

**Pedro Castillo Pineda & Asociados**

ABOGADOS

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

DIVISIÓN DE NUEVAS CREACIONES

E. S. D.

Ref: EXPEDIENTE N° 04-01768b

Solicitud de patente a nombre de KRAFT FOODS

HOLDINGS, INC

Con respecto al Oficio 07929, notificado en este asunto y contentivo del concepto técnico N° 0877, me permito presentar los siguientes documentos:

1- Copias del examen de patentabilidad elaborado en relación con la patente correspondiente EP 1 452 097 B1, recién otorgada.

2- Copia de la referencia exigida por el Examinador:

JP 07-277991 A (SNOW BRAND MILK PROD, CO., LTD), Octubre 24,1995. Se acompaña igualmente la traducción al inglés de dicho documento.

3- Copia de la notificación de la Oficina Europea de patente sobre la intención en base a la solicitud allí relacionada y para las Reivindicaciones 1-6 presentadas el 9 de febrero de 2007.

4- Copia de la patente Europea EP 1 452 097 B1, de fecha Octubre 17,2007, mencionada en el punto anterior y donde se Reivindicó prioridad del mismo documento citado para Colombia.

En cuanto al Oficio 07925, contentivo del concepto técnico N° 0876 también notificado en la solicitud de la referencia me permito transcribir las observaciones formuladas por los solicitantes al respecto "Sirvase corregir las Reivindicaciones actuales de nuestra solicitud de patente para que correspondan a la patente EP 1 452 097 B1"

— sobre el particular, también adjunto al texto en español de las Reivindicaciones 1 a

6, las cuales rempazan a las originalmente presentadas y sobre las cuales de realizarse el examen de novedad de la presente invención.

Continúan argumentando los solicitantes que "la Reivindicación 1 incluye las limitaciones de la Reivindicación 3 en su versión original, así como algunas de las limitaciones de la Reivindicación 2 en su versión original. Se prefiere no hacer mas correcciones a la Reivindicación 1, porque no creemos que tales correcciones sean necesarias para defiir claramente los complejos minerales Reivindicados.

#### Rechazo de la Novedad

El examinador rechazó las reivindicaciones 1-12 como carentes de novedad a la luz de D1 (JP 07-277991). La presente invención contiene un complejo mineral preparado combinando ácido lactobiónico, un ácido comestible y un mineral, que forman un complejo que ya tiene el mineral absorbido, y en donde la cantidad de mineral se conoce antes de la adición a una bebida o alimento. La presente invención se relaciona con agregar minerales extra en la forma de un complejo mineral a un alimento o bebida. No existe nada en D1 para sugerir que un complejo mineral pueda absorberse igualmente en el agente de absorción o que pueda agregarse posteriormente a un alimento o bebida para aportar alrededor del 5% a alrededor del 200% de valor diario recomendado en los Estados Unidos de un mineral, por tamaño de porción única. El complejo mineral de la presente invención proporciona una fuente mineral estable, soluble, de sabor definido, apropiada para fortificación mineral de productos alimenticios y bebidas.

No hay nada en D1 para indicar que forme asimismo un complejo mineral similar y que posea igualmente estas propiedades. D1 divulga agregar ácido lactobiónico a bebidas, alimentos, o tabletas como promotor de absorción de minerales. D1 no divulga un proceso para elaborar un complejo mineral combinando ácido lactobiónico, un mineral y un ácido comestible apropiado para la adición en un alimento o bebida, como se reivindica en la presente solicitud. No existe enseñanza en D1 en el sentido que complejos minerales sean apropiados para uso con un alimento con una bebida.

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En contraste, los Ejemplos 1 y 2 de D1 describen una bebida a base de jugo y una jalea, los cuales promueven la absorción de minerales, pero las recetas en las Tablas 1 y 2 no incluyen minerales de ninguna clase. Los Ejemplos 1 y 2 se dirigen a promover la absorción de minerales, no de complejos minerales, como se especifica por la presente solicitud.

Más aún, en D1 en el párrafo 0006, la divulgación establece que el ácido lactobiónico actúa como una sustancia para promover la absorción de minerales en cuerpos humanos, cuando se ingiere como una tableta o píldora, o mezclándolo en bebidas o alimentos (la divulgación no establece específicamente que la absorción de minerales tenga lugar en la bebida, o solución acuosa, sino más bien parece afirmar que la bebida o alimento, que contiene el ácido lactobiónico, promueve la absorción de minerales En el cuerpo luego de la ingestión). La reivindicación 1 de la presente invención requiere agregar una "fuente mineral" al ácido lactobiónico y al ácido comestible, donde todos los tres se mezclan entre sí en una solución acuosa y, luego, se agregan a un alimento o bebida. D1 no divulga agregar un mineral al ácido lactobiónico y al ácido cítrico (es decir, el ácido comestible) antes de ingerirlo en el cuerpo. En ninguna parte en la referencia D1 se divulga que se puede combinar ácido lactobiónico, un ácido comestible Y un mineral conjuntamente para obtener un complejo mineral a fin de incorporarlo a bebidas, alimentos o tabletas. Ni es obvio utilizar un complejo mineral en un jugo de fruta basándose en la divulgación en D1. Por lo tanto, D1 no divulga la formación de un complejo mineral para la fortificación mineral de alimentos y bebidas, como en nuestra invención, sino más bien un promotor de absorción de minerales, que carece de un elemento importante de nuestra invención, es decir, el mineral ya unido a la estructura ácido lactobiónico-ácido comestible.

Adicionalmente D1, como promotor de absorción de minerales, se convierte en una herramienta inútil donde la dieta de la persona es baja en minerales o carece de ellos. El promotor de absorción de minerales no absorbe minerales de ninguna clase

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o absorbe únicamente cantidades mínimas, y la dieta no se aumenta en la ingesta de minerales ingiriendo el promotor. Mientras que, en la invención reivindicada, ingiriendo el complejo ácido lactobiónico – ácido comestible – mineral en un alimento o bebida, el cuerpo está seguro de recibir una cantidad dada de mineral. En D1, la persona que ingiere el promotor de absorción de minerales no tiene forma de saber cuánto mineral está absorbiendo su cuerpo, si es que lo absorbe. Con la invención reivindicada, una cantidad conocida de mineral se ha combinado con la estructura ácido lactobiónico – ácido comestible, y el usuario sabe qué cantidad recibe. En consecuencia, no existe garantía que, al ingerir el promotor de absorción de minerales de D1, o, como en el Ejemplo 1, al tomar el jugo de fruta, la persona obtenga algunos minerales.

Además, debido a que el complejo mineral de la presente invención se prepara como un ingrediente separado que ya ha absorbido el mineral, la cantidad de mineral y su forma son conocidas antes de la adición a un alimento o bebida. Por lo tanto, usando las mezclas descritas en los Ejemplos 1 y 2 y D1, no es posible hacer una evaluación exacta de la cantidad final de mineral ingerido, o su forma.

El Ejemplo 3 de D1 describe tabletas que contienen calcio, almidón, celulosa cristalina, carboximetilcelulosa, éster graso de sacarosa y ácido lactobiónico. El Ejemplo 3 no incluye un ácido comestible, ni sugiere el límite superior de mineral citado en las reivindicaciones de la solicitud pendiente.

El Ejemplo 4 de D1 describe una comida para animales para promover la absorción de minerales, comida que contiene minerales y ácido lactobiónico como ingredientes separados. El Ejemplo 4 no sugiere mezclar los minerales, el ácido lactobiónico y el ácido comestible para formar complejos minerales.

Más aún, la presente invención provee fortificación mineral e ingesta mejoradas, sin afectar negativamente las propiedades organolépticas. Una persona de habilidad ordinaria esperaría que los minerales, especialmente los minerales

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agregados, reaccionaran con un número de componentes que podrían estar presentes en un alimento o bebida. La reacción podría resultar en precipitación, cambios indeseados de color, cambios indeseados de sabor y reacciones que inutilicen el mineral para absorción. Inesperadamente los inventores descubrieron un método en donde pudieron mezclar ácido lactobiónico, una fuente mineral y un ácido comestible en las cantidades reivindicadas, sin experimentar ninguno de los resultados indeseados cuya probable ocurrencia esperaría una persona de habilidad ordinaria. La referencia D1 no aborda este problema en absoluto, puesto que no agregan minerales de ninguna clase. Los minerales agregados podrían actuar ciertamente en forma muy diferente a algún elemento ya existente allí. Por consiguiente, el resultado se considera sorpresivo e inesperado.

En vista de las significativas diferencias entre D1 y la presente invención, la invención reivindicada es novedosa y no obvia.

Rechazos de la Actividad Inventiva

El examinador ha rechazado las reivindicaciones 1-8 como carentes de actividad inventiva a la luz de D2 (ES 8406196A) y D3 (Patente de los Estados Unidos No. 5,290,766).

D2 se dirige a un producto farmacéutico inyectable para el tratamiento de deficiencia de hierro. La solución inyectable, preparada de acuerdo con el proceso de D2, incluye únicamente un mineral y ácido lactobiónico, pero no un ácido comestible. Aún cuando en las primeras etapas del proceso se agrega ácido acético (es decir, un ácido comestible), el ácido acético se agrega a un compuesto de hidróxido de sodio únicamente para efectos de formar acetato de hierro, y cualquier ácido acético en exceso se elimina de la solución antes de agregar el ácido lactobiónico. En consecuencia, el ácido comestible requerido en la presente invención falta en la solución final de D2.

Más aún, D2 utiliza un proceso de dos pasos que implica perfiles de reacción diferentes de la presente invención y, por lo tanto, es probable que resulte en productos diferentes. En D2, el mineral reacciona con el ácido, independientemente de la presencia del ácido lactobiónico. El producto resultante de la primera reacción

se agrega entonces al ácido lactobiónico. En la presente invención, el ácido lactobiónico, el mineral y el ácido comestible se mezclan conjuntamente en una solución acuosa.

Las soluciones de D2 se divulgan únicamente para uso con un complejo de hierro (II) polinuclear que tiene que inyectarse en el cuerpo en una forma acuosa. No existe enseñanza o sugerencia en el sentido que se esperaría que D2 proporcione complejos minerales similares a la presente invención, ni existe alguna enseñanza de que D2 tenga las mismas propiedades de la presente invención.

D3 se dirige a una solución cardioplégica que comprende NaCl, KCl, CaCl<sub>2</sub>, MgCl<sub>2</sub>, NaHCO<sub>3</sub>, D-glucosa, ácido L-aspartico y ácido lactobiónico para mejorar la viabilidad de corazones almacenados o para uso en cirugía a corazón abierto. D2 enseña que las cantidades requeridas de ácido aspártico y ácido lactobiónico se disuelven cada uno en una pequeña cantidad de agua destilada, y el pH se ajusta a pH 7.5 con NaOH. A continuación, los ingredientes restantes se agregan y mezclan, seguidos por burbujeo con una mezcla gaseosa de oxígeno y dióxido de carbono.

D3 no divulga un proceso para preparar un complejo mineral combinando ácido lactobiónico, un mineral y un ácido comestible, apropiado para adición a un alimento o bebida como se reivindica en la presente solicitud. D3 simplemente enseña una mezcla de ingredientes. No hay nada en D3 para indicar que forme complejos minerales de ninguna clase. No hay enseñanza en D3 en el sentido que complejos minerales sean apropiados para uso con un alimento o bebida, ni que los complejos minerales podrían agregarse a un alimento o bebida para proporcionar alrededor del 5% a alrededor del 200% del valor diario recomendado en los Estados Unidos de un mineral por tamaño de porción única.

La invención reivindicada es inventiva a la luz de D2 y D3. D2 y D3, solos o en combinación, no enseñan un complejo mineral soluble que contenga un mineral, un ácido comestible y ácido lactobiónico susceptibles de agregarse a alimentos o bebidas para suministrar cantidades pre-definidas de los minerales. Más aún, como D2 y D3 se encuentran en campos técnicos separados (medicamentos intravenosos para el tratamiento de deficiencia de hierro y soluciones cardioplégicas para mejorar la función cardíaca, respectivamente), una persona de habilidad ordinaria en el arte no estaría motivada a consultar las enseñanzas de D2 y D3 al intentar abordar los problemas resueltos por la presente solicitud.

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En los términos anteriores doy respuesta a los oficios y conceptos técnicos mencionados, por lo que pido se continúe con los trámites de la solicitud.

Atentamente,



JERÓNIMO CASTILLO BONILLA

C.C. 79.462.057 de Bogotá

T.P.104167 C. S. Judicatura

- 1- Método para preparar un complejo mineral de ácido lactabiónico que comprende ácido lactabiónico, una fuente mineral y un ácido comestible, caracterizado porque el complejo mineral se prepara mezclando ácido lactabiónico, la fuente mineral y el ácido comestible en una solución acuosa y en donde el complejo mineral se prepara mezclando del 5 al 95 por ciento de peso de ácido lactabiónico, 1 a 50% de peso de una fuente mineral, y 1 a 50% de peso de ácido comestible en una solución acuosa y en el que la fuente mineral es un hidróxido mineral, un carbonato mineral, un óxido mineral o mezclas de los mismos.
- 2- El método de la Reivindicación 1, caracterizado por que el ácido comestible es ácido cítrico, ácido láctico, ácido acético, ácido málico, ácido glucónico, ácido tartárico, ácido fumárico, ácido adípico, ácido succínico, ácido ascorbico, ácido fosfórico o mezclas de los mismos.
- 3- El método de las Reivindicaciones 1 y 2, caracterizado porque el complejo mineral se prepara mezclando 50 a 90% de peso del ácido lactabiónico, 5 a 25% de peso de la fuente mineral y, 2 a 25% de peso de ácido comestible en una solución acuosa.
- 4- El método de una cualquiera de las Reivindicaciones 1 a 3, caracterizado porque el mineral es calcio, magnesio, potasio, sodio, hierro, cinc, cobre, cromo, selenio, manganeso o mezclas de los mismos.
- 5- El método de una cualquiera de las Reivindicaciones 1 a 4, caracterizado porque el mineral es calcio.
- 6- Un producto alimenticio o bebida con mineral fortificado, que comprende 0.2 a 20% de peso de un complejo mineral obtenible de acuerdo con el método de una cualquiera de las Reivindicaciones 1 a 5.

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**RECEIVED**  
18 OCT 2006  
**RECEIVED**  
**LONDON**



Formalities Officer

Name: Longo, Eleonora

Tel.: 8141

ENTERED BY *AOC*  
DUE DATE *22/12/06*  
*22/2/07*

Date  
12-10-2006

|                                                    |                                                 |
|----------------------------------------------------|-------------------------------------------------|
| Reference<br>GHS/P504586EP                         | Application No./Patent No.<br>04251080.0 - 2114 |
| Applicant/Proprietor<br>KRAFT FOODS HOLDINGS, INC. |                                                 |

**Summons to attend oral proceedings pursuant to Rule 71(1) EPC**

You are hereby summoned to attend oral proceedings arranged in connection with the above-mentioned European patent application.

The matters to be discussed are set out in the communication accompanying this summons (EPO Form 2906).

The oral proceedings, which will not be public, will take place before the examining division

on 22.02.07 at 09.00 hrs at the EPO,  
Pschörrhöfe, Bayerstr. 34, D-80335 München

No changes to the date of the oral proceedings can be made, except on serious grounds (see OJ EPO 10/2000, 456).

If you do not appear as summoned, the oral proceedings may continue without you (R. 71(2) EPC). Your attention is drawn to Rule 2 EPC, regarding the language of the oral proceedings, and to the OJ EPO 9/1991, 489, concerning the filing of authorisations for company employees and lawyers acting as representatives before the EPO.

The final date for making written submissions and/or amendments (Rule 71a EPC), is 22.12.06.

The actual room number as well as the waiting room numbers will be given to you by the porter in the foyer at the above EPO address.

Parking is available free of charge in the underground car park. However, this applies only in the case of accessing the car park via the entrance "Zollstrasse".

1st Examiner:  
Smeets D

2nd Member:  
Felder C

Chairman:  
Toulacis C

For the Examining Division

Annexes:  
Confirmation of receipt (Form 2936)  
Communication (EPO Form 2906)



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| Bescheld/Protokoll (Anlage) |            | Communication/Minutes (Annex)                   | Notification/Procès-verbal (Annexe) |
|-----------------------------|------------|-------------------------------------------------|-------------------------------------|
| Datum<br>Date               | 12.10.2006 | Blatt<br>Sheet<br>Feuille                       | 1                                   |
|                             |            | Anmelde-Nr.:<br>Application No.:<br>Demande n°: | 04 251 080.0                        |

The examination is being carried out on the **following application documents**:

**Description, Pages**

2-5, 7, 11, 12, 14, 15 as originally filed

1, 6, 8-10, 13 received on 26.09.2005 with letter of 26.09.2005

**Claims, Numbers**

1-7 received on 26.09.2005 with letter of 26.09.2005

**Drawings, Sheets**

1/4-4/4 as originally filed

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- 1 The applicant is summoned to oral proceedings due to the request as filed with the letter of 13.04.2006 and as it is held expedient by the examining division (Art. 116(1) EPC).

Subject of the oral proceedings will be whether the application fulfills the requirements of Art. 84, 54 and 56 EPC.

It is pointed out that novelty and inventive step will only be discussed once the claims meet the requirements of Article 84 EPC.

- 2 The examining division is of the preliminary and non-binding opinion that the present application has to be refused under Article 97(1) EPC based on the following grounds:

**i) Art. 84 EPC**

The feature "wherein the mineral complex can be incorporated [...] beverage product" renders the scope of claim 1 unclear. Neither the mineral, nor the quantity per serving size is disclosed. As the US Daily Value (DV) is subject to changes, the percentage

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**Bescheid/Protokoll (Anlage)**

Datum  
Date 12.10.2006  
Date

**Communication/Minutes (Annex)**

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**Notification/Procès-verbal (Annexe)**

Anmelde-Nr.:  
Application No.: 04 251 080.0  
Demande n°:

DV is not a fixed value but is also subject to changes.

Indeed, if the DV of a particular mineral increases from 100 mg to 200 mg, the range 5% of DV - 200% of DV will also shift from 5-200 mg to 10-400 mg.

**ii) Art. 54 EPC**

The argumentation of the applicant in his letter dated 13.04.2006 with respect to the objections in view of Article 54 was not found to be convincing for the examining division for the following reasons:

Whether or not minerals have been *added* to the fruit juice is irrelevant as fruit juice *per se* (and actually also the water used in the example of D1) *implicitly* comprises a variety of minerals (Ca, Mg, Na, Fe, K,...) in a variety of concentrations. Therefore, the term "fruit juice" anticipates the broad and vague expression "mineral source". Consequently, D1 anticipates the subject-matter of independent claims 1 and 7. It is also pointed out that the expression in claim 7 "02-20% of a mineral complex" does not give any indication of the amount of mineral in the food or beverage as it is not disclosed how much of a particular mineral is incorporated in the aqueous "mineral complex".

**iii) Art. 56 EPC**

If novelty of an independent claim can be established, it will be discussed whether said claim involves an inventive step.

If the applicant restricted the claims by specifying e.g., that the aqueous composition comprises 1-50% calcium hydroxide, the following observations are made:

The mineral absorption accelerating effect of compositions comprising lactobionic acid has already been acknowledged in D1. According to said document (paragraph 6), it can be incorporated in beverages, soups, and the like.

The applicant argues that adding a particular mineral to be absorbed (e.g. calcium in the form of CaOH) to the lactobionic acid in a particular concentration has the advantage that one knows exactly how much calcium his body is absorbing.

This is however not correct, as this only gives information about how much calcium was added in the "aqueous mineral complex" and not about how much calcium is

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**Bescheld/Protokoll (Anlage)**

Datum  
Date 12.10.2006  
Date

**Communication/Minutes (Annex)**

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Sheet 3  
Feuille

**Notification/Procès-verbal (Annexe)**

Anmelde-Nr.:  
Application No.: 04 251 080.0  
Demande n°:

actually absorbed.

D1 (application example 1) teaches that a person, following a diet containing a certain amount of minerals can increase the actual mineral absorption by a composition comprising lactobionic acid and citric acid.

This is essentially the same as the teaching of the present application.

As the mineral content of most food ingredients and mineral supplements is known, it is not considered important whether calcium under the form of CaOH is administrated together with the composition of example 1 of D1.

- 3 According to the established case law of the Boards of Appeal, the introduction of additional features in the independent claim will make the subject-matter of said claims novel and inventive only in those cases in which said features have an **unknown or unexpected effect or contribution** to the solution of the objective technical problem.
- 4 The attention of the applicant is drawn to the fact that the application may not be amended in such a way that it contains subject-matter which extends beyond the content of the application as filed (Article 123(2) EPC).
- 5 In case the Applicant intends to provide auxiliary requests, he is also requested to provide for each auxiliary request adapted description pages.
- 6 The Applicant is reminded that any submission filed after the time limit under R. 71(a) EPC will be considered as late filed.



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27 FEB 2006  
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(Formalities and other matters)



|                                         |                       |                    |
|-----------------------------------------|-----------------------|--------------------|
| Application No.<br>04 251 080.0 - 2114  | Ref.<br>GHS/P504586EP | Date<br>23.02.2006 |
| Applicant<br>KRAFT FOODS HOLDINGS, INC. |                       |                    |

**Communication pursuant to Article 96(2) EPC**

The examination of the above-identified application has revealed that it does not meet the requirements of the European Patent Convention for the reasons enclosed herewith. If the deficiencies indicated are not rectified the application may be refused pursuant to Article 97(1) EPC.

You are invited to file your observations and insofar as the deficiencies are such as to be rectifiable, to correct the indicated deficiencies within a period

**of 2 months**

from the notification of this communication, this period being computed in accordance with Rules 78(2) and 83(2) and (4) EPC.

One set of amendments to the description, claims and drawings is to be filed within the said period on separate sheets (Rule 36(1) EPC).

**Failure to comply with this invitation in due time will result in the application being deemed to be withdrawn (Article 96(3) EPC).**



|            |         |
|------------|---------|
| ENTERED BY | ALM.    |
| DUE DATE   | 23/4/06 |

Smeets, D  
Primary Examiner  
for the Examining Division

Enclosure(s): 2 page/s reasons (Form 2906)

**Bescheid/Protokoll (Anlage)**

Datum  
Date 23.02.2006  
Date

**Communication/Minutes (Annex)**

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Sheet 1  
Feuille

**Notification/Procès-verbal (Annexe)**

Anmelde-Nr.:  
Application No.: 04 251 080.0  
Demande n°:

The examination is being carried out on the **following application documents**:

**Description, Pages**

2-5, 7, 11, 12, 14, 15 as originally filed

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**Claims, Numbers**

1-7 received on 26.09.2005 with letter of 26.09.2005

**Drawings, Sheets**

1/4-4/4 as originally filed

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1 The present application does not meet the requirements of Article 52(1) EPC, because the subject-matter of independent claims 1 and 7 is not new in the sense of Article 54(1) and (2) EPC.

1.1 The essential technical features of claim 1 on file are:

- i) A method of preparing a mineral complex of lactobionic acid
- ii) comprising lactobionic acid, a mineral source and an edible acid
- iii) by mixing the lactobionic acid, mineral source and an edible acid in an aqueous solution.

1.2 D1 anticipates the subject-matter of claim 1 as it discloses a method of making an aqueous beverage (= aqueous solution) by mixing lactobionic acid, citric acid and minerals in said beverage.



Bescheid/Protokoll (Anlage)

Communication/Minutes (Annex)

Notification/Procès-verbal (Annexe)

Datum  
Date 23.02.2006  
DateBlatt  
Sheet 2  
FeuilleAnmelde-Nr.:  
Application No.: 04 251 080.0  
Demande n°:

Said drink is consequently regarded to be an aqueous solution and it is also suitable for incorporation into other foods or beverages.

Thus, D1 also anticipates the subject-matter of claim 7 on file.

- 2 Moreover, the subject-matter of claim 1 does not meet the requirements of Article 84 EPC as the feature "current recommended United States daily value" is not a fixed value but a parameter which is susceptible to changes.
- 3 Anyway, mineral absorption accelerators comprising lactobionic acid are described in D1.  
It is clear that the present application merely relates to obvious modifications of the subject-matter of D1 and does not disclose additional features which provide an inventive contribution to said document (Art. 56 EPC).
- 4 At least some of the objections raised above are such that there appears to be no possibility of overcoming them by amendment. **Refusal of the application under Article 97(1) EPC is therefore to be expected.**



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(Formalities and other matters)



|                                         |                       |                    |
|-----------------------------------------|-----------------------|--------------------|
| Application No.<br>04 251 080.0 - 2114  | Ref.<br>GHS/P504586EP | Date<br>31.05.2005 |
| Applicant<br>Kraft Foods Holdings, Inc. |                       |                    |

**Communication pursuant to Article 96(2) EPC**

The examination of the above-identified application has revealed that it does not meet the requirements of the European Patent Convention for the reasons enclosed herewith. If the deficiencies indicated are not rectified the application may be refused pursuant to Article 97(1) EPC.

You are invited to file your observations and insofar as the deficiencies are such as to be rectifiable, to correct the indicated deficiencies within a period

**of 4 months**

from the notification of this communication, this period being computed in accordance with Rules 78(2) and 83(2) and (4) EPC.

One set of amendments to the description, claims and drawings is to be filed within the said period on separate sheets (Rule 36(1) EPC).

**Failure to comply with this invitation in due time will result in the application being deemed to be withdrawn (Article 96(3) EPC).**



|            |         |
|------------|---------|
| ENTERED BY | ALI     |
| DUE DATE   | 30/9/05 |

Smeets, D  
Primary Examiner  
for the Examining Division

Enclosure(s): 3 page/s reasons (Form 2906)

**Bescheid/Protokoll (Anlage)**

Datum  
Date 31.05.2005  
Date

**Communication/Minutes (Annex)**

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Sheet 1  
Feuille

**Notification/Procès-verbal (Annexe)**

Anmelde-Nr.:  
Application No.: 04 251 080.0  
Demande n°:

The examination is being carried out on the **following application documents**:

Text for the Contracting States:

AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PT RO SE SI SK TR LI

**Description, pages:**

1-15 as originally filed

**Claims, No.:**

1-7 as originally filed

**Drawings, sheets:**

1/4-4/4 as originally filed

\*\*\*\*\*

- 1 The following documents (D) are referred to in this communication; the numbering will be adhered to in the rest of the procedure:

D1: DATABASE WPI Section Ch, Week 199551 Derwent Publications Ltd., London, GB; Class B05, AN 1995-400900 XP002280248 -& JP 07 277991 A (SNOW BRAND MILK PROD CO LTD), 24 October 1995 (1995-10-24)

D2: GB-A-2 129 821 (RICHTER GEDEON VEGYESZET) 23 May 1984 (1984-05-23)

- 2 The present application does not meet the requirements of Article 52(1) EPC, because the subject-matter of independent claim 1 is not new in the sense of Article 54(1) and (2) EPC. It is pointed out that the feature relating to the method of preparation is not taken into consideration for assessing novelty. Indeed, the step "mixing in aqueous solution" could also be an intermediate step of

**Bescheid/Protokoll (Anlage)**

Datum  
Date 31.05.2005  
Date

**Communication/Minutes (Annex)**

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Sheet 2  
Feuille

**Notification/Procès-verbal (Annexe)**

Anmelde-Nr.:  
Application No.: 04 251 080.0  
Demande n°:

the preparation process before, e.g. drying the composition.

The feature "wherein the mineral complex can be incorporated [...] beverage product" of claim 1 does also not add limiting product features to the composition of claim on file.

2.1 D1 discloses a mineral absorption-stimulating agent containing lactobionic acid and citric acid, having a high absorption-stimulating effect for minerals such as Ca, Fe and Mg, and used for an additive to medicines or beverages. Thus, this document anticipates the subject-matter of independent claim 1.

2.2 D2 (claims 1, 2) discloses iron complexes comprising lactobionic acid und acetate. This document is also novelty destroying for claim 1.

3 The question whether the application involves an inventive step (Article 56 EPC) is only of relevance once novelty of the independent claim has been established. However, it appears that D1 already acknowledges all essential features of the application.

Consequently, it is not at present apparent which part of the application could serve as a basis for a new and inventive claim. Should the applicant nevertheless regard some particular matter as patentable, an independent claim should be filed taking account of Rule 29(1) EPC. The applicant should also indicate in the letter of reply the difference of the subject-matter of the new claim vis-à-vis the state of the art and the significance thereof.

It is suggested to use the problem-solution approach.

4 The attention of the applicant is drawn to the fact that the application may not be amended in such a way that it contains subject-matter which extends beyond the content of the application as filed (Article 123(2) EPC).

Any information the applicant may wish to submit concerning the subject-matter of the invention, for example further details of its advantages or of the problem it solves, and for which there is no basis in the application as filed, should be confined to the



Bescheid/Protokoll (Anlage)

Communication/Minutes (Annex)

Notification/Procès-verbal (Annexe)

Datum  
Date 31.05.2005  
Date

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Feuille

Anmelde-Nr.:  
Application No.: 04 251 080.0  
Demande n°:

letter of reply and not be incorporated into the application (Article 123(2) EPC and the Guidelines, C-VI, 5.7 et seq.).

(19)日本国特許庁 (J P)

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(54)【発明の名称】 ミネラル吸収促進剤

(57)【要約】

【目的】 ラクトビオン酸を有効成分とするミネラル吸収促進剤を提供する。

【構成】 ミネラルの吸収性を促進する効果を有するラクトビオン酸を有効成分としてミネラル吸収促進剤とする。

【効果】 このミネラル吸収促進剤を配合した医薬、飲食品及び飼料は、ミネラルの補給に有用である。

## 【特許請求の範囲】

【請求項1】 ラクトビオン酸を有効成分とするミネラル吸収促進剤。

## 【発明の詳細な説明】

【0001】

【産業上の利用分野】本発明は、ガラクトースとグルコン酸が結合したラクトビオン酸を有効成分とするミネラル吸収促進剤に関する。

【0002】

【従来の技術】日本人のカルシウム摂取量は、長年にわたり栄養必要量を下回っている現状にあり、カルシウムの摂取が求められている。しかしながら、日本人の平均的な食習慣では十分な量のカルシウムを含む献立を継続して摂取するのに相当の努力を要する。また、カルシウム以外に亜鉛、銅、マグネシウムなどのミネラルについても不足しがちであり、ミネラルの吸収性が高い食品と共に、ミネラルの吸収を促進する物質に対しても関心が高まっている。さらには、出血や鉄欠乏による貧血の治療や改善には、クエン酸鉄、ピロリン酸鉄、塩化鉄、硫酸鉄などの鉄剤やビタミンB<sub>12</sub>製剤などが用いられているが、これらの鉄剤は体内での吸収率が非常に低いため比較的少量に投与しなければならない。しかし、これらの製剤を経口投与の場合、多量に投与すると鉄剤は消化管壁の鉄症や様々な副作用（吐気、むかつき、便秘など）を引き起こすという問題があった。

【0003】一方、既知の物質としてO-β-D-ガラクトピラノシルー（1-4）-D-グルコン酸の一般式で表される二糖類のラクトビオン酸が知られているが、このラクトビオン酸がカルシウムの吸収を促進するということは知られていない。

【0004】

【発明が解決しようとしている課題】本発明者らは、上述したようにカルシウムの吸収を促進する物質を求めて鋭意研究を重ねた結果、一般式がO-β-D-ガラクトピラノシルー（1-4）-D-グルコン酸で表されるラクトビオン酸がカルシウムの吸収を促進することを見出\*

\*し、本発明を完成するに至った。したがって、本発明は、ラクトビオン酸を有効成分とするミネラル吸収促進剤を提供することを課題とする。

【0005】

【課題を解決するための手段】本発明では、一般式がO-β-D-ガラクトピラノシルー（1-4）-D-グルコン酸で表されるラクトビオン酸をミネラル吸収促進剤の有効成分として用いる。このラクトビオン酸は、乳糖を基質としてラクトースデヒドロゲナーゼ活性を有するシュードモナス・グラヴェオレンスなどの微生物を作用させることにより得ることができ、また、乳糖を臭素などで酸化することにより得ることもできる。

【0006】このミネラル吸収促進効果を有するラクトビオン酸は、ヒトや家畜の生体内で効果を発揮させるために、例えば、糖衣錠やタブレットなどの錠剤、顆粒剤、液剤、もしくはカプセルなどとして経口的に投与できる医薬品として、また、飲料、スープ、チーズ、ゼリー、パン、麺類、ソーセージなど、あるいはガムやキャンディーなどの菓子類に添加することにより、ミネラル吸収促進食品素材として用いることもできる。さらには、飼料添加物として用いることもできる。なお、ラクトビオン酸の摂取量については、特に制約はないが、成人男子の場合、1mg/kg体重/日以上、望ましくは1～1,000mg/kg体重/日が適当である。

【0007】本発明のラクトビオン酸を有効成分とするミネラル吸収促進剤は、カルシウム、鉄、マグネシウム、亜鉛、銅などの生体に必要なミネラルの吸収を促進するので、食事性因子によるミネラルの摂取を改善すると共に、骨粗鬆症や鉄欠乏性貧血などの症状を改善する効果も期待される。次に実施例及び試験例を挙げて本発明を具体的に説明する。

【0008】

【実施例1】常法に従い、表1の配合比によって、ミネラル吸収促進効果を賦与した果汁飲料を製造した。

【0009】

【表1】

（単位：重量％）

|                 |      |
|-----------------|------|
| 混合異性化糖          | 15.0 |
| 果汁              | 10.0 |
| クエン酸            | 1.0  |
| ラクトビオン酸（和光純薬社製） | 0.1  |
| 香料              | 0.1  |
| 水               | 73.8 |

【0010】

【実施例2】常法に従い、表2の配合比によって、ミネラル吸収促進効果を賦与したゼリーを製造した。

【0011】

【表2】

（単位：重量％）

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| 3                | 4    |
|------------------|------|
| 果汁               | 20.0 |
| グラニュー糖           | 15.0 |
| 水飴               | 5.0  |
| 寒天               | 1.0  |
| ラクトビオン酸 (和光純薬社製) | 0.5  |
| 香料               | 0.1  |
| 水                | 58.4 |

【0012】

【実施例3】本発明のラクトビオン酸を配合したカルシウム吸収促進剤を調製した。カルシウム2,200g、コーンスターチ1,232g、結晶セルロース100g、カルボキシメチルセルロースカルシウム 68g及びラクトビオン酸 (和光純薬社製) 400gをニーダーで混合した後、水 500mlを噴霧滴下しながら混練した。次に、この混練物を20メッシュのスクリーンをセットした単軸オシレーターで造粒し、流動槽型乾燥機で乾燥した。そして、この乾燥品をフラッシュミルで粉碎し、整粒して打錠用粉体を得た。\*

\*この打錠用粉体に滑沢剤としてショ糖脂肪酸エステル 80gをV型混合機で混合した後、直径11mmの杵をセットした錠剤機で打錠し、平均重量 0.35gのタブレットを得た。

【0013】

【実施例4】常法に従い、表3の配合比によって、ミネラル吸収促進効果を賦与した犬飼育用飼料 (ドッグフード) を製造した。

【0014】

【表3】

(単位:重量%)

|                  |      |
|------------------|------|
| 大豆粕              | 13.7 |
| 脱脂粉乳             | 14.0 |
| 大豆油              | 4.0  |
| コーン油             | 2.0  |
| パーム油             | 2.0  |
| トウモロコシ澱粉         | 23.0 |
| 小麦粉              | 15.0 |
| ふすま              | 8.0  |
| ビタミン混合物          | 2.0  |
| ミネラル混合物          | 9.0  |
| セルロース            | 2.3  |
| ラクトビオン酸 (和光純薬社製) | 0.5  |

なお、ビタミン混合物の組成を表4に、ミネラル混合物の組成を表5にそれぞれ示す。

【0015】

【表4】

|                     |          |
|---------------------|----------|
| ビタミンA               | 1,500 IU |
| ビタミンD <sub>3</sub>  | 300 IU   |
| ビタミンE               | 6.8 mg   |
| ビタミンB <sub>1</sub>  | 0.9 mg   |
| ビタミンB <sub>2</sub>  | 0.4 mg   |
| ビタミンB <sub>6</sub>  | 0.5 mg   |
| ビタミンB <sub>12</sub> | 3.4 mg   |
| ビタミンC               | 50.0 mg  |
| パントテン酸              | 4.0 mg   |
| 葉酸                  | 0.2 mg   |
| コリン                 | 200.0 mg |
| ビオチン                | 24.4 μg  |
| イノシトール              | 50.0 mg  |
| ナイアシン               | 10.5 mg  |

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ショ糖を加えて全量を2gとした。

\*【表5】

【0016】

\*

|                                                      |         |
|------------------------------------------------------|---------|
| CaCO <sub>3</sub>                                    | 3.0 g   |
| KH <sub>2</sub> PO <sub>4</sub>                      | 2.0 g   |
| NaH <sub>2</sub> PO <sub>4</sub>                     | 1.5 g   |
| MgO                                                  | 0.5 g   |
| MnCO <sub>3</sub>                                    | 40.0 mg |
| FeC <sub>2</sub> H <sub>5</sub> O <sub>7</sub>       | 30.0 mg |
| 70%ZnO                                               | 10.0 mg |
| 55%CaCO <sub>3</sub>                                 | 4.5 mg  |
| KIO <sub>3</sub>                                     | 0.65 mg |
| Na <sub>2</sub> SeO <sub>3</sub> · 5H <sub>2</sub> O | 0.05 mg |
| CrK(SO <sub>4</sub> ) · 12H <sub>2</sub> O           | 5.0 mg  |

ショ糖を加えて全量を9gとした。

※ラットを用い、1群6匹で行なった。実験食は、表6に

【0017】

示したように各糖質を5重量%配合したものをを用いた。

【試験例1】ラクトビオン酸のミネラル吸収促進効果に

【0018】

ついて動物実験を行った。動物実験には8週齢のSD系雄※20

【表6】

(単位: g/100g)

|          | A群   | B群   | C群   |
|----------|------|------|------|
| カゼイン     | 20.0 | 20.0 | 20.0 |
| コーンスターチ  | 65.2 | 60.2 | 60.2 |
| セルロース    | 5.0  | 5.0  | 5.0  |
| コーンオイル   | 5.0  | 5.0  | 5.0  |
| ビタミンミックス | 1.0  | 1.0  | 1.0  |
| メチオニン    | 3.5  | 3.5  | 3.5  |
| DL-メチオニン | 0.3  | 0.3  | 0.3  |
| ラクトース    | —    | 5.0  | —    |
| ラクトビオン酸  | —    | —    | 5.0  |

A群: 対照群、B群: ラクトース投与群、C群: ラクト

★【0019】

ビオン酸投与群

【表7】

また、各実験食の成分値を表7及び表8に示した。

★

(単位: g/100g)

|    | A群    | B群    | C群    |
|----|-------|-------|-------|
| 糖質 | 63.19 | 64.19 | 64.09 |
| 蛋白 | 17.45 | 17.39 | 17.31 |
| 脂肪 | 5.45  | 5.58  | 5.45  |
| 水分 | 10.82 | 9.81  | 10.10 |
| 灰分 | 3.09  | 3.03  | 3.05  |

A群: 対照群、B群: ラクトース投与群、C群: ラクト

【0020】

ビオン酸投与群

【表8】

(単位: mg/100g)

|        | A群   | B群   | C群   |
|--------|------|------|------|
| ナトリウム  | 109  | 108  | 97   |
| カリウム   | 350  | 350  | 350  |
| カルシウム  | 490  | 490  | 495  |
| マグネシウム | 41   | 42   | 42   |
| 鉄      | 3.8  | 3.9  | 4.0  |
| 亜鉛     | 3.6  | 3.7  | 3.6  |
| 銅      | 0.55 | 0.55 | 0.56 |
| マンガン   | 4.7  | 5.0  | 5.0  |
| リン     | 600  | 610  | 610  |

A群：対照群、B群：ラクトース投与群、C群：ラクトビオン酸投与群

【0021】また、ミネラル吸収率の評価については、実験食投与1週目に糞便と尿を採取し、排泄されたカルシウムとマグネシウムを測定して、次式により算出した。

ミネラル吸収率(%) = [(摂取ミネラル量 - 排泄ミネラル量) / (摂取ミネラル量) × 100

【0022】その結果を図1に示す。それによると、ラクトビオン酸投与群は、カルシウム吸収物質として知られているラクトース投与群に比べて、カルシウムやマグネシウムなどのミネラル吸収を促進させることが判った。

【0023】

【試験例2】21日齢のウィスター系ラット（体重が45～50g）に、鉄含量を0.25mg/100g飼料とした除鉄食（オリ＊

\*エンタル酵母社製）を3週間与え、血中ヘモグロビン値が7g/100ml以下の貧血ラットを作成した。そして、1群5匹とし、その後も除鉄食を与え続けながら、下記の試験飼料を1ml/日、6週間強制経口投与した。

試験群1：除鉄食のみ

試験群2：硫酸第一鉄を鉄として0.2mg/ml

試験群3：硫酸第一鉄を鉄として0.2mg/ml + ラクトビオン酸を200mg/ml

試験群4：硫酸第一鉄を鉄として0.2mg/ml ラクトースを200mg/ml

試験飼料投与後6週間目に、尾静脈より採血し自動血球計測装置（東亜医用電子社製）でヘモグロビン値を測定した。その結果を表9に示した。

【0024】

【表9】

ヘモグロビン値（平均値±標準偏差）

|      |                |
|------|----------------|
| 試験群1 | 4.9±0.3 (g/ml) |
| 試験群2 | 10.5±0.8       |
| 試験群3 | 16.1±1.0       |
| 試験群4 | 11.6±0.9       |

【0025】このように、ラクトビオン酸投与群は、無機鉄である硫酸第一鉄の単独投与群及びラクトース投与群よりも優れた貧血治療効果を示すことが判った。

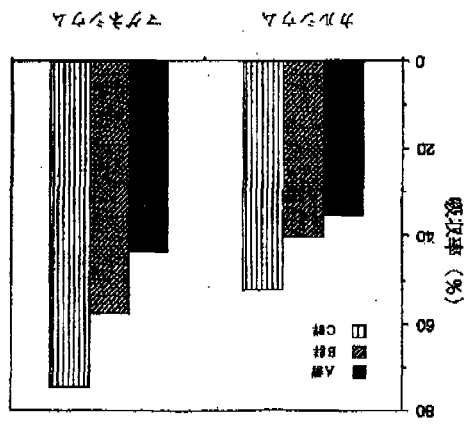
【0026】

【発明の効果】本発明のラクトビオン酸は、ミネラルの吸収性を促進する作用を有するので、このラクトビオン

酸を配合した医薬、飲食品及び飼料は、ミネラルの補給に有用である。

【図面の簡単な説明】

【図1】は、試験例1のミネラル吸収促進効果についての実験結果を示す。



【図1】

(6)

特開平7-277991

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11  
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JAPANESE PATENT OFFICE  
PATENT JOURNAL (A)  
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MINERAL ABSORTPION PROMOTER

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## Abstract

### Objective

To provide a mineral absorption promoter having lactobionic acid as an active ingredient.

### Constitution

A mineral absorption promoter containing lactobionic acid having the effect of promoting mineral absorption as the active ingredient.

### Effect

Drugs, beverages, food and feeds blended with this mineral absorption promoter are useful for supplementing minerals.

## Claim

A mineral absorption promoter containing lactobionic acid as the active ingredient.

## Detailed explanation of the invention

[0001]

### Industrial application field

This invention pertains to a mineral absorption promoter containing lactobionic acid prepared from bonding lactose and gluconic acid as the active ingredient.

[0002]

### Prior art

The intake of calcium by the Japanese has been below the daily nutritional requirement for many years and a higher intake of calcium has been encouraged. However, judging from the regular diets of the Japanese in general, substantial efforts are required if food containing sufficient amounts of calcium is to be served day after day continuously. In addition, intake of minerals other than calcium such as zinc, copper and magnesium tends to be insufficient as well, and the public has been focusing on diets having highly absorbable calcium and materials capable of promoting mineral absorption. Additionally, iron remedies such as iron citrate, iron pyrophosphate, ferric chloride and iron sulfate and vitamin B12 preparations are used for treating or improving anemia due to bleeding or iron deficiency, but in general, relatively high doses of these remedies are necessary because the absorption rates of these iron preparations are very low. However, if high doses of such drugs are administered orally, the iron drugs can cause siderosis to the walls of the digestive tract or other side effects (nausea, vomiting, constipation, etc.).

[0003]

Also, disaccharide lactobionic acid having a general formula [sic] of O- $\beta$ -D-galactopyranosyl-(1-4)-D-gluconic acid is a known substance, but said lactobionic acid is not known to promote absorption of calcium.

[0004]

Problems to be solved by the invention

The present inventors conducted investigations rigorously in search of such previously mentioned substances for promoting calcium absorption, and as a result, discovered that lactobionic acid having the general formula of O- $\beta$ -D-galactopyranosyl-(1-4)-D-gluconic acid could promote absorption of calcium, thus achieving the present invention. Accordingly, the objective of the present invention lies in providing a mineral absorption promoter containing lactobionic acid as the active ingredient.

[0005]

Mean to solve the problems

In the present invention, lactobionic acid having the general formula of O- $\beta$ -D-galactopyranosyl-(1-4)-D-gluconic acid is utilized as the active ingredient in the calcium absorption promoter. Said lactobionic acid can be obtained by employing microorganisms such as *Pseudomonas graveolens* having lactose dehydrogenase activity to act on lactose as the substrate; also, it can be obtained by oxidizing lactose with bromine, etc.

[0006]

With regard to said lactobionic acid having the effect of promoting calcium absorption, to exercise its effect fully in the human body or the bodies of domestic animals, it is made into preparations for oral ingestion including tablets such as sugar-coated tablets or other tablets, granules, liquid preparations and capsules, or it can be used as a substance for promoting mineral absorption by blending into beverages, soups, cheese, jellies, breads, noodles, sausages, or into gums or candies. In addition, it can be utilized as an additive in feeds. Also, there is no particular restriction on the amount of intake of lactobionic acid, but more than 1 mg/kg body weight/day is considered the appropriate quantity for an adult, preferably 1-1000 mg/kg body weight/day.

[0007]

Because the mineral absorption promoter of the present invention having lactobionic acid as the active ingredient promotes the absorptions of minerals such as calcium, iron, magnesium, zinc and copper required by the body, improvement of mineral absorption associated with dietary

factors as well as improvement from diseases such as osteoporosis or iron-deficiency anemia can be expected. The present invention is further explained in detail using the following application examples and test examples.

[0008]

Application Example 1

A juice beverage furnished with the effect of promoting mineral absorption was produced by a conventional method using the blending ratio shown in Table 1.

[0009]

Table 1

|   |                  | ① (単位: 重量%) |
|---|------------------|-------------|
| ② | 混合異性化糖           | 15.0        |
|   | 果汁               | 10.0        |
|   | クエン酸             | 1.0         |
|   | ラクトビオン酸 (和光純薬社製) | 0.1         |
|   | 香料               | 0.1         |
|   | 水                | 73.8        |

Key 1 Unit: wt%  
 2 Mixed isomerized sugars  
 Juice  
 Citric acid  
 Lactobionic acid (product of Wako Junyaku Co.)  
 Flavor  
 Water

[0010]

Application Example 2

A jelly furnished with the effect of promoting mineral absorption was produced by a conventional method using the blending ratio shown in Table 2.

12) 30  
5  
HA

[0011]

Table 2

| ① (単位: 重量%)      |      |
|------------------|------|
| 3                | 4    |
| ② 果汁             | 20.0 |
| グラニュー糖           | 15.0 |
| 水飴               | 5.0  |
| 珪藻土              | 1.0  |
| ラクトビオン酸 (和光純薬社製) | 0.5  |
| 香料               | 0.1  |
| 水                | 58.4 |

Key 1 Unit: wt%  
 2 Juice  
 Granular sugar  
 Syrup  
 Agar  
 Lactobionic acid (product of Wako Junyaku Co.)  
 Flavor  
 Water

[0012]

Application Example 3

A calcium absorption promoter incorporated with the lactobionic acid of the present invention was prepared. After 2200 g calcium, 1232 g starch, 100 g crystalline cellulose, 68 g carboxymethylcellulose and 400 g lactobionic acid (product of Wako Junyaku Co.) were mixed in a kneader, mixing was continued while spraying 500 mL water. Subsequently, granulation of the mixture was conducted on a uniaxial oscillator equipped with a 20-mesh screen, followed by drying in a flow tank drying machine. The dried product was then pulverized in a flash mill and the particle size was rectified to provide powder for tableting. The powder for tableting was mixed with 80 g of sucrose fatty ester as a lubricant, followed by tableting with a tableting machine equipped with a pestle of 11 mm diameter to give tablets of 0.35 g average weight.

[0013]

Application Example 4

A feed for raising dogs (dog food) furnished with the effect of promoting mineral absorption was produced by a conventional method using the blending ratio shown in Table 3.

[0014]

Table 3

| ① (単位: 重量%)      |      |
|------------------|------|
| ② 大豆粕            | 13.7 |
| 脱脂粉乳             | 14.0 |
| 大豆油              | 4.0  |
| コーン油             | 2.0  |
| パーム油             | 2.0  |
| トウモロコシ澱粉         | 23.0 |
| 小麦粉              | 15.0 |
| ふすま              | 8.0  |
| ビタミン混合物          | 2.0  |
| ミネラル混合物          | 9.0  |
| セルロース            | 2.8  |
| ラクトビオン酸 (和光純薬社製) | 0.5  |

|     |   |                                                |
|-----|---|------------------------------------------------|
| Key | 1 | Unit: wt%                                      |
|     | 2 | Soybean lees                                   |
|     |   | Fat-free powder milk                           |
|     |   | Soybean oil                                    |
|     |   | Corn oil                                       |
|     |   | Palm oil                                       |
|     |   | Cornstarch                                     |
|     |   | Wheat starch                                   |
|     |   | Wheat bran                                     |
|     |   | Vitamin mixture                                |
|     |   | Mineral mixture                                |
|     |   | Cellulose                                      |
|     |   | Lactobionic acid (product of Wako Junyaku Co.) |

The composition of the vitamin mixture and the composition of the mineral mixture are shown in Tables 4 and 5, respectively.

[0015]

Table 4

|   |                     |              |
|---|---------------------|--------------|
| ① | ビタミンA               | 1,500 IU     |
|   | ビタミンD <sub>3</sub>  | 300 IU       |
|   | ビタミンE               | 6.8 mg       |
|   | ビタミンB <sub>1</sub>  | 0.9 mg       |
|   | ビタミンB <sub>2</sub>  | 0.4 mg       |
|   | ビタミンB <sub>6</sub>  | 0.5 mg       |
|   | ビタミンB <sub>12</sub> | 3.4 mg       |
|   | ビタミンC               | 50.0 mg      |
| ② | パントテン酸              | 4.0 mg       |
|   | 葉酸                  | 0.2 mg       |
|   | コリン                 | 200.0 mg     |
|   | ビオチン                | 24.4 $\mu$ g |
|   | イノシトール              | 50.0 mg      |
|   | ナイアシン               | 10.6 mg      |
|   | 5                   | 6            |

Key 1 Vitamin \_\_\_\_\_  
 2 Pantothenic acid  
 Folic acid  
 Choline  
 Biotin  
 Inositol  
 Niacin

Sucrose was added to the above to 2 g in total weight.

[0016]

Table 5

|                                                      |         |
|------------------------------------------------------|---------|
| $\text{CaCO}_3$                                      | 3.0 g   |
| $\text{KH}_2\text{PO}_4$                             | 2.0 g   |
| $\text{NaH}_2\text{PO}_4$                            | 1.5 g   |
| $\text{MgO}$                                         | 0.5 g   |
| $\text{MnCO}_3$                                      | 40.0 mg |
| $\text{FeC}_2\text{H}_5\text{O}_7$                   | 30.0 mg |
| 70% $\text{ZnO}$                                     | 10.0 mg |
| 55% $\text{CaCO}_3$                                  | 4.5 mg  |
| $\text{KIO}_3$                                       | 0.65 mg |
| $\text{Na}_2\text{SeO}_3 \cdot 5\text{H}_2\text{O}$  | 0.05 mg |
| $\text{CrK}(\text{SO}_4) \cdot 12\text{H}_2\text{O}$ | 5.0 mg  |

Sucrose was added to the above to 9 g in total weight.

[0017]

Test example 1

An animal experiment was conducted to investigate the effect of lactobionic acid in promoting mineral absorption. 8-week-old SD male rats, 6 head per group, were utilized as the experimental animal. As shown in Table 6, the experimental diets used were added with 5 wt% of the sugars, respectively.

[0018]

Table 6

| ① (単位: g/100g) |      |      |      |
|----------------|------|------|------|
|                | ② A群 | B群   | C群   |
| ③ カゼイン         | 20.0 | 20.0 | 20.0 |
| コーンスターチ        | 65.2 | 60.2 | 60.2 |
| セルロース          | 5.0  | 5.0  | 5.0  |
| コーンオイル         | 5.0  | 5.0  | 5.0  |
| ビタミンミックス       | 1.0  | 1.0  | 1.0  |
| メチオニン          | 3.5  | 3.5  | 3.5  |
| DL-メチオニン       | 0.3  | 0.3  | 0.3  |
| ラクトース          | —    | 5.0  | —    |
| ラクトビオン酸        | —    | —    | 5.0  |

Key 1 Unit: g/100 g)  
 2 Group \_\_\_\_  
 3 Casein  
 Cornstarch  
 Cellulose  
 Corn oil  
 Vitamin mixture  
 Methionine  
 DL-Methionine  
 Lactose  
 Lactobionic acid

Group A: Control group; Group B: group administered with lactose; Group C: group administered with lactobionic acid.

Also, the values of the components of the experimental diets are shown in Tables 7 and 8, respectively.

[0019]

Table 7

| ① (單位: g/100g) |       |       |       |
|----------------|-------|-------|-------|
|                | ② A群  | B群    | C群    |
| ③ 糖質           | 63.19 | 64.19 | 64.09 |
| 蛋白質            | 17.45 | 17.39 | 17.31 |
| 脂肪             | 5.45  | 5.58  | 5.45  |
| 水分             | 10.82 | 9.81  | 10.10 |
| 灰分             | 3.09  | 3.03  | 3.05  |

Key 1 Unit: wt%  
 2 Group \_\_\_\_  
 3 Sugar  
 Protein  
 Fat  
 Water  
 Ash

Group A: Control group; Group B: group administered with lactose; Group C: group administered with lactobionic acid.

[0020]

Table 8

| ① (単位: mg/100g) |      |      |      |
|-----------------|------|------|------|
| 7               | 8    |      |      |
|                 | ② A群 | B群   | C群   |
| ③ ナトリウム         | 109  | 108  | 97   |
| カリウム            | 350  | 350  | 350  |
| カルシウム           | 490  | 490  | 485  |
| マグネシウム          | 41   | 42   | 42   |
| 鉄               | 3.8  | 3.9  | 4.0  |
| 亜鉛              | 3.6  | 3.7  | 3.6  |
| 銅               | 0.55 | 0.55 | 0.56 |
| マンガン            | 4.7  | 5.0  | 5.0  |
| リン              | 600  | 610  | 610  |

Key 1 Unit: wt%  
 2 Group  
 3 Sodium  
 Potassium  
 Calcium  
 Magnesium  
 Iron  
 Zinc  
 Copper  
 Manganese  
 Phosphorus

Group A: Control group; Group B: group administered with lactose; Group C: group administered with lactobionic acid.

[0021]

For evaluating the absorption rate of calcium, the feces and urine were collected in week one of administering the experimental diets and the excreted calcium and magnesium were determined and calculated by the following equation.

$$\text{Absorption rate of mineral (\%)} = \frac{[(\text{Amount of mineral intake} - \text{amount of mineral excreted}) / (\text{Amount of mineral intake})] \times 100}$$

[0022]

Figure 1 shows the result. The result showed that absorption of minerals including calcium and magnesium in the group administered with lactobionic acid was promoted, compared with the group administered with lactose, known to be a calcium absorbing agent.

[0023]

#### Test example 2

21-day-old Wistar rats (body weight 45-50 g) were made anemic, having blood hemoglobin of 7 g/100 mL or lower, by giving them an iron-depleted diet (product of Oriental Yeast Co.) containing 0.25 mg iron/100 g feed for 3 weeks. Afterward, 5 animals were put in each group and the iron-depleted diet was given continuously while the following experimental diets were orally fed forcefully at 1 mL/day for 6 weeks.

Experimental group 1: Iron-depleted diet solely

Experimental group 2: ferric sulfate at 0.2 mg/mL as iron

Experimental group 3: ferric sulfate at 0.2 mg/mL as iron + 200 mg/mL lactobionic acid

Experimental group 4: ferric sulfate at 0.2 mg/mL as iron + 200 mg/mL lactose

Blood was sampled from the caudal vein 6 weeks after administering the experimental diets and the hemoglobin values were determined using an automatic blood cell testing apparatus (Toa Medical Electronic Co.). Table 9 shows the results.

[0024]

Table 9

| ① ヘモグロビン値 (平均値±標準偏差) |                |
|----------------------|----------------|
| ② 試験群 1              | 4.9±0.3 (g/ml) |
| 試験群 2                | 10.5±0.8       |
| 試験群 3                | 16.1±1.0       |
| 試験群 4                | 11.6±0.9       |

Key 1 Hemoglobin value (mean ± standard deviation)  
2 Experimental group \_\_\_\_

[0025]

The results revealed that a better effect of treating anemia was obtained in the group administered with lactobionic acid compared with those in the group administered with inorganic iron ferric sulfate solely and the group administered with lactose.

[0026]

Effect of the invention

The lactobionic acid of the present invention has the effect of promoting mineral absorption and is useful in supplementing minerals when said lactobionic acid is incorporated into drugs, beverages and feeds.

Brief description of the figure

Figure 1 shows the experimental result of the mineral absorption effect of Test example 1.

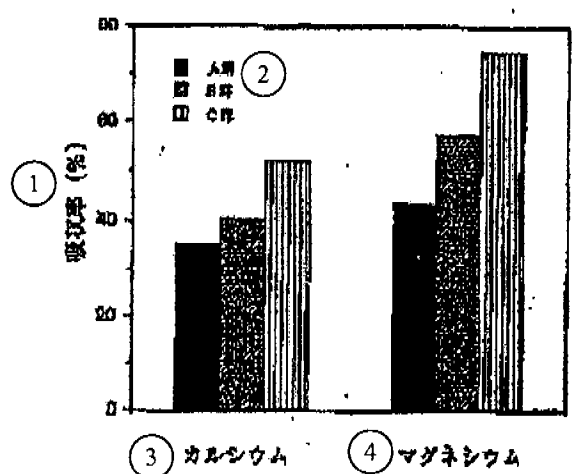


Figure 1

- Key    1    Absorption rate  
      2    Group \_\_\_\_  
      3    Calcium  
      4    Magnesium



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|                                         |                       |                    |
|-----------------------------------------|-----------------------|--------------------|
| Application No.<br>04 251 080.0 - 2114  | Ref.<br>GHS/P504586EP | Date<br>03.04.2007 |
| Applicant<br>KRAFT FOODS HOLDINGS, INC. |                       |                    |

#### Communication under Rule 51(4) EPC

You are informed that the Examining Division intends to grant a European patent on the basis of the above application with the text and drawings as indicated below:

In the text for the Contracting States:

AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LU MC NL PT RO SE SI SK TR

#### Description, Pages

|                    |                                                  |
|--------------------|--------------------------------------------------|
| 2-4, 11, 12, 14    | as originally filed                              |
| 1, 9, 13           | received on 26.09.2005 with letter of 26.09.2005 |
| 5, 5a, 6-8, 10, 15 | received on 09.02.2007 with letter of 09.02.2007 |

#### Claims, Numbers

|     |                                                  |
|-----|--------------------------------------------------|
| 1-6 | received on 09.02.2007 with letter of 09.02.2007 |
|-----|--------------------------------------------------|

#### Drawings, Sheets

|         |                     |
|---------|---------------------|
| 1/4-4/4 | as originally filed |
|---------|---------------------|

With the following amendments to the above-mentioned documents by the examining division

|                    |                    |
|--------------------|--------------------|
| Description, Pages | 5*, 10*, 11*, 15** |
| Claims, Numbers    | 1, 3, 6***         |

#### Comments

\* EPC Guidelines C-II, 4.18  
\*\* EPC Guidelines C-III, 4.3a



Date 03.04.2007

Sheet 2

Application No.: 04 251 080.0

\*\*\* Art. 84 EPC, EPC Guidelines C-III, 4.5a, amendment of the feature "by weight" has support on page 11, lines 9-10 of the application as originally filed

A copy of relevant documents is enclosed

The title of the invention in the three official languages of the European Patent Office, the international patent classification, the designated Contracting States, the registered name of the applicant and the bibliographic data are shown on the attached EPO Form 2056.

You are requested within a **non-extendable** period of four months of notification of this communication

|     |                                                                                                        |               |        |
|-----|--------------------------------------------------------------------------------------------------------|---------------|--------|
| 1.  | to file 1 set of translations of the claim(s) in the two other EPO official languages;                 |               | EUR    |
| 2a. | to pay the fee for grant including the fee for printing up to and including 35 pages;<br>Reference 007 |               | 750.00 |
| 2b. | to pay the printing fee for the 36th and each additional page;<br>number of pages: 0                   | Reference 008 | 0.00   |
| 3.  | to pay the additional claim fee(s) (Rule 51(7) EPC);<br>number of claims fees payable: 0               | Reference 016 | 0.00   |
|     |                                                                                                        | Total amount  | 750.00 |

Concerning the possibility of a request for accelerated grant pursuant to Article 97(6) EPC, reference is made to OJ EPO 2001, 459.

If you do not approve the text intended for grant but wish to request amendments or corrections, the procedure described in Rule 51(5) EPC is to be followed.

If this communication is based upon an auxiliary request, and you reply within the time limit set that you maintain the main or a higher ranking request which is not allowable, the application will be refused (Article 97(1) EPC, see also Legal Advice 15/05 (rev. 02), OJ 6/2005, 357).

If the enclosed claims contain amendments proposed by the Examining Division, and you reply within the time limit set that you cannot accept these amendments, refusal of the application under Article 97(1) EPC would result in the case that agreement cannot be reached on the text for grant.

In all cases except those of the previous two paragraphs, if the grant, printing or claims fees are not paid, or the translations not filed, in due time, the European patent application will be deemed to be withdrawn (Rule 51(8) EPC).

For all payments you are requested to use EPO Form 1010 or to refer to the relevant reference number.

After publication, the European patent specification can be downloaded free of charge from the EPO publication server <https://publications.european-patent-office.org> or ordered only from the Vienna sub-office upon payment of a fee (OJ EPO 2005, 126).

Upon request in writing each proprietor will receive the certificate for the European patent **together with one copy** of the patent specification only if the request is filed within the time limit of Rule 51(4) EPC. If



such request has been previously filed, it has to be confirmed within the time limit of Rule 51(4) EPC. The requested copy is free of charge. If the request is filed after expiry of the Rule 51(4) EPC time limit, the certificate will be delivered without a copy of the patent specification.

Translation of the priority document(s)

If the translation of the priority document(s), as required by Article 88(1) EPC, or the declaration according to Rule 38(5) EPC has not yet been filed, Form 2530 will be despatched separately. The translation is to be filed within the above mentioned time limit (Rule 38(5) EPC).

Note on payment of renewal fees

If a renewal fee falls due between notification of the present communication and the proposed date of publication of the mention of the grant of the European patent, publication will be effected only after the renewal fee and any additional fee have been paid (Rule 51(9) EPC).

Under Article 86(4) EPC, renewal fees are payable to the European Patent Office until the year in which the mention of the grant of the European patent is published.

Filing of translations in the Contracting States

Pursuant to Article 65(1) EPC the following Contracting States require a translation of the specification of the European patent in their/one of their official language(s) (Rule 51(10) EPC), **insofar** this specification will not be published in their/one of their official language(s)

- within **three** months of publication of the mention of such decision:

|    |                             |    |                |
|----|-----------------------------|----|----------------|
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- within **six** months of publication of the mention of such decision:

IE IRELAND

The date on which the European Patent Bulletin publishes the mention of the grant of the European patent will be indicated in the decision on the grant of the European patent (EPO Form 2006).

In case of a valid extension the following Extension States require a translation of the **claims** in their official language within **three** months after publication of the mention of the grant of the European patent:

|    |           |    |           |
|----|-----------|----|-----------|
| AL | ALBANIA   | LV | LATVIA    |
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The translation must be filed with the national Patent Offices of the Contracting or Extension States in accordance with the provisions applying thereto in the State concerned. Further details (e.g. appointment



Date 03.04.2007

Sheet 4

Application No.: 04 251 080.0

of a national representative or indication of an address for service within the country) are given in the EPO information brochure "National law relating to the EPC", and in the supplementary information published in the Official Journal of the EPO, or available on the EPO website.

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Note to users of the automatic debiting procedure

Unless the EPO receives prior instructions to the contrary, the fee(s) will be debited on the last day of the period of payment. For further details see the Arrangements for the automatic debiting procedure (see Supplement to OJ EPO 2, 2002).

**Examining Division:**

|                      |                |
|----------------------|----------------|
| <b>Chairman:</b>     | TOULACIS, C    |
| <b>2nd Examiner:</b> | Popa, Marian   |
| <b>1st Examiner:</b> | Smeets, Dieter |



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Enclosure(s):      Form 2056  
                         22 Copies of the relevant documents

133 42  
+ST

Annex to EPO Form 2004, Communication under Rule 51(4) EPC

Bibliographical data of European patent application No. 04 251 080.0

For the intended grant of a European patent, the bibliographical data are set out below, for information:

**Title of invention:**

- Mineralkomplex enthaltend Lactobionsäure und Verfahren zur Verwendung für Mineralanreicherung von Nahrungsmitteln
- Mineral complexes of lactobionic acid and method of using for mineral fortification of food products
- Complexe mineral comprenant de l'acide lactobionique et méthode d'utilisation pour l'enrichissement en minéraux de produits alimentaires

**Classification:**

INV. A23L1/304

**Date of filing:**

26.02.2004

**Priority claimed:**

US / 28.02.2003 / USA377541

**Contracting States\***  
for which fees have  
been paid:

AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LU MC NL  
PT RO SE SI SK TR

**Extension States\***  
for which fees have  
been paid:

AL LT LV MK

**Applicant(s)\*\*:**

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(54) **Mineral complexes of lactobionic acid and method of using for mineral fortification of food products**

Mineralkomplex enthaltend Lactobionsäure und Verfahren zur Verwendung für Mineralanreicherung von Nahrungsmitteln

Complexe mineral comprenant de l'acide lactobionique et méthode d'utilisation pour l'enrichissement en minéraux de produits alimentaires

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136 45  
+136**Description****FIELD OF THE INVENTION**

5 [0001] The present invention generally relates to the preparation of mineral complexes, especially calcium complexes, of lactobionic acid which are especially useful for mineral fortification of food and beverage products. The calcium complex of lactobionic acid provided in the present invention delivers a soluble, stable, clean tasting calcium source suitable for calcium fortification of a wide variety of food and beverage products.

**BACKGROUND OF THE INVENTION**

10 [0002] Food products manufactured for public consumption are often modified by adding nutritional or other types of additives in order to enhance their nutritional properties. Nutritional fortification of food products may include additives that benefit the overall state of health of the human body. Examples of nutritional fortification include addition of vitamins, minerals, and comparable materials. These additives are either absolutely essential for human metabolism or enhance the provision of substances that may not be available in sufficient amounts in a normal diet.

15 [0003] In recent years, calcium fortification of foods and beverages has received significant attention. Calcium fortification and increased calcium intake is reported to be especially useful in the prevention or moderating the effects of osteoporosis. Increased dietary intake of calcium has been shown to be effective in minimizing bone loss in adults and the elderly. Moreover, increased consumption of calcium earlier in life may build reserves that enable a greater tolerance of a negative calcium balance in later years. Increased consumption of calcium, regardless of age, is expected to mitigate or delay the effects of osteoporosis. Thus, persons of all ages could benefit from increased calcium consumption. Unfortunately, many of the people in greatest need of calcium, including children, women, and the elderly, do not consume the recommended daily levels of calcium. For example, according to United States Department of Agriculture surveys, as many as nine out of ten women in the United States do not consume the recommended levels of calcium. And the elderly often have difficulty in increasing their calcium consumption due to decreasing appetites and metabolism. In addition to bone health, recent research suggests the importance of calcium in improving colon health, weight management, and other health issues.

20 [0004] A large number of calcium compounds or salts have been used to fortify food products. Calcium salts which have been suggested for use or have been used as food supplements include, for example, calcium pyrophosphate, calcium hexametaphosphate, monobasic calcium phosphate, calcium glycerophosphate, tricalcium phosphate, calcium acetate, calcium ascorbate, calcium citrate, calcium citrate malate, calcium carbonate, calcium gluconate, calcium lactate, calcium lactate gluconate, calcium malate, calcium oxide, calcium hydroxide, calcium sulfate, calcium tartrate, dicalcium citrate lactate, calcium fumarate, and calcium chloride.

25 [0005] These calcium supplements have been used in a wide variety of food products. For example, U.S. Patent 4,784,871 (November 15, 1988) provided a calcium fortified yogurt. According to the patent, any calcium compound which is acid soluble could be used. U.S. Patent 5,449,523 (September 12, 1995) and U.S. Patent 5,820,903 (October 13, 1998) also provided calcium-enriched yogurts. U.S. Patent 5,478,587 (December 27, 1995) provided calcium-enriched desserts.

30 [0006] U.S. Patent 5,834,045 (November 10, 1998) provided calcium fortified acid beverages. This patent reported that the use of a calcium source comprising calcium hydroxide and calcium glycerophosphate with any acidulant will result in a beverage product having a marked improvement in storage stability. U.S. Patent 5,855,936 (January 5, 1999) provided a blend of calcium salts balanced with soluble and insoluble salts which are stabilized with a source of glucuronic acid. This composition is capable of fortifying milk beverages and other dairy-based products without coagulation and sedimentation, and with improved palatability. The calcium salts must be stabilized with the glucuronic acid source. Other calcium sources could optionally be included. Other calcium-enriched beverages are disclosed in, for example, U.S. Patent 4,642,238 (February 10, 1987; dietary and nutritionally balanced drinks); U.S. Patent 4,701,329 (October 20, 1987; milk); U.S. Patent 4,737,375 (April 12, 1988; carbonated and non-carbonated beverages containing solubilized calcium and specific amounts of citric acid, malic acid, and phosphoric acid as determined from specific ternary diagrams provided therein); U.S. Patent 4,740,380 (April 26, 1988; soft drinks); U.S. 4,871,554 (October 3, 1989; fruit drink); U.S. Patent 4,851,243 (July 25, 1989; milk); U.S. Patent 4,840,814 (June 20, 1989; milk); U.S. 4,906,482 (March 6, 1990; soy milk); U.S. Patent 5,397,589 (March 14, 1995; milk); U.S. Patent 5,690,975 (November 25, 1997; fermented milk); U.S. Patent 5,597,596 (January 28, 1997; low pH beverage); U.S. Patent 5,780,081 (July 14, 1998; milk); U.S. Patent 5,928,691 (July 27, 1999; milk); and U.S. Patent 5,897,892 (April 27, 1999; milk base products).

35 [0007] U.S. Patent 4,673,583 (June 16, 1987) provided a calcium-enriched soy bean curd. U.S. Patent 5,215,769 (June 1, 1993) provided sauces and salad dressings containing a soluble calcium source comprising specific molar ratios of calcium citrate malate or calcium acetate. U.S. Patent 5,514,387 (May 7, 1996) provided calcium enriched crackers and other baked goods; an emulsifier was used to avoid adverse effect on texture and mouthfeel. U.S. Patent

5,840,354 (November 24, 1998) provided calcium-enriched dried fruit products. U.S. Patent 5,945,144 (August 31, 1999) provided a calcium fortified pasta product.

[0008] U.S. Patent 5,075,499 (December 24, 1991) provides dicalcium citrate-lactate for use as a calcium supplement. Tablets of dicalcium citrate-lactate were preferably taken on a daily basis. U.S. Patent 6,007,852 (December 28, 1999) relates to a calcium enriched natural cheese. The preferred calcium source is tricalcium phosphate. The patent indicates that other calcium sources (but does not specifically mention any specific sources) can be used so long as the calcium source forms a suspension rather than a solution in water, skim milk, or cheese milk. U.S. Patent 6,106,874 (August 22, 2000) provides a low pH nutritional beverage which uses pectin-free fruit juice and a calcium source selected from the group consisting of natural milk mineral concentrate, calcium lactate gluconate, and mixtures thereof.

[0009] Calcium sulfate has been found to significantly and adversely affect the organoleptic properties of food products to which it is added. Generally, added calcium sulfate results in bitterness and undesirable strong flavors with added at significant levels. See, e.g., U.S. Patents 5,820,903 and 5,840,354. Tricalcium phosphate, although widely used, often contributes an undesirable "gritty" texture which, of course, limits the levels at which it can be incorporated in food products. See, e.g., U.S. Patent 5,449,523.

[0010] Calcium enrichment or fortification can adversely affect the organoleptic properties of the food or beverage product to which it is added. Examples of such unacceptable properties include off-flavors, flavor changes, off-colors, textural changes, and the like. Some calcium compounds have more adverse effects than others, especially at higher levels of calcium addition. Thus, much of the currently available technology related to calcium addition does not provide the high levels of calcium addition desired. Further, the cost of some calcium forms is high and, thus, limits their usefulness.

Thus, it is desirable to provide additional calcium compounds and/or other dietary minerals for use in food and beverage products which can provide significant levels of dietary calcium or other dietary minerals without adverse effects on organoleptic properties and at lower cost. Additionally, the form of calcium can influence absorption and use by and in the body. Additionally, the absorption of calcium can be enhanced or inhibited by other compounds. For example, some carbohydrates can improve calcium absorption. Greger, "Nondigestible Carbohydrates and Mineral Bioavailability," J. Nutr., 129, 1434S-1435S (1999); Weaver, "Calcium in Food Fortification Strategies," Internat. Dairy J., 8, 443-449 (1998); Brommage et al., "Intestinal Calcium Absorption in Rats Is Stimulated by Dietary Lactulose and Other Resistant Sugars," J. Nutr., 123, 2186-2194 (1993).

[0011] Lactobionic acid (4-O- $\beta$ -D-galactopyranosyl-D-gluconic acid; CAS Reg. No. 96-82-2) is a water soluble, white crystalline compound. It can be synthesized from lactose by oxidation of the free aldehyde group in lactose as carried out catalytically, chemically, electrolytically, or enzymatically. Harju, Bulletin of the IDF 289, ch. 6., pp. 27-30, 1993; Satory et al., Biotechnology Letters 19 (12) 1205-08, 1997. The use of lactobionic acid or its salts as additives in food products previously has been suggested for several specific applications. Calcium or iron chelate forms of lactobionic acid has been described for dietary mineral supplementation. Riviera et al., Amer. J. Clin. Nutr., 36 (6) 1162-69, 1982. U.S. Patent 5,851,578 describes a clear beverage having a non-gel forming fiber, and water soluble salts of calcium, with or without water soluble vitamins, with or without additional mineral salt supplements and buffered with food acids. The food acid buffering agent includes citric, lactic, maleic, adipic, succinic, acetic, acetic gluconic, lactobionic, ascorbic, pyruvic, and phosphoric acids, as well as combinations thereof. Calcium lactobionate, a salt form of lactobionic acid, has been approved for use as a firming agent in dry pudding mixes. 21 C.F.R. §172.720 (1999). Also, the possible use of lactobionic acid as a general food acidulant has been proposed, albeit without exploration or illustration. Timmermans, Whey: Proceedings of the 2nd Int'l Whey Conf., Int'l Dairy Federation, Chicago, October 1997, pp. 233, 249. This article generally describes lactobionic acid as being useful as an antibiotics carrier, an organ transplant preservative, mineral supplement, growth promoter of bifidobacteria, or as a co-builder in detergents in its potassium salt form. More recently, the use of lactobionic acid in cheese and other dairy products has been described in copending U.S. Patent Application Serial Number PCT US02/14337, filed May 7, 2002, (International Publication WO 02/089592) which is owned by the same assignee as the present application.

[0012] JP7277991 describes a mineral absorption-stimulating agent containing lactobionic acid comprising the combination of product of galactose with gluconic acid as an active ingredient. The agent is said to have a high absorption-stimulating effect for minerals required for living bodies such as Ca, Fe and Mg. It is used as an additive to medicines, beverages, confectionary etc.

[0013] The present invention provides mineral complexes of lactobionic acid which are very effective as mineral fortification agents and which do not significantly affect the organoleptic or textural properties of the food or beverage to which they are added. Such mineral complexes can be produced in a cost effective manner from inexpensive starting materials such as lactose or whey.

## SUMMARY OF THE INVENTION

[0014] The present invention generally relates to the preparation of mineral complexes, especially calcium complexes, of lactobionic acid which are especially useful for mineral fortification of food and beverage products. For the purposes

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of this invention, the use of the term "lactobionic acid" also includes its lactone as well as mixtures of the acid and its lactone. (See, e.g., Dutta et al., "Study of the Lactone-Acid-Salt Equilibria and Hydrolysis Kinetics for Lactobionic - Lactone," Indian J. Chem., vol 9, 229-232 (March 1971).) The mineral complexes produced according to the present invention include calcium complexes of lactobionic acid, magnesium complexes of lactobionic acid, potassium complexes of lactobionic acid, sodium complexes of lactobionic acid, iron complexes of lactobionic acid, zinc complexes of lactobionic acid, copper complexes of lactobionic acid, chromium complexes of lactobionic acid, selenium complexes of lactobionic acid, manganese complexes of lactobionic acid, and the like. Mixtures of these mineral complexes may also be used. The mineral complexes of lactobionic acid provided in the present invention delivers a soluble, stable, clean tasting mineral source suitable for mineral fortification of a wide variety of food and beverage products. The high solubility of the mineral complexes produced according to the present invention in water allows for the preparation of mineral-fortification of foods and beverages which are clean tasting and non-gritty. The preferred mineral complex produced according to the present invention is the calcium complex of lactobionic acid.

[0015] The mineral complexes of lactobionic acid produced according to the present invention are prepared by mixing lactobionic acid with a mineral source selected from a mineral hydroxide, a mineral carbonate, a mineral oxide, or mixtures thereof with an edible acid such as citric acid, lactic acid, acetic acid, malic acid, gluconic acid, tartaric acid, fumaric acid, adipic acid, succinic acid, ascorbic acid, phosphoric acid, or mixtures thereof. Thus, the preferred calcium complex of lactobionic acid produced according to the present invention is prepared by mixing lactobionic acid with a calcium source such as calcium hydroxide, calcium carbonate, calcium oxide, or mixtures thereof with an edible acid such as citric acid, lactic acid, acetic acid, malic acid, gluconic acid, tartaric acid, fumaric acid, adipic acid, succinic acid, ascorbic acid, phosphoric acid, or mixtures thereof. Generally, an aqueous solution containing about 1 to about 95 percent lactobionic acid is mixed with about 1 to about 50 percent of the mineral source (e.g., calcium source) and about 1 to about 50 percent of the edible acid to form the desired mineral complex; generally the pH of the final aqueous solution is about 2 to about 8. More preferably, an aqueous solution containing about 50 to about 90 percent lactobionic acid is mixed with about 5 to about 25 percent of the mineral source (e.g., calcium source) and about 2 to about 20 percent of the edible acid to form the desired mineral complex. An especially preferred calcium complex of lactobionic acid is prepared by mixing lactobionic acid with calcium hydroxide and citric acid.

[0016] The present invention is also directed to mineral-fortified food and beverage products comprising about 0.2 to about 20 percent of obtainable by the above method

[0017] Preferably, a single serving of the mineral-fortified food or beverage products of the present invention contain sufficient quantities of the mineral in the form of the corresponding mineral complex of lactobionic to provide about 5 to about 200 percent of the recommended United States Daily Value of calcium, more preferably about 10 to about 35 percent of the recommended United States Daily Value of that mineral. Calcium fortification of food and beverage products using the calcium complex of lactobionic acid of the present invention is especially preferred.

#### BRIEF DESCRIPTION OF THE DRAWING

[0018]

Figure 1 shows the Differential Scanning Calorimetry results (top portion of each panel) and the Thermal Gravimetric Analysis results (bottom portion of each panel) for crystalline calcium salt of lactobionic acid (Panel A), crystalline citric acid (Panel B), a mixture of crystalline calcium salt of lactobionic acid and crystalline citric acid (Panel C), and an inventive calcium lactobionic acid complex (Panel D).

#### DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS OF THE INVENTION

[0019] The mineral complexes produced according to the present invention are prepared by mixing lactobionic acid, a mineral source, and an edible acid in an aqueous solution. The mineral complexes produced according to the present invention include calcium complexes, magnesium complexes, potassium complexes, sodium complexes, iron complexes, zinc complexes of lactobionic acid and the like. Mixtures of these mineral complexes may also be used. The calcium complex of lactobionic acid is especially preferred. The mineral sources are selected from mineral hydroxides, mineral carbonates, mineral oxides, or mixtures thereof. Generally, the preferred mineral source is the corresponding mineral hydroxide. Suitable edible acids include citric acid, lactic acid, acetic acid, malic acid, gluconic acid, tartaric acid, fumaric acid, adipic acid, succinic acid, ascorbic acid, phosphoric acid, or mixtures thereof. Generally, the preferred edible acid is citric acid.

[0020] The mineral complexes produced according to the present invention are sufficiently soluble in food or beverage products to provide at least about 5 percent, and in some cases, depending on the actual product, much higher, of the current United States recommended Daily Value of the mineral per single serving size of the food or beverage product. For purposes of this invention, a single serving size for a food product is about 28 g and for a beverage product is about

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240 ml or 8 ounces. For purposes of this invention, the current United States recommended Daily Value of the mineral is considered to be the value published by the United States Food and Drug Administration as of the filing date of the current application. The current United States recommended Daily Value for calcium is 1000 mg per day.

[0021] The preferred calcium complex of lactobionic acid produced according to the present invention is prepared by mixing lactobionic acid with a calcium source such as calcium hydroxide, calcium carbonate, calcium oxide, or mixtures thereof with an edible acid such as citric acid, lactic acid, acetic acid, malic acid, gluconic acid, tartaric acid, fumaric acid, adipic acid, succinic acid, ascorbic acid, phosphoric acid, or mixtures thereof. Generally, an aqueous solution containing about 5 to about 95 percent lactobionic acid is mixed with about 1 to about 50 percent of the mineral source (e.g., calcium source such as calcium hydroxide in the preferred embodiment) and about 1 to about 50 percent of the edible acid (e.g., citric acid in the preferred embodiment) to form the desired mineral complex; generally the pH of the final aqueous solution is about 2 to about 8. More preferably, an aqueous solution containing about 50 to about 90 percent lactobionic acid is mixed with about 5 to about 25 percent of the mineral source and about 2 to about 20 percent of the edible acid to form the desired mineral complex. Generally, mixing of the components is carried out at or near room temperature. An especially preferred calcium complex of lactobionic acid is prepared by mixing lactobionic acid with calcium hydroxide and citric acid. Mixed complexes can also be prepared if desired by mixing two or more mineral sources with lactobionic acid and the edible acid. Physical mixtures of two or more separately prepared mineral complexes can also be used.

[0022] The mineral complexes produced according to this invention can be prepared by combining the lactobionic acid, mineral source, and edible acid in an aqueous solution. The mineral complex may be maintained as formed in the aqueous solution or may be collected as a solid complex by removing the water medium using any conventional drying technique. Generally it is preferred that the mineral complexes are collected in a solid form; the solid complexes will generally be easier to store and use. Conventional methods can be used to collect the solid mineral complex. Generally, however, gentle methods such as freeze drying, spray drying, drum drying, and the like are preferred to remove the water and obtain the solid mineral complex.

[0023] Lactobionic acid is generally a white crystalline powder. Lactobionic acid may be obtained commercially (e.g., Lonza Inc., Fairlawn, N.J.; Sigma, St. Louis, MO) or prepared through chemical or enzymatic oxidation of lactose or a lactose-containing substrate. The lactobionic acid can be prepared by saccharide chemical oxidation or bioconversion processes (e.g., catalytic action of a carbohydrate oxidase enzyme) using lactose or a lactose-containing substrate (e.g., whey or whey permeate) as the starting material. Suitable carbohydrate oxidase enzymes include, for example, lactose oxidase, glucose oxidase, hexose oxidase, and the like, as well as mixtures thereof. Generally, lactose oxidase is preferred. A particularly suitable enzyme for lactose oxidation has been developed by Novozymes A/S and is described in WO 9931990.

[0024] Cellobiose dehydrogenase is also a useful enzyme for converting lactose to lactobionic acid. Canevascini et al., Zeitschrift für Lebensmittel Untersuchung und Forschung, 175: 125-129 (1982). This enzyme is, however, complex and requires the use of a relatively expensive co-factor (e.g., quinones, cytochrome C, Fe(III), and the like); it also requires immobilization. Also, a second enzyme, laccase, is required to regenerate the co-factor used with cellobiose dehydrogenase. The use of glucose-fructose oxidoreductase to oxidize lactose results in two products, sorbitol and lactobionic acid, and a further separation procedure is necessary to recover the lactobionic acid product. Nidetzky et al., Biotechnology and Bioengineering, Vol. 53 (1997). Nonetheless, glucose-fructose oxidoreductase also is a suitable enzyme for the practice of this embodiment of the invention. Of course, other methods can be used to prepare the lactobionic acid for use in the present invention.

[0025] The mineral complexes produced according to the present invention can be incorporated into various food and beverage products to provide mineral-fortification food and beverage products. The mineral-fortified food and beverage products of this invention will contain about 0.2 to about 20 percent of the mineral complex of lactobionic acid. Preferably, a single serving of the mineral-fortified food or beverage products of the present invention contain sufficient quantities of the mineral in the form of the corresponding mineral complex of lactobionic to provide about 5 to about 200 percent of the recommended United States Daily Value of calcium (i.e., about 50 to about 2000 mg calcium), more preferably about 10 to about 35 percent of the recommended United States Daily Value of calcium (i.e., about 100 to about 350 mg calcium). Calcium fortification of food and beverage products using the calcium complex of lactobionic acid of the present invention is especially preferred.

[0026] Having generally described the embodiments of the process illustrated in the figures as well as other embodiments, the invention will now be described using specific examples which further illustrate various features of the present invention but are not intended to limit the scope of the invention, which is defined in the appended claims. All percentages used herein are by weight, unless otherwise indicated.

**EXAMPLE 1.** Lactobionic acid crystals (58 g; Lonza Inc., Fairlawn, NJ) were completely dissolved in 500 g deionized water. Citric acid (6 g; Sigma, St. Louis, MO) was then completely dissolved in the solution; calcium hydroxide (10 g; Sigma, St. Louis, MO) was then completely dissolved in the solution. The final pH of the calcium complex solution was about 4.6. The aqueous solution was mixed for about 10-30 minutes at room temperature and then freeze dried. About

65 g (about 87 percent yield) of the desired white solid calcium complex containing about 8 percent calcium was obtained. The calcium complex was dissolved in water at room temperature to provide a clear solution with about 2000 mg calcium per single beverage serving size (i.e., about 240 ml or 8 ounces). The calcium complex was more soluble than calcium citrate; it contained more calcium and had better flavor than pure calcium lactobionate available commercially. Thus, the calcium complex was better suited in food and beverage applications than other calcium salts or commercially available calcium lactobionate.

**EXAMPLE 2.** A fortified liquid beverage was prepared using the calcium complex of Example 1. The following formulations were prepared by simply mixing the components together at room temperature:

|                                                              | Inventive (%) | Control (%) |
|--------------------------------------------------------------|---------------|-------------|
| Calcium Complex                                              | 2.1           | 0           |
| Water                                                        | 96.8          | 98.9        |
| Flavor                                                       | 0.3           | 0.3         |
| Citric Acid/Malic Acid                                       | 0.5           | 0.5         |
| Colorant                                                     | 0.0001        | 0.0001      |
| Preservative (EDTA, sorbate, benzoate, or potassium citrate) | 0.17          | 0.17        |
| Artificial Sweetener<br>(sucralose or acesulfame K)          | 0.05          | 0.05        |
| Clouding Agent (Givaudan Flavors Corp.)                      | 0.06          | 0.06        |

The inventive sample provided about 300 mg calcium per serving (about 240 ml). The control sample was prepared in the same manner as the inventive sample except that it did not contain any of the calcium complex. Samples of the inventive and control samples (20 ml at room temperature) were provided to a trained panel of 17 members in a discrimination sensory test. No significant differences were detected between the inventive and the control samples. Thus, the inventive calcium fortified sample provided a sensory impression essentially identical with the control sample and had no off-flavors, objectionable sensory notes, or textural defects.

**Example 3.** Combinations of calcium lactobionic acid (Sigma, St. Louis, MO) with either monocalcium citrate or tricalcium citrate were compared with the calcium complex of Example 1 in similar beverages as described in Example 2 above. The various salts and the calcium complex were added at levels to provide about 1000 mg calcium per single serving. Beverages were prepared containing the following amounts of calcium salts or inventive calcium complex:

| Sample         | Calcium Lactobionic<br>Acid<br>(5.3% Ca) | Monocalcium Citrate<br>(9% Ca) | Tricalcium Citrate<br>(21% Ca) | Inventive Calcium<br>Complex<br>(8% Ca) |
|----------------|------------------------------------------|--------------------------------|--------------------------------|-----------------------------------------|
| Comparative #1 | 15.8 g                                   | 1.8 g                          | -                              | -                                       |
| Comparative #2 | 15.8 g                                   | -                              | 0.76 g                         | -                                       |
| Inventive      | -                                        | -                              | -                              | 12.5 g                                  |

Similar water samples containing the above amounts of calcium salts or calcium complex were also prepared. The calcium complex dissolved easily in either the beverage formulation or water to provide a clean tasting, non-gritty beverage. Comparative samples #1 and #2, however, were not completely soluble in either the beverage formulation or water.

**EXAMPLE 4.** The calcium content of the inventive beverage of Example 2 was increased to provide about 1000 mg calcium (i.e., about 100 percent of the DV of calcium) per 240 ml single serving size. The calcium complex completely dissolved in the beverage. The resulting beverage had acceptable flavor and appearance.

**EXAMPLE 5.** Beverages as prepared in Examples 2 and 3 containing the inventive calcium complex of Example 1 as well as aqueous solutions containing similar amounts of the calcium complex of Example 1 were stored under refrigerated conditions. Similar levels of conventional calcium sources (e.g., monocalcium citrate, tricalcium citrate, and calcium fumarate) were prepared in aqueous solutions or similar beverages formed noticeable sediments within about 1 week under such storage conditions. No sediments or precipitates were observed in the samples containing the calcium complex produced according to the present invention after 7 months of refrigerated storage.

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**EXAMPLE 6.** This examples illustrates several methods of preparing the calcium complex other than the one described in Example 1.

- (1) Lactobionic acid (29 g) was dissolved in 250 ml water to which was added calcium hydroxide (5 g) with stirring. Stirring was continued for about 10 minutes, after which citric acid (3 g) was added. Within a few minutes, all solids were completely dissolved. The final pH of the resulting calcium complex solution was about 6.0.
- (2) Lactobionic acid (29 g) and citric acid (3 g) were dissolved in water (250 ml). Calcium hydroxide (5 g) was then completely dissolved in the water solution to provide the calcium complex. The final pH of the resulting calcium complex solution was 7.0.
- (3) A calcium complex was prepared as in subpart (1) above except that the amount of lactobionic acid was increased to 35.5 g. The final pH of the resulting calcium complex solution was 4.2.

The calcium complexes prepared in subparts (1) - (3) were evaluated in the same manner as in Examples 2, 3, and 4 above. Performance was essentially the same as the calcium complex as prepared in Example 1.

**EXAMPLE 7.** A zinc complex was prepared by mixing water (250 g), lactobionic acid (55 g), zinc carbonate (10 g), and citric acid (10 g). The final pH of the solution was about 3.4. A portion of the zinc complex was freeze dried. The freeze dried zinc complex was sufficiently soluble in water such that a clean tasting beverage could be prepared containing 200 percent of the United States Daily Value of zinc.

**EXAMPLE 8.** A calcium complex of lactobionic acid was prepared as in Example 1 except that lactic acid was used according to the following fomulation.

|  | Ingredient        | Weight (g) |
|--|-------------------|------------|
|  | Water             | 400        |
|  | Lactobionic Acid  | 60         |
|  | Calcium Hydroxide | 10         |
|  | Lactic Acid (85%) | 9          |

The resulting calcium complex solution had a final pH of about 4.7. A portion of the calcium complex was freeze dried. It exhibited good solubility in water.

**Example 9.** Differential Scanning Calorimeter and Thermal Gravimetric Analyst of (A) crystalline calcium salt of lactobionic acid, (B) crystalline citric acid, (C) a mixture of crystalline calcium salt of lactobionic acid and crystalline citric acid, and (D) an inventive calcium lactobionic acid complex as prepared in Example 1 above. The results are shown in Figure 1 wherein for each Panel the Differential Scanning Calorimetry is on the top and the Thermal Gravimetric Analysis is on the bottom. The results obtained shown that the inventive calcium lactobionic acid complex (Panel D) is very different from the calcium salt of lactobionic acid (Panel A), citric acid (Panel B), or mixtures thereof (Panel C).

#### Claims

1. A method of preparing a mineral complex of lactobionic acid comprising lactobionic acid, a mineral source, and an edible acid, wherein the mineral complex is prepared by mixing lactobionic acid, the mineral source, and the edible acid in an aqueous solution and wherein the mineral complex is prepared by mixing 5 to 95 percent by weight lactobionic acid, 1 to 50 percent by weight of the mineral source, and 1 to 50 percent by weight of the edible acid in the aqueous solution; and wherein the mineral source is a mineral hydroxide, a mineral carbonate, a mineral oxide or mixtures thereof
2. The method of Claim 1, wherein the edible acid is citric acid, lactic acid, acetic acid, malic acid, gluconic acid, tartaric acid, fumaric acid, adipic acid, succinic acid, ascorbic acid, phosphoric acid, or mixtures thereof.
3. The method of Claim 1 or 2, wherein the mineral complex is prepared by mixing 50 to 90 percent by weight lactobionic acid, 5 to 25 percent by weight of the mineral source, and 2 to 20 percent by weight of the edible acid in the aqueous solution.
4. The method of any one of Claims 1 to 3,

wherein the mineral is calcium, magnesium, potassium, sodium, iron, zinc, copper, chromium, selenium, manganese, or mixtures thereof.

5. The method of any one of Claims 1 to 4, wherein the mineral is calcium.
6. A mineral-fortified food or beverage product comprising 0.2 to 20 percent by weight of a mineral complex obtainable according to the method of any one of Claims 1 to 5

#### Patentansprüche

1. Verfahren der Herstellung eines Lactobionsäure, eine Mineralquelle und eine Speisesäure enthaltenden Mineralkomplexes der Lactobionsäure, bei dem der Mineralkomplex durch Mischen von Lactobionsäure, der Mineralquelle und der Speisesäure in einer wässrigen Lösung hergestellt wird und bei dem der Mineralkomplex durch Mischen von 5 bis 95 Gew.-% Lactobionsäure, 1 bis 50 Gew.-% der Mineralquelle und 1 bis 50 Gew.-% der Speisesäure in der wässrigen Lösung hergestellt wird und bei dem die Mineralquelle ein mineralisches Hydroxid, ein mineralisches Carbonat, ein mineralisches Oxid oder Gemische davon ist.
2. Verfahren des Anspruchs 1, bei dem die Speisesäure Zitronensäure, Milchsäure, Essigsäure, Äpfelsäure, Gluconsäure, Weinsäure, Fumarsäure, Adipinsäure, Bernsteinsäure, Ascorbinsäure, Phosphorsäure oder Gemische davon ist.
3. Verfahren des Anspruchs 1 oder 2, bei dem der Mineralkomplex durch Mischen von 50 bis 90 Gew.-% Lactobionsäure, 5 bis 25 Gew.-% der Mineralquelle und 2 bis 20 Gew.-% der Speisesäure in der wässrigen Lösung hergestellt wird.
4. Verfahren eines der Ansprüche 1 bis 3, bei dem das Mineral Calcium, Magnesium, Kalium, Natrium, Eisen, Zink, Kupfer, Chrom, Selen, Mangan oder Gemische davon ist.
5. Verfahren eines der Ansprüche 1 bis 4, bei dem das Mineral Calcium ist.
6. Mineralangereichertes Nahrungsmittel- oder Getränkeprodukt mit 0,2 bis 20 Gew.-% eines Mineralkomplexes, der nach dem Verfahren eines der Ansprüche 1 bis 5 erhältlich ist.

#### Revendications

1. Procédé de préparation d'un complexe minéral de l'acide lactobionique contenant de l'acide lactobionique, une source minérale et un acide comestible, dans lequel le complexe minéral est préparé en mélangeant l'acide lactobionique, la source minérale et l'acide comestible dans une solution aqueuse et dans lequel le complexe minéral est préparé en mélangeant de 5 à 95 pour cent en poids d'acide lactobionique, de 1 à 50 pour cent en poids de la source minérale et de 1 à 50 pour cent en poids de l'acide comestible dans une solution aqueuse ; et dans lequel la source minérale est un hydroxyde minéral, un carbonate minéral, un oxyde minéral ou leurs mélanges.
2. Procédé selon la revendication 1, dans lequel l'acide comestible est l'acide citrique, l'acide lactique, l'acide acétique, l'acide malique, l'acide gluconique, l'acide tartrique, l'acide fumarique, l'acide adipique, l'acide succinique, l'acide ascorbique, l'acide phosphorique ou leurs mélanges.
3. Procédé selon la revendication 1 ou 2, dans lequel le complexe minéral est préparé en mélangeant de 50 à 90 pour cent en poids d'acide lactobionique, de 5 à 25 pour cent en poids de la source minérale et de 2 à 20 pour cent en poids de l'acide comestible dans une solution aqueuse.
4. Procédé selon l'une quelconque des revendications 1 à 3, dans lequel le minéral est du calcium, du magnésium, du potassium, du sodium, du fer, du zinc, du cuivre, du chrome, du sélénium, du manganèse ou leurs mélanges.

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5. Procédé selon l'une quelconque des revendications 1 à 4, dans lequel le minéral est du calcium.
6. Produit alimentaire ou boisson enrichis en minéraux comprenant de 0,2 à 20 pour cent en poids d'un complexe minéral pouvant être obtenu selon le procédé de l'une quelconque des revendications de 1 à 5.

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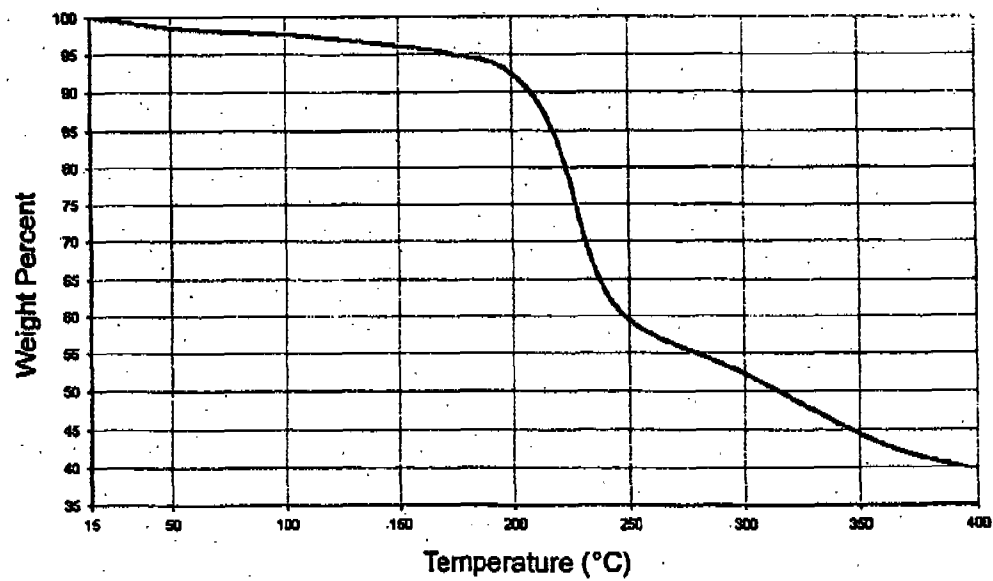
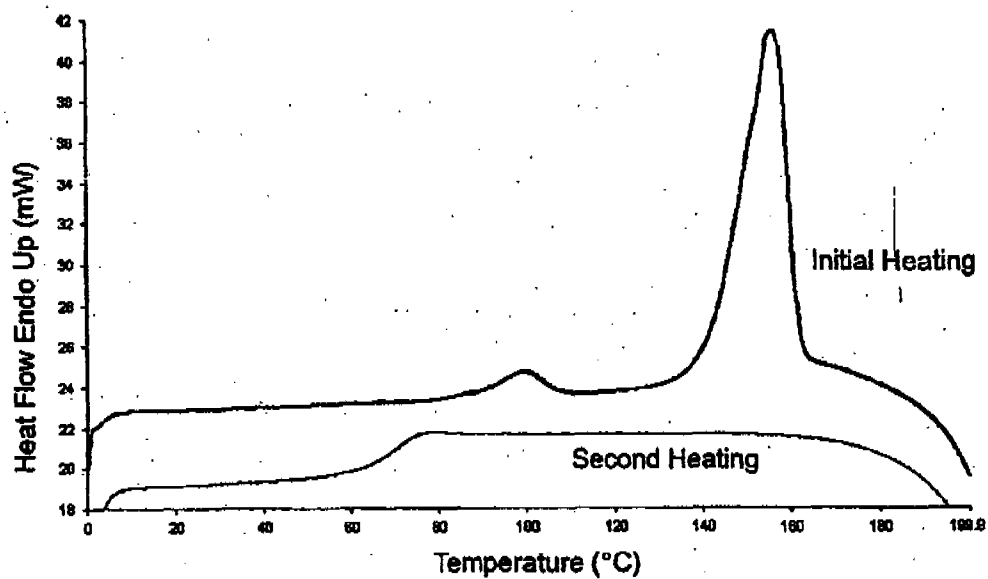
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Figure 1

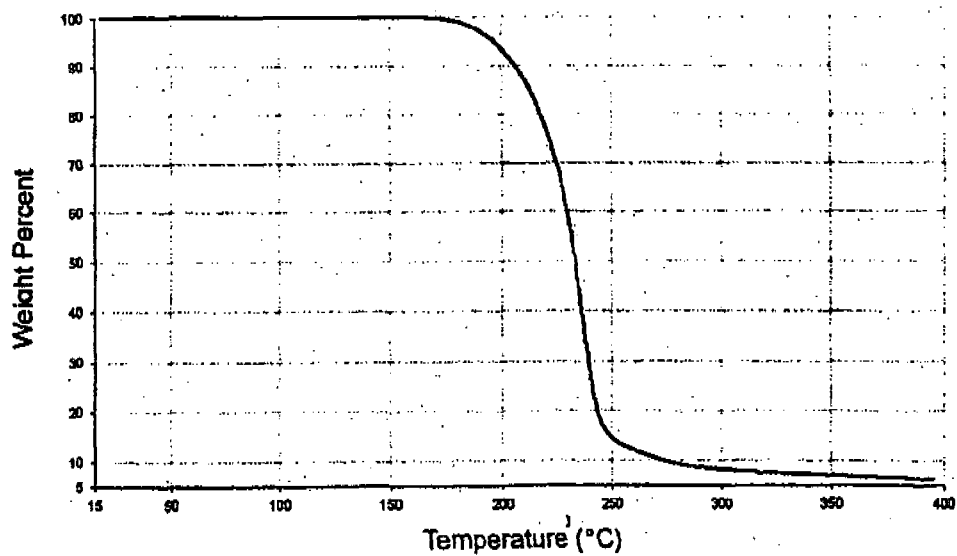
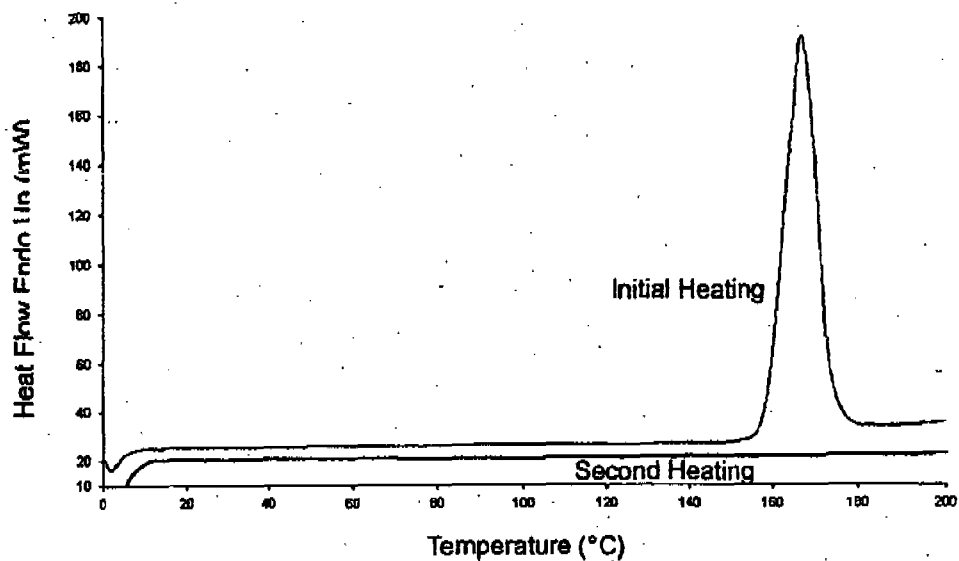


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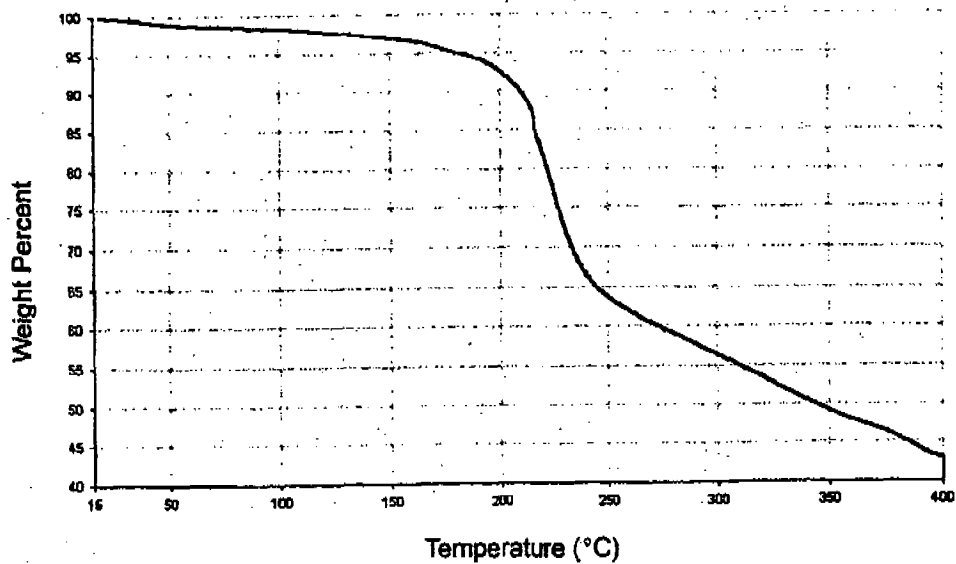
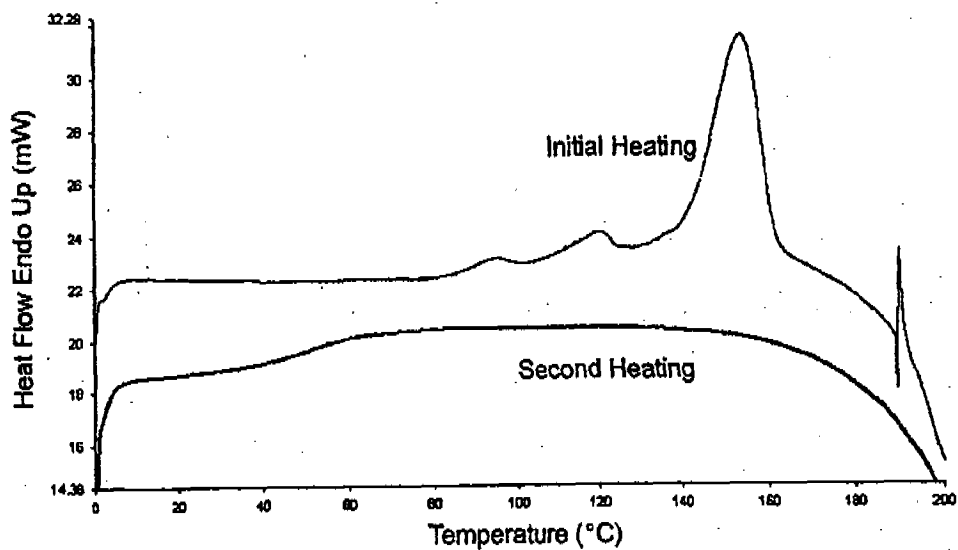
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S4

Figure 1 (cont)

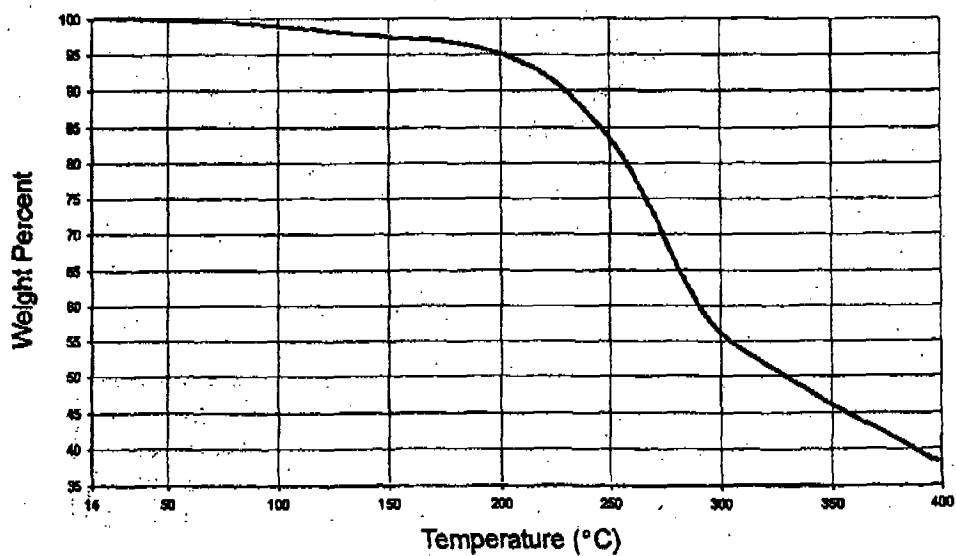
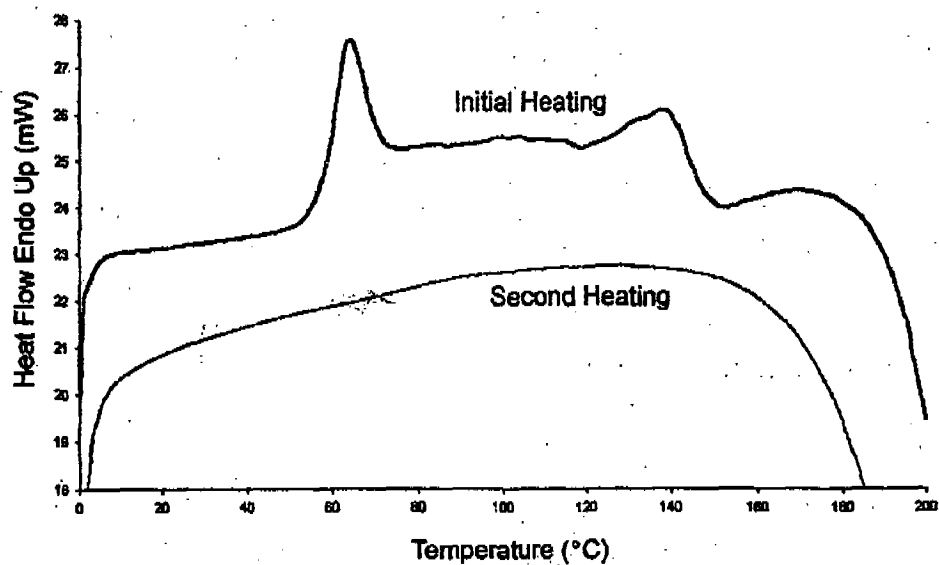


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**Figure 1 (cont)****C**

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**Figure 1 (cont)**



**D**

REFERENCES CITED IN THE DESCRIPTION

*This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.*

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

**Radicación No. 04-17688**

**Clasificación Internacional (IPC): A23L 2/02 y A23L 1/304.**

**Concepto Técnico No. 4101**

Como resultado del examen definitivo, realizado con fundamento en el artículo 48 de la Decisión 486 de la Comisión de la Comunidad Andina, se le comunica:

**1. DOCUMENTOS ESTUDIADOS.**

- Capítulo descriptivo: folios 9 al 11
- Capítulo reivindicatorio: folios 12 al 15 (capítulo reivindicatorio original)  
Folio: 97 (capítulo reivindicatorio modificado)
- Respuesta del solicitante: Folios: 90 a 96

Se acepta reivindicación de prioridad US 10/377.541 del 28 de Febrero de 2003

**2. OBJETO DE LA INVENCION.**

**Título:** "Complejos minerales de ácido lactobiónico y método de usarlos para fortificación mineral de productos alimenticios".

La invención se refiere a :

Reivindicación 1: Método para preparar un complejo mineral de ácido lactobiónico que comprende ácido lactobiónico, una fuente mineral y un ácido comestible ; caracterizado por que el complejo mineral se prepara mezclando ácido lactobiónico, la fuente mineral y el ácido comestible en una solución acuosa y en donde el complejo mineral se prepara mezclando del 5 al 95% de peso de ácido lactobiónico 1 a 50% de peso de una fuente mineral y 1 a 50% de peso de ácido comestible en una solución acuosa y en el que la fuente mineral es un hidróxido mineral , un carbonato mineral, un óxido mineral o mezclas de los mismos..

Reivindicaciones 2 a 6: El ácido comestible es ácido cítrico, ácido láctico, ácido acético, ácido málico, ácido glucónico, ácido tartárico, ácido fumárico, ácido adipico, ácido succínico, ácido ascórbico, ácido fosfórico o mezclas de los mismos. El mineral es calcio, magnesio, potasio, sodio, hierro, cromo, cobre, selenio, manganeso o mezclas.

Clasificación Internacional de Patentes: A23L 2/02 y A23L 1/304.

El solicitante realizó modificaciones al capítulo reivindicatorio las cuales fueron aceptadas y sobre dicho capítulo reivindicatorio modificado se presenta este concepto.

### 3. DETERMINACIÓN DEL ESTADO DE LATÉCNICA

*La fecha que se ha tenido en cuenta para determinar el Estado de la Técnica es la fecha de presentación de la solicitud prioritaria la cual corresponde al 28 de Febrero del 2003.*

*Teniendo en cuenta la fecha indicada se realizó la búsqueda en el estado de la técnica de documentos relacionados con la solicitud encontrándose los siguientes documentos más relevantes:*

| Nº | DOCUMENTO    | TÍTULO                                                                                                                          | FECHA DE PUBLICACIÓN |
|----|--------------|---------------------------------------------------------------------------------------------------------------------------------|----------------------|
| D1 | JP 07-277991 | Mineral absorption-stimulating agent                                                                                            | 1995-10-24           |
| D2 | ES 8406196 A | Procedimiento de obtención de una solución inyectable a base de un complejo mixto de hierro férrico polinuclear y electroneutro | 1983-10-14           |
| D3 | US 5,290,766 | Cardioplegic Composition                                                                                                        | 1976-10-26           |

### 4. EVALUACIÓN DE LOS REQUISITOS DE PATENTABILIDAD

#### 4.1. Evaluación de NOVEDAD.

La anterioridad D1 presenta un agente que estimula la absorción mineral; dicho agente contiene ácido lactobiónico como principio activo. Para este agente se observa un gran efecto que estimula la absorción de minerales requeridos por los organismos vivos; tales como calcio, hierro y magnesio. Dicho agente es utilizado como aditivo para medicinas, bebidas y otros. Para que se presente el efecto estimulante es preferible ingerir dosis de  $> 1$  mg/Kg peso/día para un hombre adulto. El ácido lactobiónico se puede formular en cualquier tipo de alimento; incluso en dulces o gomas de mascar. En la anterioridad D1 se presenta a manera de ejemplo la preparación de una formulación que contiene calcio, almidón de maíz, celulosa cristalina, carboximetil celulosa de calcio y ácido lactobiónico. Como otro ejemplo se presenta una formulación para una bebida de jugo de frutas el cual incluye azúcar, jugo de fruta, ácido cítrico, ácido lactobiónico, perfume y agua.

Como se puede apreciar en esta anterioridad las composiciones que contienen ácido lactobiónico con minerales y ácido comestible son conocidas en el arte previo así como el efecto que presenta el ácido lactobiónico en la absorción de minerales tales como el calcio, uno de los principales para el organismo humano. El complejo formado por el ácido lactobiónico con el mineral y el ácido comestible es posible adicionarlo a productos alimenticios. Por lo anterior, tal como se presenta la solicitud; esta carece de novedad ya que la composición reivindicada es conocida en el arte previo.

#### 4.2. Evaluación del NIVEL INVENTIVO

La anterioridad D2 se encuentra presentando una formulación para un compuesto inyectable la cual consta de ácido lactobiónico, dextrano, ácido acético. Se prefiere la utilización del ácido lactobiónico en lugar del contenido en dextrano completo. El átomo de hierro central de éste complejo se une a ligandos lactobionato, acetato o hidróxido. La esfera de coordinación formada con varios ligandos asegura que se libera hierro in vivo en varias etapas a partir del complejo. Esto se

traduce en una absorción más prolongada y en menor toxicidad que las observadas con los preparados de uso comercial.

En la anterioridad D3 se esta presentando una solución acuosa que proporciona función cardiaca después de un periodo de exposición a cardioplegia. Esta solución contiene NaCl, KCl,  $\text{CaCl}_2$ ,  $\text{MgCl}_2$ ,  $\text{NaHCO}_3$ , D-Glucosa, L-aspartico y ácido lactobiónico.

Como se puede observar en las anterioridades citadas el ácido lactobiónico es conocido como un compuesto acomplejante de cationes minerales, el cual permite una liberación controlada del metal. Este se ha formulado con metales tales como calcio y hierro. En la anterioridad D2 se ha observado en presencia de formulaciones con ácido acético.

La composición presenta en la anterioridad D3 contiene sales provenientes de sodio, potasio y calcio, las cuales se encuentran acomplejadas con ácido lactobiónico. En esta composición también se encuentra Glucosa y ácido aspartico. Esta solución es utilizada para la recuperación de la función cardiaca en pacientes que presentan alguna disfunción cardiaca.

De esta manera, la composición reivindicada es posible derivarla de una manera evidente del estado de la técnica ya que el efecto acomplejante del ácido lactobiónico es conocido por lo que es posible conocer los ligandos que pueden hacer parte del complejo entre ellos los minerales, los cuales presentarán mayor biodisponibilidad que al encontrarse en su forma libre. Por lo tanto la solicitud carece de nivel inventivo.

En conclusión los requisitos de patentabilidad de la presente solicitud se encuentran afectados así:

| Nº | DOCUMENTO    | REIVINDICACIONES AFECTADAS | REQUISITO QUE AFECTA |
|----|--------------|----------------------------|----------------------|
| D1 | JP 07-277991 | 1 a 6                      | NOVEDAD              |
| D2 | ES 84(6196 A | 1 a 6                      | NIVEL INVENTIVO      |
| D3 | US 5,290,766 | 1 a 6                      | NIVEL INVENTIVO      |

##### 5. Respuesta a los argumentos del solicitante:

El método que se presenta en la reivindicación 1 no muestra características técnicas por medio de las cuales se pueda diferenciar de una mezcla convencional de principios activos. Por lo tanto, la anterioridad D1 afecta la novedad de la solicitud ya que en ella se presenta la mezcla del ácido lactobiónico con calcio en solución acuosa (folio 119) de igual forma que en la solicitud. Por su parte, la anterioridad D1 se encuentra presentando a manera de ejemplos las mezclas de ácido lactobiónico con diferentes mezclas minerales (folio 120), así como estudios en los cuales se observa una mayor absorción de calcio y magnesio al adicionar a la composición ácido lactobiónico.

Por su parte, la combinación de los documentos D2 y D3 afecta el nivel inventivo de la composición presentada ya que en dichas anterioridades se presentan mezclas de ácido lactobiónico con minerales y ácido lactobiónico con ácido acético; por lo que en estos documentos se presentan los componentes principales de la composición de la solicitud; así se demuestra que los complejos de ácido lactobiónico con minerales y ácidos orgánicos se conocen en el estado

del arte; por lo que una persona de nivel medio versada en la materia preparar la composición de la solicitud.

En consecuencia y por todo lo expuesto anteriormente, se recomienda **Negar** las reivindicaciones: 1 a 6 (folios: 97).

Bogotá, D.C., 28 de Noviembre del 2009.

|                                            |                                               |
|--------------------------------------------|-----------------------------------------------|
| <b>CONCEPTO TECNICO No.</b><br><b>4101</b> | <b>EXAMINADOR TECNICO</b><br>Código No.202064 |
|--------------------------------------------|-----------------------------------------------|