la presente invención.
3. Me permito recordar a usted, que tal como se informó en el Petitorio de la invención, la presente solicitud corresponde a Capítulo II.
4. Anexo me permito acompañar recibo número 08-10.993, expedido por la Superintendencia de Industria y Comercio, que acredita el pago de la tasa que dicho examen causa.

Señor Superintendente,


ALICIA LLOREDA RICAURTE
T.P. 53.215

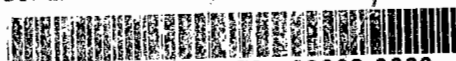
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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

NIT : 800176089-2

RECIBO OFICIAL DE CAJA : 08 - 10,993
A : FEBRERO 11 DE 2008

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 06-018273-00003-0000

Fecha: 2008-02-13 16:42:30 Dep. 2020 NUECREACIONE
Tra. 11 PATENTE I y II Eve: 379 FASE NACIONAL II
Act. 538 PETICION Folios: 2

***** CONSIGNACION *****

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PGO	Vr. PAGO
LLOREDA Y CIA S. A	CONSIGNACION	BANCO DE BOGOTA	062754387	2660849	11/02/2008	4,643,000.00

***** CONCEPTO *****

RENTISTICO	CONCEPTO	TOTAL CONCEPTO
1 50005-01-01 SOLICITUDES	114 PTC CAP-II EXAMEN DE PATENTE I y II	210,000.00
	TOTAL :	\$ 210,000.00

SDN: DOSCIENTOS DIEZ MIL PESOS

RESPONSABLE :

DIVISIÓN DE NUEVAS CREACIONES

RADICACIÓN EXPEDIENTE No. 06-18273

EL EXTRACTO DE LA PRESENTE SOLICITUD DE **PATENTE DE INVENCION**

FUE PUBLICADO EN LA GACETA DE PROPIEDAD INDUSTRIAL No **579** DE

FECHA **31 DE AGOSTO DE 2007** EL TÉRMINO HÁBIL SEÑALADO POR LA

LEY EXPIRA EL **28 DE NOVIEMBRE DE 2007**

NOTA: Dentro del plazo de los seis (6) meses siguientes a partir de la fecha de publicación en la gaceta de Propiedad Industrial, deberá solicitar y cancelar el examen de patentabilidad so pena de que la solicitud caiga en abandono, de acuerdo con lo establecido en el Artículo 44 de la Decisión 486/2000.

SE PRESENTARON OPOSICIONES POR PARTE DE TERCEROS.

SI _____

NO X

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1 100

**SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIVISIÓN DE NUEVAS CREACIONES**

202012

Bogotá, D.C., 06 de mayo de 2009

Apoderado: Alicia Lloreda Ricaurte

ASUNTO

Radicación 06-18273
Trámite 002
Evento 001
Actuación 430
Oficio **5 9 7 3**
Folios

Patente de Invención



Vía PCT (fase nacional)



Cap. I



Cap. II



No. Sol. Internacional

PCT/EP2004/010200

Fecha de Presentación Internal.

WO2005/025335

Como resultado del examen de fondo, realizado con fundamento en el artículo 45 de la Decisión 486 de la Comisión de la Comunidad Andina, se le comunica:

Documentos estudiados

Descripción:

Folios: 14 a 73

Como se radicó inicialmente.

Reivindicaciones:

Folios 74 a 24

Como se radicó inicialmente.

Prioridad:

Folios: 56 a 61; GB 9930058.4; 20/12/1999

§ Objeto de la invención

El título de la invención "FRACCIONES DE LECHE Y PREPARACIONES DE LECHE PARA EL TRATAMIENTO Y/O PREVENCIÓN DE LAS ENFERMEDADES MEDIADAS POR COX-2".

Tiene como objeto las composiciones nutricionales y farmacéuticas que comprenden una o más fracciones de proteína de leche.

El campo de la invención, según la Clasificación Internacional de Patentes: A23L 1/305.

De la solicitud de Patente

Reivindicaciones (Artículo 30 D 486 de la C.A.N.)

-La reivindicación 2 esta referida a la descripción, lo cual no es aceptable puesto que la descripción no delimita el alcance, lo correcto es que la característica a la que se refiere quede explícitamente establecida en la reivindicación.

-La reivindicación 4, no es clara puesto que la "característica técnica" a que hace referencia esta sólo enunciada como un resultado a obtener.

-La reivindicación 13 no es clara, ya que se refiere según el encabezado a un proceso, pero el resto del texto de la reivindicación no es consecuente técnicamente con el encabezado, hace referencia al uso tácito del uso de proteínas de la leche, con un efecto deseado.

Las reivindicaciones objetadas no cumplen con el requisito de definición, claridad, concisión o sustento por la descripción de acuerdo al art. 30 de la Decisión 486 y/o art.22 Tratado PCT.

§ No es una invención (Artículo 15 D 486 literal b) de la C.A.N.)

La reivindicación 18 reclama una fracción de leche, con características deseables, para usarse en composiciones nutricionales esa materia corresponde a material biológico existente en la naturaleza, por lo tanto esta bajo el alcance de del artículo 15 D 486 literal b), D 486 de la C.A.N.

§ Reivindicaciones relativas a un uso o a un segundo uso (Artículos 14 y 21 D 486)

-Las reivindicaciones 7-12 reclaman el uso de una fracción de la leche, y de acuerdo con la D 486, Artículos 14 y 21 el uso reclamado no se considera para protección por patente, como se lee en el artículo 14 de la Decisión 486 de la C.A.N "... Los Países Miembros otorgarán patentes para las invenciones sean de productos o procedimientos en todos los campos de la tecnología..."; aquí no se hace alusión al uso como materia patentable.

Los usos o segundos usos no son patentables, de conformidad con la sentencia del TJAC 89-AI-2000, los usos en general no son patentables.

§ Determinación del Estado de la Técnica

La fecha que se ha tenido en cuenta para determinar el Estado de la Técnica es:
Fecha de presentación de la solicitud prioritaria 12/09/2003

	Documento No.	Título	Publicación
D1	US5.492.716	Method of harvesting natural milk proteins	20-feb-1996
D2	US4.550.028	Method of re-suspending flocculated milk casein to obtain enriched daily raw material	29-oct-1985
D3	Us4.981.704	Partial hydrolysate of whey	01-ene-1991

		proteins, enzymatic process for the preparation of this hydrolysate, and hypoallergenic dietetic mil food containing it.	
D4	US5.436.020	Method for producing a formulated milk for infants analogous to human milk	25-jul-1995
D5	EP 0080933	Procedé de recuperation des protéines du lactosérum, application á la production des fromages et fromages obtenus	08-jun-1983
D6	GB 200.185	Process for the recovery of proteins and milk-sugar from whey	05-jul-1923
D7	WO01/11990	Composition for infant formula having a low theonine content	22-feb-2001
D8	US5.290.571	Biologically active whey protein concentrate	01-mar-1991
D9	WO82/01806	Process and apparatus for making chees base and a novel intermediate product of said process	10-jun-1982
D10	US5.230.902	Undenatured whey protein concentrate to improve active systemic humoral immune response	27-jul-1993

§ Análisis de patentabilidad (Artículo 14 D 486 de la C.A.N.)

Novedad (artículo 16 D486)

La solicitud en estudio reclama una composición farmacéutica una composición nutricional y/o farmacéutica para el tratamiento y/o prevención de enfermedades mediadas por la ciclooxigenasa 2, CARACTERIZADA porque comprende una cantidad terapéuticamente efectiva de una o más fracciones de proteína de leche y/o una o más preparaciones de proteína de leche, en donde dichas una o más fracciones de proteína de leche y/o una o más preparaciones de proteína de leche proveen actividad inhibidora de ciclooxigenasa 2.

-Tal como se reclama la materia a proteger, que consiste en una composición que comprende "una cantidad de una o más fracciones de proteína de leche", se reclama es la leche natural proveniente de cualquier mamífero o cualquier composición que comprenda leche. Ahora la otra parte reclamada "y/o una o más preparaciones de proteína de leche", se reclama propiedad sobre cualquier producto derivado lácteo del mercado [ejemplos: arequipe de leche, yogures, cuajadas, quesos, cortados de queso, leche deslactosada, leche descremada, leche semidescremada etc.] todos esos productos comprenden proteína de leche o partes de proteína de leche y

además el hecho de que se indique un uso o propiedad deseada para la proteína de la leche o parte de la proteína de la leche o a la leche misma no la hace patentable.

-D1-D5 describen procesos para la separación de las proteínas de la leche y otras fracciones de proteína de leche y los productos obtenidos con el uso de las proteínas de la leche en las composiciones, entonces la materia que se reclama no es nueva e inventiva. (Véase los documentos completos).

-La anterioridad D6 describe procesos para recuperar cada una de las fracciones de la leche, especialmente recuperar las diferentes fracciones proteicas, para diferentes usos, entonces tal como se puede ver la materia reclamada en la presente solicitud no es nueva ni inventiva.

D7 describe composiciones alimenticias o medicamentos para niños que comprenden proteínas de la leche, las cuales son bajas en treonina, por la remoción de un glico péptido de caseína (véase todo el documento especialmente, pag 1, ejemplos 4 y 5, pag 16, tabla 4)

-D8- describe composiciones que comprenden concentrados de proteína biológicamente activos, comprende múltiples composiciones que comprenden una o mas fracciones de proteínas de la leche, por lo tanto la materia reclamada en la presente solicitud no es nueva.

-D9 describe aparato, métodos para separar los componentes de la leche y queso que comprende toda la caseína y todas las proteínas del suero las cuales están originalmente en la leche.

-D10 describe:

Whey and whey protein have been utilized from time immemorial for nutritional purpose. In addition, whey was recommended in folk and ancient medicine for the treatment of various diseases and, in one instance, life-time feeding of hamsters with a whey protein diet has been shown to promote longevity with no explanation given. We have shown, in controlled experiments, for the first time, that whey protein feeding specifically enhances mice immune response to sheep red blood cells (SRBC), resistance to pneumococcal infection, inhibits the development of colon cancer and delays the process of aging independently of its nutritional quality.

Tal como esta anterioridad enseña las composiciones reclamadas por la solicitud en estudio no son nuevas. (véase toda la anterioridad especialmente Figs.4-7, colum.1-6).

No. Documento	Reivindicaciones	Requisito que afecta
D1	1-6,13-18	NOVEDAD
D2	1-6,13-18	NOVEDAD
D3	1-6,13-18	NOVEDAD
D4	1-6,13-18	NOVEDAD
D5	1-6,13-18	NOVEDAD
D6	1-6,13-18	NOVEDAD
D7	1-6,13-18	NOVEDAD
D8	1-6,13-18	NOVEDAD
D9	1-6,13-18	NOVEDAD
D10	1-6,13-18	NOVEDAD

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 60 días contados a partir de la fecha de 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 e), del capítulo quinto del título primero de la Circular Única N° 10 de 2001.

ALIX CARMENZA CÉSPEDES DE VERGEL
Jefe de División de Nuevas Creaciones

El anterior requerimiento fue notificado por fijación en lista, de fecha

22 MAYO 2009

22 MAYO 2009

CONCEPTO TÉCNICO No. 1547 | EXAMINADOR TÉCNICO Código No.202012

105

5,492,716

METHOD OF HARVESTING NATURAL MILK PROTEINS

BACKGROUND OF THE INVENTION

The present invention concerns a method of harvesting natural milk proteins by treating a fraction of the milk with a precipitant. This treatment separates the mixture into concentrated natural casein and a fraction that contains the precipitant.

Dividing milk into three fractions, specifically fat, casein, and whey, by centrifuging is known. Although all components of the milk can be considered nutritious, it has been impossible until now to process milk without some form of waste occurring. This situation has resulted in main products and byproducts with no other value widely divergent physical value and time.

German Patent No. 233 suggests adding concentrated pectin to separate the milk into concentrated casein and pectin in whey. This approach made it possible for the first time to obtain a solution of natural casein as a separate concentrated fraction. The approach was not really successful, however, because it took so much pectin (approximately 250 kg/tonne of casein concentrate) and pectin is expensive. No one has been able to discover a way to exploit the whey that will recover the cost of the pectin.

SUMMARY OF THE INVENTION

The object of the present invention is accordingly a method of harvesting concentrated natural casein with a low fat content that requires only a little precipitant.

This object is attained by using an anionic polysaccharide solution as a precipitant, separating the mixture in a centrifuge into a polysaccharide fraction and a milk fraction, and using the polysaccharide fraction to separate the milk fraction into concentrated casein and another polysaccharide fraction.

Separating the mixture in a centrifuge and exploiting the first polysaccharide fraction saves a lot of polysaccharide. Only 70 to 220 kg of polysaccharide per 1,000 kg of dried concentrate milk protein is needed.

Advantages and embodiments of the invention are set forth in the following claims and they will now be specified with reference to the following examples.

DETAILED DESCRIPTION OF THE INVENTION

EXAMPLE 1

900 kg of non-fat milk or defatted buttermilk are treated with 100 kg of a 7% aqueous solution of pectin, with a 3.7% solution of carboxymethylcellulose, or with a 3.5% solution of Rhodigel-200 (Xanthan Gum). The batch is thoroughly agitated for up to 15 minutes and separated in a high-speed centrifuge into 120 to 130 kg of a solution of natural casein (a protein-lipide concentrate for buttermilk) and approximately 870 to 880 kg of a polysaccharide fraction containing approximately 6.7% solids. The latex can either be processed into food or further concentrated to 33.9% solids, which is 170 kg of concentrated polysaccharide. The concentrated protein is further concentrated in a spray dryer and/or used for food.

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The concentrated polysaccharide fraction is used to make food or mixed with 900 kg of non-fat milk or buttermilk and separated in a centrifuge into approximately 130 to 130 kg of concentrated natural casein and 420 kg of another polysaccharide fraction containing 11.7% solids. The protein is further concentrated in a spray dryer and/or used for food. The concentrated polysaccharide obtained from the second polysaccharide fraction is used to make food and/or concentrated to 4% in 50% solids, which is 220 to 230 kg of concentrate. The concentrate is used to make food or mixed with 900 kg of non-fat milk or buttermilk and separated in a centrifuge into approximately 120 to 130 kg of concentrated natural casein and approximately 880 kg of a third polysaccharide fraction. The concentrated casein and the polysaccharide fraction are dried and/or used to make food. Approximately 400 kg of concentrated milk protein, including approximately 20% solids, and approximately 580 kg of a polysaccharide fraction with up to 18% solids are accordingly harvested from 2700 kg of non-fat milk or buttermilk or mixtures thereof.

EXAMPLE 2

900 kg of non-fat milk or concentrated buttermilk containing 24% solids are treated with 100 kg of a 6% solution of pectin, a 12.5 to 2.0% solution of carboxymethylcellulose, and a 1.5 to 2.0% solution of Rhodigel-200 (Xanthan Gum) and thoroughly mixed for up to 15 minutes. The batch is subsequently separated in a high-speed centrifuge into approximately 400 kg of concentrated milk proteins with approximately 31% solids, including 17.5% casein, and approximately 600 kg of a polysaccharide fraction containing approximately 15% solids, including 1.8% whey protein. The concentrated casein and the polysaccharide fraction are dried and/or used to make food.

What is claimed is:

1. A method of harvesting natural milk proteins comprising treating a fraction of the milk with a precipitant to separate the mixture into concentrated natural casein and a fraction that contains the precipitant by using an anionic polysaccharide solution as a precipitant, separating the mixture in a centrifuge into a polysaccharide fraction and a milk fraction, and centrifuging the polysaccharide fraction to separate the milk fraction into concentrated casein and another polysaccharide fraction.
2. The method as in claim 1, wherein the concentrated polysaccharide accounts for 0.5 to 0.6% of the mixture.
3. The method as in claim 2, wherein the concentrated polysaccharide accounts for 0.5 to 0.6% of the mixture.
4. The method as in claim 1, wherein the first polysaccharide fraction is, before being centrifuged, concentrated at a temperature of 40° to 70° C. to a solids content of 30 to 35%.
5. The method as in claim 1, wherein the second polysaccharide fraction is centrifuged to separate a milk fraction into concentrated casein and a third polysaccharide fraction.
6. The method as in claim 5, wherein the second polysaccharide fraction is, before being centrifuged, concentrated to a solids content of 45 to 50%.
7. The method as in claim 1, wherein the milk fraction is non-fat milk.
8. The method as in claim 1, wherein a concentrated milk fraction is employed.
9. The method as in claim 1, wherein the milk fraction is concentrated buttermilk with a solids content of 15 to 25%.

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United States Patent (19)
Molochnikov et al.

(11) Patent Number: 5,492,716
(45) Date of Patent: Feb. 20, 1996

METHOD OF HARVESTING NATURAL MILK PROTEINS

(75) Inventors: Valery Molochnikov, Sverdlovsk, Russian Federation; Karl Heinz Zentler, Oelde, Germany

(77) Assignee: Westfalia Separator AG, Detteln, Germany

(21) Appl. No.: 109,800

(22) Filed: Aug. 20, 1993

(30) Foreign Application Priority Data

Aug. 21, 1992 (DE) Germany 42 37 646.7

(51) Int. Cl.⁴ A23 1/20; A23 3/30

(52) U.S. Cl. 426/658

(58) Field of Search 426/658

References Cited

FOREIGN PATENT DOCUMENTS

053573 A-1992 Germany

OTHER PUBLICATIONS

U.S. Pharmacopeia, Jan. 1, 1990, p. 1096

Primary Examiner: David H. Crete

Assistant Examiner: Charles P. Kutz

Attorney, Agent, or Firm: Spring Horn, Krone & Woods

ABSTRACT

A method of harvesting natural milk proteins by treating a fraction of the milk with a precipitant. The treatment separates the mixture into concentrated natural casein and a fraction that contains the precipitant. The object is to use less polysaccharide. An anionic polysaccharide solution is used as a precipitant. The mixture is separated in a centrifuge into a polysaccharide fraction and a milk fraction. The polysaccharide fraction is exploited to separate the milk fraction into concentrated casein and another polysaccharide fraction.

9 Claims, No Drawings

105

105

106

4,550,028

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METHOD OF RE-SUSPENDING FLOCCULATED MILK CASEIN TO OBTAIN PROTEIN ENRICHED DAIRY RAW MATERIAL

BACKGROUND OF THE INVENTION

1. Field of the Invention

The invention relates to the field of dairy technique. It has for its object a method of re-suspending flocculated milk casein for the obtaining of a protein-enriched dairy raw material. Such a raw material may find applications especially for cheese production, but also for obtaining products for alimentary or dietetic use, such as milk powders enriched in protein substances. The field wherein the invention finds a particularly advantageous application is that of cheese-making.

2. Description of the Prior Art

Casein is the main protein in milk. Being sensitive to acidity and to rennet, it represents almost the 4/5ths of the proteic matters in milk. The other proteic substances, called "whey proteins" or "seric proteins", which are insensitive to the action of rennet while sensitive to that of heat, represent somewhat more than the remaining 1/5th.

The methods used for separating the milk proteins have been improved in the course of time with a view to recover them in an ever increasing proportion and in the least possible denatured state. To the rudimentary, while economical, method consisting of industrial casein preparation there was added the so-called coprecipitation technique. Among the more recent treatments for milk, ultrafiltration was proposed to provide a retentate suitable as a pre-cheese, i.e. a raw material with a composition quite similar to that of drained cheese. Such a retentate contains all the proteins of the original milk in a non-denatured state, said proteins having undergone no flocculation. Ultrafiltration, apart from the cyclic character of its operation, does not allow full control of the retentate composition, due to its non-instantaneous nature which permits the evolution of the product subjected to filtration. From the technological standpoint, recovery of the whey proteins in the soluble state while desirable for some uses, might prove unsuitable for cheese-making, for example, where those proteins being in fluidity instead of firmness. From the technological standpoint, ultrafiltration is a gentle, but costly technique. Practically, care should be had of using membranes of sufficiently warranted strength, life-time and aptness to be cleaned without being damaged. In the present state of the art, ultrafiltration of milk for cheese-making, is quite valuable from the theoretical standpoint but liable to raise practical difficulties.

Among the known methods mention may also be made of the so-called CENTRI-WHEY method developed by the firm ALFA-LAVAL, which consists in flocculating the whey proteins in the absence of casein, i.e. in the whey itself, and after their separation by centrifuging, in incorporating said flocculated proteins in the milk for the following cheese-making step. The whey proteins are coagulated by heating and are present under the form of a suspension sufficiently stable not to settle during renneting. The method thus leads to a milk proteic concentrate wherein the casein is in the form of a colloidal dispersion, and which contains the whey proteins in the flocculated state. From the dietetic standpoint, nutritionists are of opinion that it is not objectionable, to coagulate whey proteins in the coagulated state instead of the soluble state. While valuable both from the dietetic and economical standpoint, the CENTRI-WHEY method does not lead to a dairy raw material constituting a genuine pre-cheese. The protein milk resulting from the whey protein flocculating step is incorporated in the process milk, this causing a further synthesis, whereby carrying out of the method may be construed

SUMMARY OF THE INVENTION

The present invention has for its purpose to remove most of the drawbacks of the methods of the prior art, even the most recent thereof, such as those used in particular for cheese production. Thus, while entirely consistent with cheese-making tradition, the method provides a dairy raw material usable as a pre-cheese of a composition perfectly suited to the requirements. In this connection, the invention also has for its object a method for obtaining a dairy raw material, usable in cheese-making, wherein the inorganic substance content, also called the mineralization ratio, may be accurately adjusted. The method of the invention may be carried out continuously and uses equipment already in use in the dairy industry. As previously set forth, the preferred field of application of the present invention is that of cheese production since, by resuspension of the casein, the method provides a dairy raw material sensitive to coagulation by rennet. However the method of the invention is not limited to cheese-making applications, since said raw material may be used for alimentary or dietetic purposes, for example for manufacturing products liable to be dehydrated, which are enriched in proteic matters derived from milk.

Under its most general form, the invention has for its object a method for re-suspending flocculated milk casein for the obtaining of a protein-enriched dairy raw material, characterized in that the milk is subjected to a combined acidifying and heat treatment under such conditions as to provide a whey and a proteic flocculate (or curd), consisting of casein and/or whey proteins. In that after cooling, the curd and whey are separated, the latter containing substantially no milk proteins, while the curd coagulates substantially all the milk proteins in the flocculated state, in that the curd is subjected to a so-called "frigo-compression" treatment combining a compression step at a pressure exceeding 100 bars and a cooling step to a temperature ranging from 0° to 5° C., this leading to a liquid product concentrated in proteins, wherein the casein is re-suspended.

DESCRIPTION OF THE INVENTION

The method of the invention is applicable to the widest variety of milks, irrespective of their nature or origin. These may include as well whole or skimmed milk, natural milk or milk reconstituted, especially upon rehydration of milk powder. Use may be made of milk from any milk-producing female animals, viz. cows, goats, ewes, cow-buffalo, she-asses and similar. The starting milk may have undergone a previous homogenizing treatment or a heat treatment. There may thus be used pasteurized milks or UHT (ultrahigh temperature) milks.

The first stage of the method of the invention consists in subjecting the milk to a combined acidifying and heating treatment. The conditions for this treatment are varying since the acidity of the medium and the temperature are correlated. Thus, the temperature affording

United States Patent (19)

Montigny

(31) Patent Number: 4,550,028

(43) Date of Patent: Oct. 29, 1985

(54) METHOD OF RE-SUSPENDING FLOCCULATED MILK CASEIN TO OBTAIN PROTEIN ENRICHED DAIRY RAW MATERIAL

(75) Inventor: Jean Montigny, Folleville, France

(73) Assignee: Centrale Laitiere de Haute Normandie, Maroube, France

(21) Appl. No. 392,144

(22) Filed: Jan. 25, 1982

(30) Foreign Application Priority Data

Jun 24, 1981 (FR) France 81 12323

(51) Int. Cl. A23C 19/02

(52) U.S. Cl. 426/582; 426/49

(58) Field of Search 426/582, 657, 36, 39, 426/446

(56) References Cited

U.S. PATENT DOCUMENTS

3,815,587 10/1972 Kogut et al. 426/192

4,006,800 1/1978 Rose et al. 426/392

Primary Examiner—George Yeung
Attorney, Agent, or Firm—O'Brien, Fisher, Spivak,
McClelland & Maier

ABSTRACT

Milk is subjected to a combined acidifying and heating treatment in such conditions as to provide a whey and a proteic flocculate (or curd), consisting of casein and/or whey proteins. Then after cooling the curd and whey are separated, the latter containing substantially no milk proteins, while the curd practically contains all the milk proteins in the flocculated state, the curd is subjected to a so-called "frigo-compression" step combining compression to a pressure exceeding 100 bars with cooling to a temperature ranging from 0° C. to 5° C., this leading to a protein-concentrated product, wherein the casein is re-suspended. There is thus obtained a dairy raw material which may be used as a pre-cheese and be directly processed into cheese, without syncretis, by addition of rennet.

14 Claims, 1 Drawing Figure

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Starting material: whey from pressed cheese, condensed to 22.6% dry extract by reverse osmosis. Its initial pH is 6.3 and its total nitrogenous matter represents 14.6% of the dry extract.

Hydrolysis: The pH of the whey is adjusted to 8.0 using soda then 150 g of 10% (w/v) of sodium hydroxide is put in a container with 500 g of whey, at 60° C., with slow stirring in order to maintain the temperature at 110° C.

The pH is regulated to 8.0 by the addition of soda. After 20 hours of hydrolysis, the composition is reported from the whey by decantation.

The pH of the whey is adjusted to 4.0 using hydrochloric acid and the preparation is taken to 60° C. for 1 hour, then centrifuged. The supernatant recovered represents the hydrolysate which it is wished to obtain.

It is obvious that the embodiments described are only by substituting equivalent techniques, without for that reason departing from the scope of the invention.

1. Partial hydrolysate of whey proteins which comprises peptides spread over the following distribution as a function of their molar mass:

2. Hydrolysate of whey proteins which comprises peptides spread over the following distribution as a function of their molar mass:

3. Enzymatic process for the preparation of a partial hydrolysate of whey proteins which comprises peptides spread over the following distribution, as a function of their molar mass:

4. Process according to claim 3, in which a mixture of insolubilized enzymes is used, and in which said stage (b) consists firstly in separating the insolubilized enzymes by decantation, centrifugation and/or filtration, then separating the unhydrolyzed residual proteins by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000 in order to obtain the hydrolysate.

5. Process according to claim 3, in which a mixture of soluble enzymes is used, and in which said stage (b) is carried out by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000.

6. Process according to claim 3, in which a mixture of dried proteins is used, and in which said stage (b) is carried out by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000.

7. Process according to claim 3, in which a mixture of dried proteins is used, and in which said stage (b) is carried out by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000.

8. Process according to claim 3, in which a mixture of dried proteins is used, and in which said stage (b) is carried out by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000.

9. Process according to claim 3, in which a mixture of dried proteins is used, and in which said stage (b) is carried out by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000.

10. Process according to claim 3, in which a mixture of dried proteins is used, and in which said stage (b) is carried out by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000.

11. Process according to claim 3, in which a mixture of dried proteins is used, and in which said stage (b) is carried out by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000.

12. Process according to claim 3, in which a mixture of dried proteins is used, and in which said stage (b) is carried out by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000.

13. Process according to claim 3, in which a mixture of dried proteins is used, and in which said stage (b) is carried out by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000.

14. Process according to claim 3, in which a mixture of dried proteins is used, and in which said stage (b) is carried out by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000.

15. Process according to claim 3, in which a mixture of dried proteins is used, and in which said stage (b) is carried out by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000.

16. Process according to claim 3, in which a mixture of dried proteins is used, and in which said stage (b) is carried out by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000.

17. Process according to claim 3, in which a mixture of dried proteins is used, and in which said stage (b) is carried out by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000.

18. Process according to claim 3, in which a mixture of dried proteins is used, and in which said stage (b) is carried out by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000.

19. Process according to claim 3, in which a mixture of dried proteins is used, and in which said stage (b) is carried out by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000.

20. Process according to claim 3, in which a mixture of dried proteins is used, and in which said stage (b) is carried out by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000.

21. Process according to claim 3, in which a mixture of dried proteins is used, and in which said stage (b) is carried out by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000.

22. Process according to claim 3, in which a mixture of dried proteins is used, and in which said stage (b) is carried out by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000.

23. Process according to claim 3, in which a mixture of dried proteins is used, and in which said stage (b) is carried out by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000.

24. Process according to claim 3, in which a mixture of dried proteins is used, and in which said stage (b) is carried out by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000.

25. Process according to claim 3, in which a mixture of dried proteins is used, and in which said stage (b) is carried out by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000.

26. Process according to claim 3, in which a mixture of dried proteins is used, and in which said stage (b) is carried out by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000.

27. Process according to claim 3, in which a mixture of dried proteins is used, and in which said stage (b) is carried out by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000.

28. Process according to claim 3, in which a mixture of dried proteins is used, and in which said stage (b) is carried out by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000.

29. Process according to claim 3, in which a mixture of dried proteins is used, and in which said stage (b) is carried out by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000.

30. Process according to claim 3, in which a mixture of dried proteins is used, and in which said stage (b) is carried out by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000.

31. Process according to claim 3, in which a mixture of dried proteins is used, and in which said stage (b) is carried out by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000.

32. Process according to claim 3, in which a mixture of dried proteins is used, and in which said stage (b) is carried out by ultra-filtration and/or dia-filtration using at least one membrane having a threshold of less than 10,000.

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"Procédé de récupération des protéines du lactosérum, application à la production des fromages et fromages obtenus".

La présente invention concerne le domaine de l'industrie laitière et a plus particulièrement pour objet un procédé pour la récupération des protéines du lactosérum (petit-lait) et leur utilisation dans la fabrication de fromages. L'invention est également relative à de nouveaux produits de type fromages pouvant être obtenus par un tel procédé.

Les produits fromagers naturels, par exemple de type cheddar, caillé malaxé, colby, gouda ou suisse, sont fabriqués par coagulation de lait, affinés à l'aide de bactéries convenables productrices d'acide lactique, jusqu'à l'acidité désirée, au moyen d'enzymes de caillage de lait appropriées, découpage du coagulum et éventuellement cuisson du caillé résultant dans son lactosérum. On sépare par égouttage le lactosérum du caillé, après quoi on peut transformer en cheddar ou brasser le caillé alors que de l'acide supplémentaire apparaît du fait de la transformation par fermentation dans le caillé du lactose en acide lactique. On peut soumettre ou non le caillé à un lavage à l'eau. S'il s'agit de fabriquer du fromage du type cheddar, le caillé est broyé, salé et mis par pressage sous forme d'éléments ronds, parallélépipédiques ou analogues aux fins d'affinage. Les opérations d'addition de bactéries/d'acide lactique, d'affinage du lait, de découpage du caillé, de cuisson du caillé, de brassage du caillé, de transformation du caillé en cheddar et de salage du caillé sont toutes réglées en vue de l'obtention d'un produit dans lequel le lactose résiduel et le pouvoir tampon disponible du caillé sont équilibrés de façon que la transformation totale par fermentation du lactose résiduel

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Procédé de récupération des protéines de lactosérum, application à la production des fromages et fromages obtenus.

La présente invention concerne un procédé pour la récupération des protéines du lactosérum et leur utilisation dans la fabrication de fromage.

On soumet le lactosérum, sécrété du caillé de fromage au cours du traitement normal, d'abord à une pasteurisation, puis à une ultrafiltration pour obtenir un concentré de protéines de lactosérum, ledit procédé étant caractérisé en ce qu'on mélange le concentré avec du lait et qu'on soumet le lait ainsi enrichi à une autre ultrafiltration après laquelle on le traite de la manière usuelle pour former un caillé. Suivant un autre mode de réalisation de l'invention, le procédé inclut les étapes (a) coagulation du mélange de lait et de concentré de protéines de lactosérum et (b) l'ultrafiltration du coagulum, auquel cas on obtient directement le fromage désiré après ladite ultrafiltration.

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Par exemple, on peut introduire dans le caillé, les protéines du lactosérum séchées, mais seule une quantité limitée de protéines de lactosérum peut être ajoutée de cette manière au caillé de fromage sans modifier les propriétés qu'on désire. En général, l'addition au caillé de protéines du lactosérum peut conférer au produit final une texture granuleuse et un goût amer et, par conséquent, les protéines de lactosérum récupérées à partir de lactosérum ne sont pas utilisées à un degré notable dans les procédés industriels de fabrication de fromage naturel.

Pour les mêmes raisons, les protéines de lactosérum récupérées de cette manière ne sont pas utilisées à un degré notable dans la fabrication industrielle de fromages élaborés. En outre, il n'est industriellement possible d'ajouter que des quantités limitées de telles protéines de lactosérum récupérées à des produits à tartiner, aliments ou autres produits à base de fromages élaborés, ou à des imitations de fromages.

De toute façon, dans tous ces procédés connus, la quantité maximale de protéines de lactosérum qu'il est possible d'introduire dans le fromage ne peut dépasser celle du lait à partir duquel le lactosérum de départ a été obtenu. On sait que la proportion des protéines dites solubles (ou protéines de lactosérum) du lait de vache est de l'ordre de 20 % en poids par rapport aux protéines totales du lait. Cette valeur peut varier quelque peu selon la femelle laitière, la saison, la nourriture de la femelle et autres paramètres bien connus de l'homme du métier. Ainsi, il n'est pas possible d'introduire dans le fromage final plus de 20 % en poids environ de protéines de lactosérum et, ainsi qu'il a été

du caillé en acide lactique donne un fromage doté du pH minimum répondant aux exigences particulières du marché, usuellement comprise entre 4,9 et 5,5.

Les procédés classiques de fabrication de fromages naturels et élaborés ne font essentiellement usage que de caséine. La plupart des protéines du lactosérum ne sont incorporées au fromage qu'à raison de quelques unités pour cent, les autres demeurant dissoutes dans le lactosérum et étant évacuées en tant que sous-produit du procédé. Or, les protéines du lactosérum représentent environ 14 à 24 % en poids de l'ensemble des protéines du lait entier ou écrémé et leur valeur alimentaire est au moins comparable à celle de la caséine. En conséquence, la perte des protéines du lactosérum subie suivant les procédés de fabrication de fromage traditionnelle limite les rendements possibles de ces procédés. L'utilisation même partielle des protéines du lactosérum dans la fabrication de fromages naturels et élaborés est d'un grand intérêt sur le plan industriel.

On a donc déjà tenté dans le passé de concevoir un procédé qui permettrait de tirer pleinement parti des protéines du lactosérum en fromagerie.

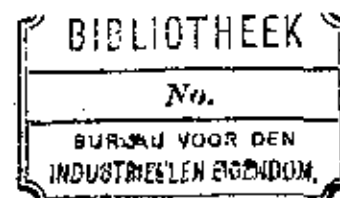
Une solution possible consiste à récupérer ces protéines à partir du lactosérum, par séchage, condensation, ultrafiltration ou osmose inverse du lactosérum. On recombine ensuite au fromage les protéines de lactosérum récupérées. De tels procédés sont décrits par exemple par F.V. Kosikowski, Cheese and Fermented Foods, Edwards Brothers, Inc., Ann Arbor, Michigan, 2e éd. 1977, pp. 451-458.

Cette solution soulève une difficulté du fait que les constituants du lactosérum récupérés sont dépourvus des caractéristiques physiques et chimiques requises pour la fabrication du fromage naturel.

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PATENT SPECIFICATION



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Complete Accepted: July 6, 1923.

PROVISIONAL SPECIFICATION.

Process for the Recovery of Proteins and Milk-Sugar (Lactose) from Whey.

I, DAVID THOMSON, O.B.E., M.B., Ch.B., D.Ph., a British subject, of 81, Harley Street, London, W., do hereby declare the nature of this invention to be as follows:—

My invention consists in an improved process for recovering protein substances and lactose, or milk-sugar, from whey.

In carrying out the process according to this invention I first determine the acidity of the whey. The first step is to reduce this acidity to a reaction of $P_{H}4.7$ in terms of hydrogen ion concentration or, in other terms, to the point at which it gives a sky blue colour with brom-phenol blue or a dirty yellowish colour with brom-cresol purple. At this stage any casein which may be present is precipitated. The whey as it leaves the cheese making process is usually too acid and an addition of $NaOH$ or Na_2CO_3 is necessary to bring it to this point which is the optimum point for precipitation of casein. Such casein as is precipitated must be removed, preferably by centrifuging before proceeding further. After the removal of the casein the second stage of the process may be carried out.

Alkali is added until a reaction of $P_{H}10.5$ is reached or, in other terms, to the point where phenolphthalein begins, in solution, to turn red. At this point a precipitate consisting of calcium phosphate together with a certain amount of lac-albumen is thrown down. Hydrochloric acid is now added until the precipitate re-dissolves, and until the reaction of $P_{H}4.7$ is again reached, and the liquid is heated to 60° Centigrade when a large precipitate of lac-albumen will be thrown down. This should be centrifuged off and then liquid alkali is again added until the reaction is once more $P_{H}10.5$ when the phosphate precipitate together with a certain amount of lac-albumen is again thrown down and may be removed by centrifuging.

The third stage of the process consists in recovering from the clear whey, which has been now thoroughly freed from phos-

phate, the milk-sugar which it still contains. It is evaporated down to a syrupy consistency and if any trace of flocculent precipitate is present in the syrup this should be centrifuged out while the liquid is still hot. The clear syrup is now passed into shallow pans and allowed to cool when it will be found that the sugar will crystallise out gradually.

The fourth stage consists in the evaporation to dryness of the brown liquor left after the crystallisation of the milk-sugar, and the residue is a brownish salty material resembling salt meat extract and contains a considerable amount of protease or albumose (water soluble protein) with stimulating extractives of an amino-acid nature.

An alternative form of process consists in the following steps. Firstly the whey is brought to a reaction of $P_{H}4.7$ as before and any casein thrown down is removed by centrifuging. In the second stage alkali is added to the clear whey until the reaction is $P_{H}10.5$ and the precipitate of phosphate and albumen which is thrown down is centrifuged off.

In the third stage the clear whey is now acidified by hydrochloric acid until the reaction of $P_{H}4.7$ is again reached when a precipitate of lac-albumen is thrown out and may be removed and the precipitation is materially assisted by heating the solution to a temperature of 60° C. and the precipitate will be found to be insoluble in water. If, however, soluble lac-albumen is required the precipitate should be rendered very faintly alkaline before drying. By this means a faintly alkaline lac-albumen powder is obtained and is soluble in water.

Dated the 5th day of April, 1922.

KINGS PATENT AGENCY LIMITED,

By BENJ. T. KING,

Director,

Registered Patent Agent,
146a, Queen Victoria Street, London,
E.C.

Agents for Applicant.

COMPLETE SPECIFICATION.

Process for the Recovery of Proteins and Milk-Sugar (Lactose) from Whey.

I, DAVID THOMSON, O.B.E., M.B., Ch.B., D.Ph., a British subject, of 81, Harley Street, London, W. 1, do hereby declare the nature of this invention and in what manner the same is to be performed, to be particularly described and ascertained in and by the following statement:—

My invention consists in an improved process for recovering protein substances and lactose or milk sugar from whey.

In carrying out my invention I take advantage of the fact that the various protein substances in whey can be classed into groups each of which has a particular optimum point of acid or alkaline reaction at which it is most thoroughly precipitated from solution. This point may be found for any particular group and the reaction of the solution containing the several groups may be so altered and adjusted that the groups are precipitated one by one with great efficiency.

The whey obtained from cheese making has usually a certain quantity of casein still remaining in solution owing to the acidity being higher than the optimum point for its precipitation. The first stage therefore is to reduce the acidity to $P_{H}4.7$ (in terms of hydrogen ion concentration) by the gradual addition of solution of $NaOH$ or Na_2CO_3 or lime. The casein settles out and may if required be removed by means of a centrifuge.

1. The casein-free whey is next heated to $60^{\circ}C$. and more alkali is added until the reaction is $P_{H}9$ at which point a precipitate of phosphates and albumen is thrown down and preferably removed with a centrifuge. It may be dried.

2. The clear whey is again heated to $60^{\circ}C$. and hydrochloric acid is added until the reaction stands at between $P_{H}4.7$ and $P_{H}5$ when a further heavy precipitate of lac albumen but free from phosphate settles out, and is removed with a centrifuge and dried. It may with advantage be rendered slightly alkaline before drying. If desired the process numbered (2) above may be carried out before the process numbered (1).

3. The whey should now be clear like water but it still contains lactose and further protein substances and salt. It is now subjected to a heating and evaporating process preferably of the type in which revolving drums dip into

the liquid which lies in a trough, the trough being provided with funnel shaped depressions into which precipitate tends to collect. As the liquid evaporates the salt and acid contents become more concentrated and a further protein precipitate settles out which may be collected and dried. If the process numbered (2) has preceded instead of followed the process (1) the liquid should be rendered slightly acid—say to $P_{H}4.7-5$ before evaporation under process 3. The evaporation is not allowed to proceed further than to reduce the liquid to a thin syrupy consistency by which time the protein precipitate will all have been thrown down and it is then transferred to evaporating pans and allowed to cool when the milk sugar will gradually crystallize out.

The brown liquor left after crystallization of the milk sugar may be evaporated when a brownish salty material resembling salt meat extract results, containing a considerable amount of water soluble protein and salt with stimulating extractives of an amino-acid nature.

I am aware of the Specification of my own prior Letters Patent No. 173,891 and I do not desire to claim anything claimed therein.

For a clear understanding of the foregoing it is pointed out that the correct hydrogen ion concentration is estimated by electrometric means or by means of appropriate indicators—see the text-book "The Determination of Hydrogen-Ions" by W. M. Clark, 1920 (Williams & Williams Company, Baltimore).

Having now particularly described and ascertained the nature of my said invention and in what manner the same is to be performed, I declare that what I claim is:—

1. A process for recovering protein substances from whey in which the whey after extraction of casein is rendered alkaline to at or about $P_{H}9$ and after removal of the precipitate is made acid to at or about $P_{H}4.7$ to 5 to remove a further precipitate or in which these stages take place in the reverse order.

2. A process for recovering protein substances from whey in which the whey after extraction of casein is rendered alkaline to at or about $P_{H}9$ and after removal of the precipitate is made acid to at or about $P_{H}4.7$ to 5 to remove a

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Composition For An Infant Formula Having a Low Threonine Content

This invention relates to a composition for an infant formula having a low threonine content; a method of producing the composition; use of the composition in the manufacture of a medicament or nutritional product for addressing the nutritional needs and providing healthy growth of an infant; and a method of addressing the nutritional needs and providing healthy growth of an infant which comprises administering an effective amount of the composition.

Within the context of this application the word "comprises" is taken to mean "includes, among other things" and it is not intended to mean "consists of only".

Mother's milk is recommended for all infants. However, in some cases mother's milk is not available and infant formulae must be used. Normal, full-term infants are usually fed cow's-milk-based formulas. These formulas contain a mixture of casein and whey as protein sources and they provide nutrition for infants, however they do not provide a protein concentration and an amino acid profile equivalent to that of mother's milk. In addition these standard formulae are not suitable for pre-term infants and those having adverse reactions to protein in cow's milk formula or to lactose.

An alternatives to cow's milk formula is soy formula; particularly for infants who are lactose intolerant. However, soy is not as good a protein source as cow's milk. Also, infants do not absorb some minerals, such as calcium, as efficiently from soy formulae.

A further alternative formula is based on hydrolysed protein. These formulas are hypoallergenic and have a decreased likelihood of an allergic reaction.

Ideally, to be as close as possible to human milk, the protein in infant formulae may be derived from both whey and casein in an appropriate ratio. However, a problem with conventional formulae having these proteins is that they have a high protein concentration to ensure that the infant gets the necessary amount of all essential amino acids. The protein concentration is higher than the concentration normally found in human milk and it may not be beneficial for an

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(54) Title: COMPOSITION FOR AN INFANT FORMULA HAVING A LOW THREONINE CONTENT

(57) Abstract: A composition for an infant formula which comprises a low threonine content; a method of producing the composition; use of the composition in the manufacture of a medicament or nutritional product for addressing the nutritional needs and providing healthy growth of an infant; and a method of addressing the nutritional needs and providing healthy growth of an infant which comprises administering an effective amount of the composition. A preferred embodiment of the composition comprises all of: i) acid whey protein or sweet whey protein from which casein-glyco-macropeptide has been removed; and ii) free arginine, and iii) free lysine; and iv) free tyrosine or free tryptophan or tryptophan-rich milk protein or a mixture thereof.

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	intake	Ur. Excr.	Fec. Excr.	Retent.
Formula having 1.83g protein /100kcal	349±83	194±21	37±15	117±62
Formula having 2.24 g protein /100kcal	284±54	136±25	31±10	117±63

The data show that adjustment of urinary nitrogen excretion enabled infants to maintain nitrogen retention at identical levels in spite of a substantial difference in intake. Absorption and retention of minerals and fat were similar with both formulae. It was concluded that a modified whey formula with protein-energy ratio 1.83g/100kcal leads to adequate nitrogen and mineral retention in normal infants. Lower urinary nitrogen excretion indicates reduced metabolic load.

Example 5

Commercially available infant formulae contain more protein (>2g/100kcal) than human milk; it is well established that plasma amino acids (AA) of formulae-fed infants deviate from breastfed infants. It has now been found that infants fed two formulae varying in amount and composition of protein (modified whey; 1.83g protein /100kcal; F-1.8 & F-1.8LCP) have AA closer to breast fed infants than infants a whey enriched formula (2.24g protein/100kcal; F-2.2). The 3 formulae were exclusively fed between 6 and 122 days of age. Blood was collected at 30, 61 and 122 days of age. Formula intake and the intervals between last feeding and blood sampling were recorded. AA (ion exchange; tryptophan: HPLC) were measured in plasma of breastfed infants (n=19) and infants fed formula F-1.8 (n=23), F-1.8LCP (n=20), F-2.2 (n=13). Statistical analysis was carried out by Kruskal-Wallis and Mann-Whitney tests. Levels of threonine, the branched chain AA, phenylalanine and lysine in the group fed F-2.2 were significantly higher than in the breastfed group. In the groups fed F-1.8 and F-1.8LCP threonine was close to the breastfed group and the branched-chain AA were not different from the breastfed group. Glycine concentrations in the groups F-1.8 and F-1.8LCP were higher than in the breastfed group. Since the time intervals between feeding and blood sampling did not differ among the groups, the dependence of citruline on protein load with formula (F-2.2, F-1.8, F-1.8LCP)

Protein	1.9 g
Hydrolysed whey	1.86 g
Free amino acids	0.04 g
Lipids	5.1 g
Palm olein	
Coconut oil	
Sunflower oil	
Canola oil	
Egg phospholipids	
Carbohydrates	11.6 g
Lactose	11.6 g
Vitamins and minerals	To meet regulations

The infant formula is suitable for full term, hypoallergenic infants and has a balanced amino acid profile.

Example 4

To compensate for the lesser quality of bovine milk proteins, infant formulae contain more protein than human milk. By improving the quality of the protein it is possible to use less protein. It has now been found that a formula containing modified sweet whey (having caseino-glyco-macropetide removed) with about 1.83g protein /100kcal results in similar nitrogen retention as a conventional whey-enriched formula with 2.24g protein /100kcal. This has been tested by performing metabolic balance studies with 8 normal infants (2 girls, 6 boys, aged between 39 and 139 days) in a balanced cross-over design. A metabolic balance study (72 hours) was performed with each formula after a washout period of 11 days. The formula having 1.83g protein /100kcal contained modified sweet whey and casein and casein in a ratio of 70:30. The formula having 2.24 g protein /100kcal contained demineralised whey and casein in a ratio of 60:40. In other respects the compositions were similar to commercially available infant formulae.

Results

	Nitrogen (mg/kg/d)
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120

11/9

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was found to be significant. The higher plasma urea values in the group F-2.2 are therefore due to increased synthesis and not decreased urinary urea excretion. It can be concluded that feeding modified whey formula with 1.8g protein/100kcal results in plasma amino acids at 30, 61 and 122 days of age which are close to breastfed infants.

It should be understood that various changes and modifications to the presently preferred embodiments described herein will be apparent to those skilled in the art. Such changes and modifications can be made without departing from the spirit and scope of the present invention and without diminishing its attendant advantages. It is therefore intended that such changes and modifications be covered by the appended claims.

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BIOLOGICALLY ACTIVE WHEY PROTEIN CONCENTRATE

RELATED APPLICATIONS

This application is a continuation-in-part of U.S. application Ser. No. 289,971 filed Dec. 23, 1988, now abandoned, and a continuation of application U.S. application Ser. No. 188,271, filed Apr. 28, 1988, now abandoned.

BACKGROUND OF THE INVENTION

Throughout this application, various publications are referred to by Arabic numerals within parentheses. Full citations for these references may be found at the end of the specification, immediately preceding the claims. The disclosures of these publications are hereby incorporated by reference in order to more fully describe the state of the art at the time of the invention described and claimed herein.

The present invention is based on the surprising discovery that undenatured whey protein concentrate has an enhanced immunological effect. More specifically, the invention relates to the effect of the oral administration of whey protein concentrate in undenatured conformation on the immune response to sheep red blood cells, host resistance to pneumococcal infections, development of chemically induced colon carcinoma and tissue glutathione.

The present invention shows the correlation between the undenatured conformation of whey protein concentrate (w.p.c.) and host immunoenhancement whereby chemical indices of denaturation are given and the demonstration that the same crucial role of molecular conformation (undenatured state) applies to glutathione GSH promotion, which is the other major biological activity of w.p.c. Equally important is the demonstration that another protein source such as egg white, with the same high cysteine content as w.p.c. does not enhance GSH synthesis, further demonstrating the specificity of w.p.c. with respect to the described biological activity.

Whey and whey protein have been utilized from time immemorial for nutritional purposes. In addition, whey was recommended in folk and ancient medicine for the treatment of various diseases (1,2) and, in one instance, lifetime feeding of humans with a whey protein diet has been shown to promote longevity with no explanation given (3,4).

Dairy products are widely used as a good source of nutrition. In addition, claims have been made to the effect that fermented whole milk (yogurt) is beneficial to the management of some types of intestinal infections. Certain dietary regimes based on ill defined natural or cultured dairy products are said to be associated with long life expectancy in some regions of the U.S.S.R., for example, Georgia.

Since time immemorial, serum lactis, which is latin for milk serum or whey, has been administered to the sick for the treatment of numerous ailments. In 1603, Baricelli reported on the therapeutic use of cow or goat milk serum sometimes mixed with honey or herbs. The spectrum of illnesses treated with whey include jaundice, infected lesions of skin, those of the genito-urinary tract with purulent secretions, gonorrhea, epilepsy, quatern fever and other febrile states of different origins. Indeed, the common denominator of most of these illnesses appears to be a septic condition. Although

physicians of both ancient times and of the middle ages agreed that whey treatment should be carried out over a period of several days, a difference of opinion appears to exist concerning the daily amount prescribed. Thus, Galen, Hippocrates and Dioscorides insisted on a minimum daily amount of two 12 ounce latin libras, and up to five libras a day according to gastric tolerance. This would represent between one to two liters of whey a day. Baricelli on the other hand, reflecting the trend of his time, limited the amount prescribed to one libra a day, given in fractionated doses on an empty stomach.

Since then, numerous articles published in Europe through the 17th, 18th and 19th centuries have advocated the therapeutic use of whey. In an Italian textbook published in the middle of the 19th century (5), at the dawn of scientific medicine, an interesting distinction is made between whole milk and milk serum. Milk is recommended firstly as a nutrient especially in patients with strivers of the gastro intestinal tract. In this respect the author emphasizes that the benefits of the then popular "milk therapy" of cachexia and tuberculosis are due only to the nutritional property of milk. Secondly, the milk was prescribed in the treatment of poisoning because milk components would presumably neutralize ingested toxic material. Thirdly, milk therapy was suggested for the alleged capacity of this fluid to coat and soothe ulcers of the gastrointestinal tract. Milk serum, on the other hand, was advocated in the treatment of pneumonia, acute inflammatory diseases of the testicles and urogenital tract, in spite of its recognized lower nutritional quality. Finally, the author emphasized the ineffectiveness of whey in the treatment of disorders of the nervous system.

The prime difference between whey (serum lactis) and whole milk is the near absence in the former of the casein, the casein-bound calcium and phosphate, most of the fat and the fat soluble vitamins. The actual concentration in whey of "whey proteins" is usually similar to that in milk. Hence quantitative differences between whey and milk could not be construed to represent a key factor in the alleged therapeutic effect of whey treatment because, if any, they imply the lack, in whey, of some important nutrients. Some previously collected data (5-10) of the present inventors provide a scientific background to the presumed benefit of intensive treatment with "serum lactis". The importance of the characteristic amino acid and peptide profile of whey protein concentrate in the immune enhancing effect of the whey protein concentrate (WPC) has been shown. The caseins represent 80% of the total protein content of cows milk while WPC is only 20%. Hence, it is conceivable that it is the separation of WPC from the casein in whey which represents the crucial qualitative change, since this would render the amino acid profile and associated small peptides patterns of whey proteins unaltered by that of the casein, once the digestive process has released free amino acids from all ingested proteins.

The search for the possible mechanism of immunoenhancement by whey protein feeding has revealed to us the provocative possibility that whey protein concentrate may contribute to a broader biological effect of a protective nature involving susceptibility to cancer and general detoxification of environmental agents. All these conditions appear to be somehow related to changes in glutathione which is a ubiquitous element

United States Patent (19)

Bonnous et al.

[11] Patent Number: 5,290,571

[45] Date of Patent: * Mar. 1, 1994

BIOLOGICALLY ACTIVE WHEY PROTEIN CONCENTRATE

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[73] Assignee: Immunotec Research Corporation, Ltd., Quebec, Canada

[*] Notice: The portion of the term of this patent subsequent to Jul. 27, 2010 has been disclaimed.

[21] Appl. No.: 417,246

[22] Filed: Oct. 4, 1989

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 289,971, Dec. 22, 1988, abandoned, and a continuation of Ser. No. 188,271, Apr. 28, 1988, abandoned.

[51] Int. Cl. 6: A61K 35/20

[52] U.S. Cl.: 424/335; 514/2; 514/21; 514/251; 514/276; 514/285; 530/365; 530/833; 426/72

[56] Field of Search: 514/2, 21, 251, 276, 514/285; 530/365, 833; 424/533; 426/72

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Attorney, Agent, or Firm—John P. White

ABSTRACT

The present invention is concerned with a whey protein composition comprising a suitable concentration of whey protein concentrate wherein the whey protein concentrate contains proteins which are present in an essentially undenatured state and wherein the biological activity of the whey protein concentrate is dependent on the overall amino acid and small peptides pattern resulting from the contribution of all its protein components and a method of producing said whey protein composition. The invention also relates to several applications of said composition.

(2) Claims, 9 Drawing Sheets



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(31) Priority Application Number: PE 6782 288,885		(72) Inventors: JAMESON, Graeme, W.; 65 Main Street, Kew, Vic. 3101 (AU); SUTHERLAND, Brian, J.; 40 Wardale Road, Springvale South, Vic. 3172 (AU).
(32) Priority Date: 5 December 1980 (05.12.80) 31 July 1981 (31.07.81)		(74) Agents: SZCZEPANSKI, S., Z. et al.; Hume, Clement, Brinks, Wilham & Olds, Limited, Suite 4100, One IBM Plaza, Chicago, IL 60611 (US).
(33) Priority Countries: AU US		(81) Designated States: AT (European patent), BR, CH (Euro- pean patent), DE (European patent), DK, FL, FR (Euro- pean patent), GB (European patent), JP, NL (Euro- pean patent), NO, SE (European patent), SU.
(71) Applicants: SCHREIBER FOODS, INC. (US/US); 425 Pine Street, Green Bay, WI 54305 (US); COMMON- WEALTH SCIENTIFIC AND INDUSTRIAL RE- SEARCH ORGANIZATION (AU/AU); Limestone Avenue, Campbell, A.C.T. (AU); AUSTRALIAN DAIRY CORPORATION (AU/AU); St Kilda Road, Melbourne, Vic. (AU).		Published With international search report.

PROCESS AND APPARATUS FOR MAKING CHEESE OR
CHEESE BASE AND A NOVEL INTERMEDIATE
PRODUCT OF SAID PROCESS

FIELD OF THE INVENTION

This invention relates to processes for making food products by selective concentration of milk, food products obtained by such processes, and foods made from such food products.

BACKGROUND OF THE INVENTIONA. Definitions of Terms

"Milk" means the lacteal secretion obtained by the milking of one or more females of a mammalian species, such as cow, sheep, goat, water buffalo, or camel. Broadly speaking, such milk is comprised of casein (a phospho-protein) and soluble proteins, lactose, minerals, butterfat (milkfat), and water. The amount of these constituents in the milk may be adjusted by the addition of, or the removal of all or a portion of, any of these constituents. The term "milk" includes lacteal secretion whose content has been adjusted.

Milk obtained by milking one or more cows is referred to as "cows milk". Cows milk whose composition has not been adjusted is referred to herein as "whole milk". It is comprised of casein, whey proteins, lactose, minerals, butterfat (milkfat), and water.

The composition of "cows milk" can be adjusted by the removal of a portion of or all of any of the

(54) Title: PROCESS AND APPARATUS FOR MAKING CHEESE OR CHEESE BASE AND A NOVEL INTERMEDIATE PRODUCT OF SAID PROCESS

(57) Abstract

A process for an efficient production of cheese or cheese base containing substantially all the casein and whey proteins which were originally present in the milk comprising four phases: (1) selective concentration of milk to form a concentrate; (2) increasing the ionic strength of the concentrate so as to maintain it in the liquid phase during fermenting; (3) fermenting the concentrate; and (4) removing water from the fermented concentrate to produce cheese or cheese base containing substantially all the casein and whey proteins originally present in the milk. The concentrates and fermented concentrates are unique intermediate products in that they do not coagulate during processing even at low pH's. The process permits an efficient evaporation of water from the fermented concentrate that is maintained in the liquid state. The process also avoids the possibility of losing whey proteins by totally eliminating syneresis.

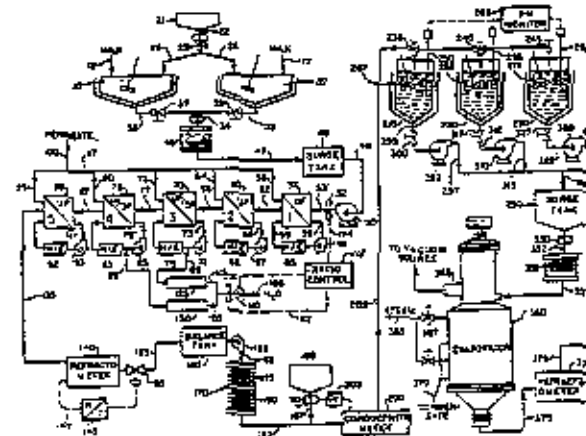
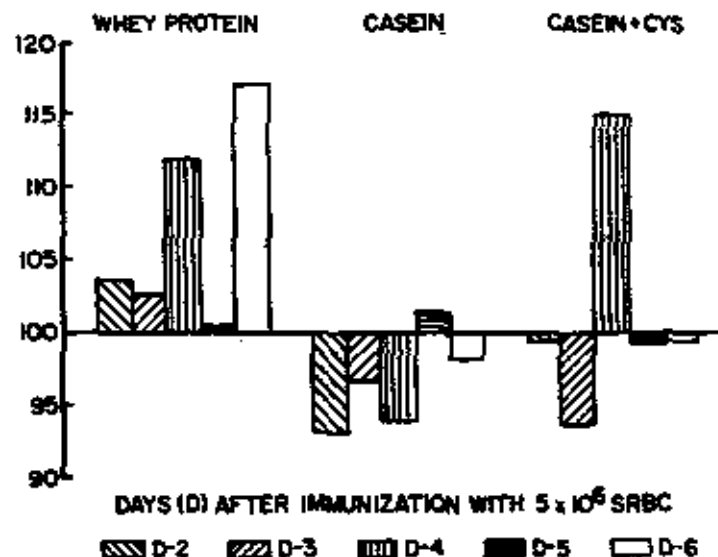


Figure 4



United States Patent [19]
Gold et al.

[11] Patent Number: 5,230,902
[45] Date of Patent: Jul. 27, 1993

[54] UNDENATURED WHEY PROTEIN CONCENTRATE TO IMPROVE ACTIVE SYSTEMIC HUMORAL IMMUNE RESPONSE

[75] Inventor: Phil Gold, Westmont; Gaston Bousquet, Montreal; Patricia A. L. Kongsara, St. Lambert, all of Canada

[73] Assignor: Immunotec Research Corporation, Montreal, Canada

[21] Appl. No.: 563,794

[22] Filed: Aug. 3, 1990

Related U.S. Application Data

[63] Continuation of Ser. No. 289,971, Dec. 23, 1988, abandoned, which is a continuation-in-part of Ser. No. 185,271, Apr. 27, 1988, abandoned.

[51] Int. Cl.⁵ A61K 35/28
[52] U.S. Cl. 424/335; 514/2; 530/365; 530/833
[58] Field of Search 514/2, 21, 251, 276; 514/885; 530/365, 833; 424/335; 426/72

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Primary Examiner—Douglas W. Robinson
Assistant Examiner—John C. Witz
Attorney Agent or Firm—John P. White, Craig J. Arnold

ABSTRACT

This invention provides a method of improving the humoral immune response or increasing the concentration levels of glucanase in mammals, which comprises administering orally to a mammal a therapeutically or a prophylactically effective amount of undenatured whey protein concentrate which has a biological activity based on the overall amino acid and associated small peptides/proteins resulting from the contribution of all its protein components. A method for improving the humoral immune response in mammals also is disclosed which comprises administering orally to a mammal the combination of a vitamin supplement containing vitamin B₁₂ in an amount in excess of minimum daily requirements and an effective amount of undenatured whey protein concentrate. This invention further provides a dietary supplement for a mammal which comprises an effective amount of vitamin B₁₂ and B₆ and a therapeutically or prophylactically effective amount of whey protein supplement.

16 Claims, 5 Drawing Sheets

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D 10

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UNDENATURIZED WHEY PROTEIN CONCENTRATE TO IMPROVE ACTIVE SYSTEMIC HUMORAL IMMUNE RESPONSE

RELATED APPLICATION

This application is a continuation of U.S. application Ser. No. 289,971, filed Dec. 23, 1988, now abandoned, which is a continuation in part of U.S. application Ser. No. 188,271 filed Apr. 27, 1988, now abandoned.

1. AREA OF INVESTIGATION

Effect of dietary whey protein on the immune response to sheep red blood cells, host resistance to bacterial infections, development of tumors, and the process of aging.

Whey and whey protein have been utilized from time immemorial for nutritional purposes. In addition, whey was recommended in folk and ancient medicine for the treatment of various diseases and, in one instance, for the feeding of infants with a whey protein diet. It has been shown to promote longevity with no expensiveness given. We have shown, in controlled experiments, for the first time, that whey protein feeding specifically enhances mice immune response to sheep red blood cells (SRBC) resistance to pneumococcal infections, inhibits the development of colon cancer and delays the process of aging independently of its nutritional quality. The search for the possible mechanism of immunoprotection by whey protein feeding has revealed to us the provocative possibility that whey protein may contribute to a broader biological effect of a protective nature involving susceptibility to cancer, diabetes of aging and general detoxification of environmental agents. All these conditions appear to be somehow related to changes in glutathione which is a ubiquitous element exerting a protective effect against superoxide radicals and other toxic agents. Our studies have shown that the observed enhancement of the immune response is associated with greater production of splenic glutathione in immunized mice fed whey protein in comparison to mice fed a control or cysteine enriched control diet. The efficiency of dietary cysteine in inducing immunoprotective glutathione levels is greater when it is delivered in the whey protein than as free cysteine. Glutathione was found at higher levels in the heart and liver of whey protein fed mice in comparison to mice fed the corresponding control diet or Purina Mouse Chow. In old mice dietary whey protein was found to delay the onset of the diabetes of aging.

2. DEFINITIONS

- (a) **Whey Protein:** Whey proteins are the group of milk proteins that remain soluble in "milk serum" or whey after precipitation of casein at pH 4.6 and 20° C. The major whey proteins in cow's milk are beta-lactoglobulin (BLG), alpha-lactalbumin (AL), immunoglobulin and serum albumin (SA) in order of decreasing amount (7).
- (b) **C-casein:**
- (c) **SRBC-Sheep red blood cells**
- (d) **FFC-Fluorescent cells (epidermal):** immunization of FFC in spleen is used to assess the humoral immune response to SRBC antigen.
- (e) **GSH (Glutathione (gamma-glutamyl-cysteinyl-glycine))**

- (f) Unless otherwise specified, the defined formula diets tested varied only in the type of protein.
- (g) Whey of bovine milk contains approximately 6 g per liter protein, most of the lactose, mineral and water soluble vitamins.

A variable source of whey protein concentrate is the material known by the trade name PROMOD, which is a protein supplement provided in powder form by Ross Laboratories, a Division of Abbott Laboratories U.S.A. This is a concentrated source of high quality protein which is useful for providing extra protein to persons having increased protein needs, or those who are unable to meet their protein needs with their normal diet. It contains whey protein concentrate and soy lecithin. It has the following nutrients:

NUTRIENTS	Per 5 g Protein (see above)
Protein	10 g
Fe	Does not exceed 0.40 g
Calcium	Does not exceed 0.87 g
Water	Does not exceed 0.40 g
Calcium	Does not exceed 21 mg (0.15 mEq)
Sodium	Does not exceed 11 mg (0.17 mEq)
Phosphorus	Does not exceed 40 mg (1.0 mEq)
Phosphorus	Does not exceed 12 mg
Chlorine	Does not exceed 75

It has the following typical amino acid composition per 100 g protein: 100 g PROMOD protein yields up to approximately 105 g of antibodies.

TYPICAL AMINO ACID COMPOSITION	Per 100 g Protein (see above)
Amino Acids	
Alanine	19 g
Aspartic Acid	15 g
Glutamic Acid	15 g
Proline	15 g
Threonine	15 g
Tyrosine	15 g
Valine	15 g
Non-Essential Amino Acids	
Alanine	19 g
Aspartic Acid	15 g
Glutamic Acid	15 g
Proline	15 g
Threonine	15 g
Tyrosine	15 g
Valine	15 g

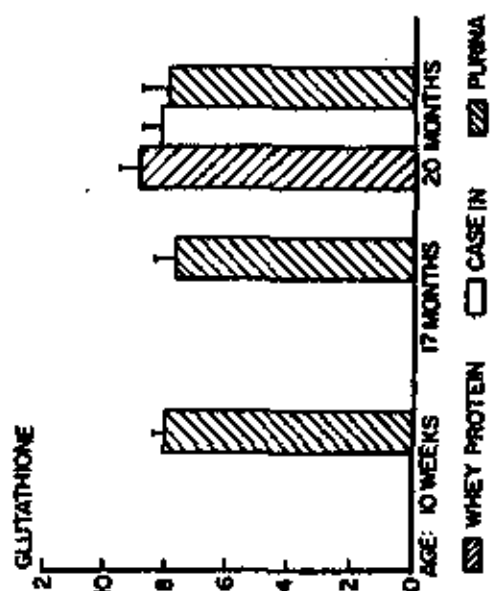
Diets

The composition of mouse vitamins in the defined formula diet used is (most of) our experiments is given in Table 1 (Diet 1). Diet 1 is prepared in the following way: 20 g of selected pure protein, 30 g of product 80556 protein free diet powder (Grand-Volant Co. Inc., U.S.A.), 18 g cornstarch, 2 g wheat bran, 0.15 g Nutritional vitamins freshly (Grand-Volant, Ontario, Canada), 2.65 g KCl, 0.85 g NaCl. Unless otherwise specified, the only variable in the various purified diets was the type of protein.

3. PREVIOUS WORK

Dairy products are widely used as a good source of nutrition. In addition, changes have been made to the effect that fermented whey (yogurt) is beneficial in the management of some types of intestinal infections.

Figure 5



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Certain dietary regimes based on ill defined cultured dairy products are said to be associated with long life expectancy in some regions of the USSR (Georgia etc).

Since lacto-macrosomia, serum lactin, lactin for milk serum or whey, has been administered to the sick for the treatment of numerous ailments. In 1603 Barthelemy reported on the therapeutic use of cow or goat milk serum, especially mixed with honey or beer. The treatment of illmen treated with whey included, jaundice, infected lesions of the skin, those of the genito-urinary tract with persistent scrofulous, gonorrhea, erysipelas, quartan fever and other febrile states of different origin. Indeed, the common decomposition of most of these physicians of both Ancient Times and of the Middle Ages agreed that whey treatment should be carried out over a period of several days, a difference of opinion appeared to exist concerning the daily amount prescribed. Thus, Galen, Hippocrates and Dioscoride insisted on a minimum daily amount of two 12 oz tins filled and up to five liters a day according to gastric tolerance. This would represent between 1 to 2 liters of whey a day. Barthelemy, on the other hand, reflected the trend of his times, limited the amount prescribed to one liter a day, given in fractionated doses in 40 empty stomachs.

In the following year, Comenius wrote about the virtues of whey in the treatment of several unrelated syndromes including bronchopneumonia and diabetes with high fever. Unfortunately, in his long dissertation, the author fails to clearly discriminate between milk and milk serum treatment.

Since then, numerous articles published in Europe throughout the 17th, 18th and 19th centuries have advocated the therapeutic use of whey. In an Italian letter, book published in the middle of the 18th century, at the dawn of scientific medicine, an interesting discussion is made between whole milk and milk serum. Milk is recommended firstly as a nutrient especially in patients with fractures of the gastrointestinal tract. In this respect the author emphasizes that the benefits of the then popular "milk therapy" of catarrhs and tuberculous are due only to the nutritional property of milk. Secondly, milk was prescribed in the treatment of poisoning because milk components would presumably neutralize ingested toxic material. Thirdly, milk therapy was suggested for the alleged capacity of this fluid to coat and wash down the gastrointestinal tract.

Milk serum, on the other hand, was advocated in treatment of psoriasis, acute inflammation diseases of the sinuses and uterine tract, in spite of its recognized lower nutritional quality. Finally the author emphasized the effectiveness of whey in the treatment of disorders of the nervous system.

The prime difference between whey, (serum lactis) and whole milk is the near absence in the former of the enzymes, the calcium-bound alkaline and phosphate, most of the fat and fat soluble vitamins. The actual concentration in whey of "whey proteins" is only about 5% higher than that in milk. Hence quantitative differences between whey and milk could not be considered to represent a key factor in the alleged therapeutic effect of whey treatment because, if any, they imply the lack, in whey, of some important nutrients. Our data (7,14) may provide a scientific background to the presumed benefit of extensive treatment with "serum lactis".

We have shown the importance of the characteristic amino acid profile of whey protein concentrate in the

immune enhancing effect of WPC. The causes represent 10% of the total protein content of cow's milk while WPC is only 20%. Hence, it is conceivable that it is the separation of WPC from the whey in which represents the crucial qualitative change, since this will render the amino acid profile of whey protein unaltered by that of the whey, once the digestive process has released free amino acids from all ingested proteins.

Although no clinical trials have been reported, some interesting information can be gathered from data of human subjects.

Whey Protein in Nutritional Nutrition

Infant feeding studies indicate that whey protein formulas are metabolically superior to casein predominant formulas (8, 9) in protein babies.

Longevity

Studies performed at the Eschery Cancer Center in Nebraska (10, 11) showed that survival (percentage in spontaneous diseases) of female and male hamsters, weaned from a 20 week period of feeding from a mixture of whey and casein was best with 20 g/100 g (from 100 g/100 g methionine and cysteine supplemented casein diet). Body weight gains were similar in both groups. In lifetime feeding studies, the mean and maximal longevity of female and male hamsters fed 10, 20 and 40 g WPC/100 g diet was increased in comparison with those fed commercial laboratory feed (estimated 24% protein from various sources). Survival was best with the 20% WPC diet; in males, longevity increased by 50%. No significant relationship was noted between food intake, maximal weight and longevity.

4. OUR STUDIES

Our interest in the effect of amino acid intake upon the immune system was prompted by an observation made several years ago (1). We fed three defined formula diets containing a free amino acid mixture and a mixture duplicating casein. Another group of mice was fed a similar diet but with moderate restriction of phenylalanine and tyrosine compensating by a corresponding increase in the non-essential amino acid mixture. The second group of mice gained weight at the same rate as the mice fed the casein equivalent mixture of Purina mouse chow. However, when challenged with sheep red blood cells, these mice produced more antibodies and plaque forming cells against sheep red blood cells than Purina or casein equivalent-fed mice.

A new concept thus emerged, namely, that changes in the amino acid profile of the diet can influence the immune response independently of any systemic effect on the nutritional status of the host. But, more importantly, changes in the amino acid profile, i.e. protein type, could conceivably enhance the humoral immune response beyond that which had traditionally been considered to represent a "nutrient" response.

We subsequently assessed the effect on the immune response of different types of proteins in nutritionally adequate diets. Mice fed formula diets containing 20% or 24% lactalbumin (WPC) were found to produce more plaque forming cells to sheep red blood cells than mice fed Purina mouse chow containing about 22% protein from various sources and of similar nutritional efficiency. The immune enhancing effect of lactalbumin was maximal at 30% concentration (21). A 20 g per