

06-122967.54
CASTELLANOS & CO LTDA
ABOGADOS
Calle 94 A No. 7 A-09
Bogotá, D.C. - COLOMBIA

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 06-122967- -00002-0000

Fecha: 2007-10-01 15:34:24 Dep. 2020 NUECREACION
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
Act. 538 PETICION Folios: 2

Señor

Jefe de la División de Nuevas Creaciones

Superintendencia de Industria y Comercio

Ministerio de Comercio, Desarrollo, Industria y Turismo

E. S. D.

Re.: Expediente No. **06.122.967**

Solicitud del examen de patentabilidad correspondiente a la Patente PCT

Entrada en Fase Nacional, para:

"NUEVA FORMULACION FARMACEUTICA DE CEFIXIMA CON MEJOR BIODISPONIBILIDAD"

Solicitante: **LUPIN LIMITED**

SOLICITUD EXAMEN DE PATENTABILIDAD

(CAPITULO I)

Yo, **MARGARITA CASTELLANOS ABONDANO**, mayor de edad, identificada y domiciliada como aparece al pié de mi firma, obrando en mi calidad de apoderada de la sociedad solicitante, atentamente me permito solicitar a Ud. que se realice el examen de patentabilidad de la invención arriba citada, para lo cual anexo el comprobante de pago **No. 07- 78.971** de **Septiembre 28 de 2007**, correspondiente a la tasa establecida para dicha solicitud.

En consecuencia, atentamente solicito a Ud. se anexe este memorial junto con el comprobante de pago al expediente correspondiente a esta solicitud de Patente PCT Entrada en Fase Nacional, y se continúe con su tramitación.

Señor Jefe,

Margarita Castellanos Abondano
C.C. No. **39.779.654** de Usaquén
T.P.A. No. **70.819** del C. S. J.
Calle 94 A No. 7 A-09 - Bogotá, D.C.
Teléfono (PBX): 610 7420

Bogotá, **01 OCT. 2007**
MCA/gcb/P1428

SS
55

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

NIT : 800176089-2

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 06-122967- -00002-0000

Fecha: 2007-10-01 15:34:24 Dep. 2020 NUECREACIONE
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RECIBO OFICIAL DE CAJA : 07 - 78,971
CHA : SEPTIEMBRE 28 DE 2007

***** CONSIGNACION *****

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PGO	Vr. PAGO
ALVARO CASTELLANOS	CONSIGNACION	BANCO POPULAR	050-00110-6	63492136	28/09/2007	12,883,000.00

***** CONCEPTO *****

ANT. RENTISTICO	CONCEPTO	TOTAL CONCEPTO
1 50005-01-01 SOLICITUDES	85 EXAMEN DE PATENTABILIDAD DE INVEN	404,000.00
	TOTAL :	\$ 404,000.00

SON: CUATROCIENTOS CUATRO MIL PESOS

RESPONSABLE :

RECIBO DE CAJA APLICADO AL EXPEDIENTE No. _____

DIVISIÓN DE NUEVAS CREACIONES

RADICACIÓN EXPEDIENTE No. 06-122967

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

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

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

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

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

SE PRESENTARON OPOSICIONES POR PARTE DE TERCEROS.

SI _____

NO X



US005514383A

United States Patent [19]

Laly et al.

[11] Patent Number: 5,514,383

[45] Date of Patent: May 7, 1996

[54] PROCESS FOR THE PREPARATION OF
TABLETS OF DERIVATIVES OF
CEPHALOSPORANIC ACID BY DIRECT
COMPRESSION

[75] Inventors: Jean-Louis Laly, Tours; Roberto
Lombardi, Saint Germain en Laye,
both of France

[73] Assignee: Rhone-Poulenc Rorer S.A., Cedex,
France

[21] Appl. No.: 64,049

[22] PCT Filed: Nov. 8, 1991

[86] PCT No.: PCT/FR91/00872

§ 371 Date: May 14, 1993

§ 102(e) Date: May 14, 1993

[87] PCT Pub. No.: WO92/00463

PCT Pub. Date: May 29, 1992

[30] Foreign Application Priority Data

Nov. 15, 1990 [FR] France 90 14210

[51] Int. Cl.⁵ A61K 9/20

[52] U.S. Cl. 424/464; 424/489; 424/470

[58] Field of Search 424/470, 489,
424/464, 246; 514/202, 210

[56] References Cited

U.S. PATENT DOCUMENTS

4,015,000 3/1977 Kocsis et al. 424/246
4,708,956 11/1987 Hirata et al. 514/210
5,151,417 9/1992 Sasho et al. 514/202

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Jun. 12, 1989, Ono Tomoi, Antiulcer agents containing
cefixime (salts) English Abstract.

Chemical Abstracts, vol. 109, No. 12, Abstract No. 98626a,
Jun. 28, 1988, Antibiotic drugs; cefixime trihydrate;
cefixime trihydrate tablets and cefixime trihydrate powder
for oral suspension English Abstract.

Derwent, Accession No. 89-327676, Sep. 27, 1989,
2-cephem cpds. having vinyl gp. at 3-position-useful as
antibacterial agents effective against Gram-positive and
English Abstract.

Primary Examiner—Thurman K. Page

Assistant Examiner—William E. Benston, Jr.

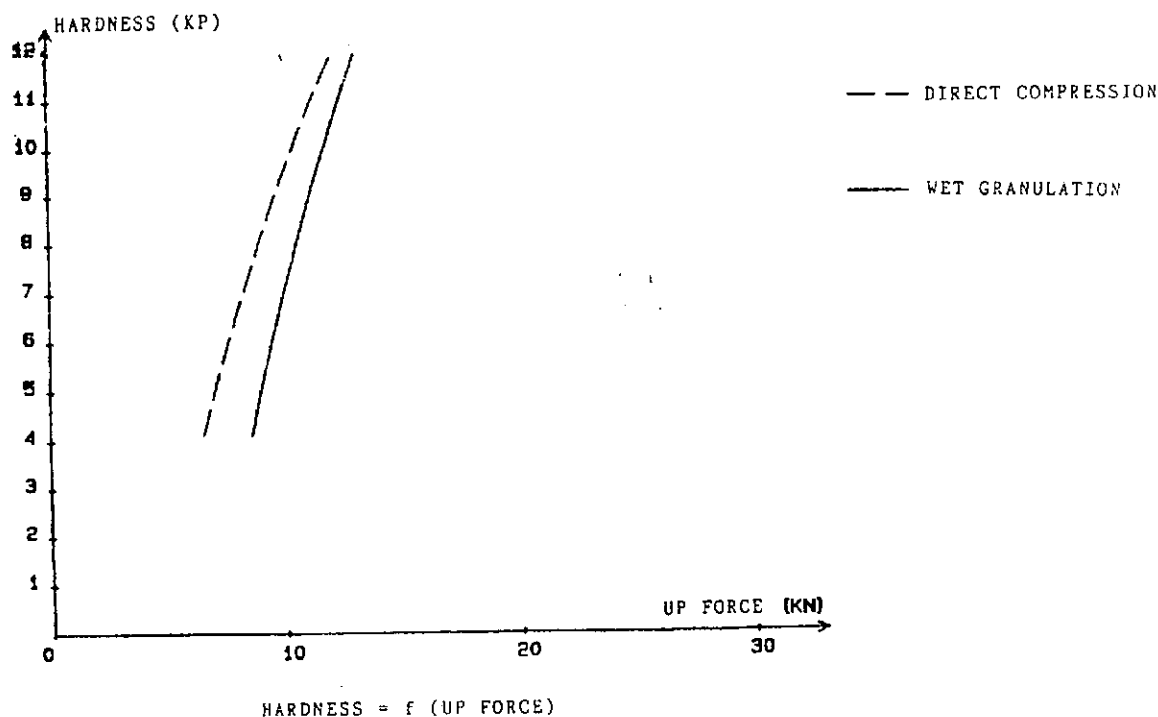
Attorney, Agent, or Firm—Ross J. Oehler

[57]

ABSTRACT

The present invention relates to a pharmaceutical form based
on cephalosporin. It relates in particular to a tableted
pharmaceutical form.

7 Claims, 1 Drawing Sheet



5,514,383

1

PROCESS FOR THE PREPARATION OF TABLETS OF DERIVATIVES OF CEPHALOSPORANIC ACID BY DIRECT COMPRESSION

The present invention relates to a new pharmaceutical form based on cephalosporin. It relates more particularly to a new tableted pharmaceutical form.

The invention relates very particularly to a new tableted pharmaceutical form based on a semi-synthetic derivative of 7-acylaminocephalosporanic acid which can be administered orally. It relates preferably to the derivatives of 7-acylamino-3-vinylcephalosporanic acid. It relates above all to the forming of (6R,7R)-7-[(Z)-2-(2-amino-4-thiazolyl)-2-carbomethoxyiminoacetamido]-8-oxo-3-vinyl-5-thia-1-aza-2-bicyclo[4.2.0]octene-2-carboxylic acid. This cephalosporin is better known under the international common name of Cefixime.

The compounds of the cephalosporin class exhibit a high antibiotic activity; their use is reserved, furthermore, to relatively severe cases when another antibiotic therapy has turned out to be unsatisfactory. These compounds from [sic] their very high activity have led some countries to create very strict legislation relating to their production. Thus, compounds of this kind may be manufactured and formed only in specific rooms, this being in order to avoid any cross-contamination with any other medication.

Another difficulty in the forming of these active substances is due to their cost. Indeed, these products are obtained by a lengthy process requiring a large number of stages of synthesis and are therefore offered, when purchased, at an extremely high material cost.

It is therefore indispensable, for the two reasons referred to above, to have a processing technique which avoids product losses as much as possible.

Insofar as the techniques of pharmaceutical forming into tablets are concerned, two preparative routes are known:

forming by a wet route

forming by direct compression.

In the first case, that is to say in the case of forming of active substances by a wet route, the following series of stages should be envisaged:

weighing the active substances and excipients

delumping and screening the various constituents of the final formulation

primary mixing of the active substance and of the excipients and checking the homogeneity of the mixture obtained

wetting of the mixture

granulation

drying

grading of the particles

dilution

final mixing

compression.

This series of stages requires the presence of eight different types of apparatus. Because of the toxicity of the active substance, the whole of the forming operation requires spotless cleaning in the case of each of these pieces of equipment. The changing of equipment on the one hand increases the cost of production significantly, since the losses cannot be reduced to a value of less than 2% and, on the other hand, prevents any automation of the process. Environmental protection and industrial hygiene are proportionally more difficult to control, the higher the number of

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stage of synthesis and of pieces of equipment. The wet route process additionally requires a drying stage with a risk of deterioration of the product which is far from being negligible. All these technical constraints, plus the legislative constraints with regard to the environment, have led industrialists to abandon forming by a wet route.

The second possible route for preparing a tableted pharmaceutical form of an active substance consists in carrying out a direct compression of a mixture of powders, a mixture which in the case of the present invention consists of the cephalosporin and excipients.

It appeared that this technique was also to be proscribed within the scope of the present invention, in view of the high proportion of the active substance in relation to excipients. The direct compression process applies generally to tablets in which the quantity of active substance is smaller than 100 mg and in which the proportion of the active substance in the tablet does not exceed 25%. Above this percentage it is impossible to "bury" the active substance in the mass of the excipients and thus to be free from the physical and chemical constraints on the active substance.

Quite astonishingly it has been found that within the scope of the present invention all these problems have been solved by carrying out a direct compression of a mixture containing a cephalosporin and one or more excipients in a weight proportion of the active substance in the tablet ranging between 20 and 90% and preferably between 30 and 70%.

The cephalosporin employed in the present invention is preferably a derivative of 7-acylamino-3-vinylcephalosporanic acid and most particularly the said derivative is that marketed under the name of Cefixime.

The excipients used are chosen especially from:

calcium carbonates

calcium phosphates

calcium sulphates

microcrystalline celluloses

cellulose powders

fructoses

the various forms of lactose

mannitols

sorbitols

starches

pregelled starches

sugars.

Lubricating agents may also be added, such as magnesium stearate, stearic acid, talc or a polyethylene glycol.

The particle size distribution of the active substance which is preferred for implementing the compression by a dry route of the present invention is the following:

fewer than 5% of particles larger than 250 μ m

between 55 and 95% of particles between 250 and 90 μ m

between 5 and 40% of particles smaller than 90 μ m.

The relative density of the active substance is preferably between 0.6 and 0.9.

The process of preparation consists in weighing the various constituents, delumping them and carrying out a first mixing with all the constituents but without the lubricating agent, and then the lubricating agent is added, the final mixing is carried out and the compression is performed. This process employs only four pieces of equipment, and this brings the advantage of reducing the losses of active substance to below 1%.

The tablets obtained by the process described above, which also form part of the invention, exhibit a friability and

cleavage criteria which are better than the same tablets manufactured by a wet-route compression. They exhibit an excellent uniformity of distribution of the active substance.

The invention will be described more completely with the aid of the following examples, which should not be considered as limiting the invention.

EXAMPLE 1

The following substances are used:

Cefixime trihydrate	184.60 kg
Pregelised starch (Starch 1500)	48.98 kg
Dicalcium phosphate dihydrate	122.44 kg
Magnesium stearate	2.03 kg
Microcrystalline cellulose (Avicel PH 102)	41.95 kg

The Cefixime trihydrate has the following particle size distribution:

The various substances, active substance and excipient are passed through a screen with a 1-mm mesh to carry out a delumping operation.

The substances are weighed and charged—except for the magnesium stearate—into a 1,000-liter mixer. Mixing is carried out for 10 minutes at a speed of 10 revolutions per minute.

The magnesium stearate, delumped beforehand on a 0.680-mm screen, is added. Mixing is again carried out for 5 minutes.

A Fette P 2000 press with a station number of 43 is employed for compressing. 200,000 tablets per hour are produced. The weight of tablets manufactured is 397 kg, which represents a production efficiency of 99.2%. The tablets have a mean weight of 491.5 mg with a scatter in accordance with the French Pharmacopoeia. The determination of Cefixime performed on 15 tablets varies from 192.7 mg to 200.8 mg.

The hardness of the tablets was measured on 20 tablets in the conventional manner on an apparatus of the Schleuniger 4M-type; the measurement gives 100 to 140 newtons.

The pressability of the mixture was also measured as a function of the force applied to the upper punch (expressed in kilonewtons) on an extensometry line using a set of sensors which measure the deformation of the upper and lower punches and the movement of the upper punch in the matrix of the compression machine. Comparative curves expressing the pressability of the mixture were established. These curves result from the measurement of the hardness of the tablets in a Schleuniger apparatus as a function of the force, in newtons, applied to the upper punch. This force is measured with a strain gauge. Comparative extensometry curves were established for tablets obtained by wet compression and by direct compression (see FIG. 1). The curve obtained shows that simple mixing offers a better response to compression. The tablets obtained by direct compression exhibit a hardness which is markedly higher than those obtained by wet granulometry.

The various materials, active substance and excipient are passed through a grid screen with a mesh opening of 0.8 mm to carry out a delumping operation.

The materials are weighed and charged—except for the magnesium stearate—into a 150-liter mixer. Mixing is carried out for 10 minutes at a speed of 10 revolutions per minute. The magnesium stearate, delumped beforehand on a 0.650-mm screen, is added. Mixing is again carried out for 5 minutes.

A Courtroy R 100 press with a station number of 24 is employed for compressing. 110,000 tablets per hour are produced.

The tablets have a mean weight of 596.3 mg with a scatter in accordance with the French Pharmacopoeia. The determination of Cefixime performed on 20 tablets varies from 394.4 mg to 407.12 mg. The hardness of the tablets measured with the Schleuniger apparatus on 20 tablets varies from 100 to 140N.

Comparative Example 1

The following materials are used:

Cefixime trihydrate	106.620 kg
Pregelised starch (Starch 1500)	6.750 kg
Dicalcium phosphate dihydrate	2.700 kg
Microcrystalline cellulose (Avicel PH 102)	7.868 kg

The starting materials are weighed, screened and then charged into a 400-liter mixer-granulator. Dry mixing is carried out for 5 minutes. 24 kg of water are then added and then 8.32 kg of water are added gradually until a granulated mass which contains 27% of water is obtained. The granulation takes 7 minutes.

The granules are then dried in a fluidised air bed drier for 1 hour 15 minutes with an air entry temperature of 45° C. and an exit temperature of 18° C.–25° C. The granulate obtained is then passed over a screen with a mesh size of 1 mm. 119.938 kg of granules are obtained.

The following are then weighed:

Microcrystalline cellulose	14.394 kg
Pregelised starch	19.948 kg
Dicalcium phosphate dihydrate	63.838 kg
Magnesium stearate	0.886 kg

The granules obtained previously are mixed with the cellulose, starch and phosphate, the stearate is then added and 217.550 kg of final product are obtained. This mixture is compressed in a Fette P 2000 press. A mass of tablets of 215.38 kg is obtained, which represents a yield of 98% based on the mass employed. The tablets have a unit weight of 490 mg and an extensometry curve as shown in the diagram of FIG. 1. The friability of the tablets, measured by the TAB method at 10 minutes is 0.3%. The hardness of the tablets varies from 85 to 95N.

We claim:

1. A dry process for the preparation of tablets of 7-acylaminocephalosporanic acid comprising carrying out a direct compression of a mixture comprising said acid and at least one pharmaceutical excipient, said acid comprising at least about 25% by weight of said mixture and wherein the 7-acylaminocephalosporanic acid has a particle size distribution such that:

fewer than 5% of particles have a diameter greater than 250µ,

between 55 and 95% of the particles have a diameter of between 250 and 90µN, and

between 5 and 40% of the particles have a diameter smaller than 90µ.

2. Process of preparation according to claim 1, wherein the mixture employed for the direct compression contains 30 to 70% by weight of the said acid relative to the weight of the final tablet.

Handwritten notes: 250µm, 250-90µm, 290µm

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3. Process according to claim 1, wherein the 7-acylaminocephalosporanic acid has a relative density of between 0.6 and 0.9.

4. Process according to claim 1, wherein the 7-acylaminocephalosporanic acid derivative is a derivative of 7-acylamino-3-vinylcephalosporanic acid.

5. A process according to claim 1, wherein the excipients are selected from the group consisting of calcium carbonates, calcium phosphates, calcium sulphates, microcrystal-

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line celluloses, cellulose powders, fructoses lactoses, mannitols, sorbitols, starches, pregelled starches and sugars.

6. Process according to claim 5, wherein a lubricating agent chosen from magnesium stearate, stearic acid, talc and a polyethylene glycol is added.

7. Tablets of derivatives of 7-acylaminocephalosporanic acid prepared using the process according to claim 1.

* * * * *

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D2



PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification⁶ : A61K 9/20, 31/545	A1	(11) International Publication Number: WO 98/46213 (43) International Publication Date: 22 October 1998 (22.10.98)
(21) International Application Number: PCT/US98/05412 (22) International Filing Date: 19 March 1998 (19.03.98) (30) Priority Data: 60/044,140 17 April 1997 (17.04.97) US (71) Applicant: BRISTOL-MYERS SQUIBB COMPANY [US/US]; 5 Research Parkway, Wallingford, CT 06492 (US). (72) Inventor: REMON, Jean, Paul, Louis, Auguste; Rijsenbergstraat 51, B-9000 Gent (BE). (74) Agent: DUBOFF, Samuel, J.; Bristol-Myers Squibb Company, 5 Research Parkway, Wallingford, CT 06492 (US).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>
(54) Title: CEFADROXIL MONOHYDRATE TABLET FORMULATION (57) Abstract This invention relates to uncoated direct compression tablets containing cefadroxil monohydrate as the active ingredient, which are capable of oral administration to human beings by swallowing, chewing or disintegrating in water resulting in a drinkable dispersion.		

people having trouble swallowing a tablet that is still intact, but yet do not have immediate access to water to disperse the same therein to form a drinkable dispersion.

Cefadroxil monohydrate is a widely used broad spectrum
5 cephalosporin antibiotic that can be administered orally in adults and children. It is sold worldwide by Bristol-Myers Squibb Company under various trade names, including Duricef® and Duracef® in the form of gelatin capsules, uncoated tablets and powder for reconstitution with
10 water to form a liquid suspension, and is dosed several times daily depending on the type of bacterial infection and the patient's needs (i.e. adult, elderly or pediatric).

Therefore, to fulfill the various diverse needs of the patient being treated, and to overcome the aforementioned disadvantages of prior art
15 tablet formulations, it would be highly desirable to provide a tablet of cefadroxil monohydrate that is uncoated (for ease of preparation) and is chewable, swallowable and easily dispersible in water to form a pleasant tasting drinkable dispersion for oral administration to a human being.

It has now surprisingly been found possible to provide such a tablet
20 formulation for cefadroxil monohydrate possessing the aforementioned attributes.

SUMMARY OF THE INVENTION

Accordingly, one embodiment of the invention is an uncoated cefadroxil monohydrate tablet obtained by direct compression of an anhydrous pharmaceutical composition comprising by weight % based on
25 the final tablet weight:

- (a) About 50% of cefadroxil monohydrate;
- (b) About 10-12% of a mixture containing 87 parts by weight of microcrystalline cellulose and 13 parts by weight of guar gum;

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- (c) About 9.5-29% of a cross-linked polyvinylpyrrolidone;
- (d) About 2.5-10% of colloidal silicon-dioxide;
- (e) About 4-19% of dibasic calcium phosphate; and
- (f) About 9-21% of mannitol or maltitol;

5 said tablet being capable of oral administration to a human being by swallowing, chewing or disintegrating in water resulting in a drinkable dispersion.

A preferred embodiment is a tablet comprising:

- | | | | |
|----|-----|--|----------|
| | (a) | Cefadroxil monohydrate | 1000 mg. |
| 10 | (b) | Cross-linked polyvinylpyrrolidone | 200 mg. |
| | (c) | Dibasic calcium phosphate | 200 mg. |
| | (d) | Microcrystalline cellulose/guar gum mixture containing 26 mg. guar gum | 200 mg. |
| | (e) | Mannitol | 350 mg. |
| 15 | (f) | Colloidal silicon dioxide | 50 mg. |
| | (g) | Magnesium stearate | 27 mg. |
| | (h) | Aspartame | 4.5 mg. |
| | (i) | Sodium saccharine | 4.5 mg. |
| | (j) | Strawberry aroma | 30 mg. |
| 20 | (k) | Raspberry aroma | 30 mg. |

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CLAIMS

What is claimed is:

1. An uncoated cefadroxil monohydrate tablet obtained by direct compression of an anhydrous pharmaceutical composition comprising by weight % based on the final tablet weight:

- (a) About 50% of cefadroxil monohydrate;
- (b) About 10-12% of a mixture containing 87 parts by weight of microcrystalline cellulose and 13 parts by weight of guar gum;
- 10 (c) About 9.5-29% of a cross-linked polyvinylpyrrolidone;
- (d) About 2.5-10% of colloidal silicon dioxide;
- (e) About 4-19% of dibasic calcium phosphate; and
- (f) About 9-21% of mannitol or maltitol;

15 said tablet being capable of oral administration to a human being by swallowing, chewing or disintegrating in water resulting in a drinkable dispersion.

2. The tablet of claim 1 comprising:

- (a) Cefadroxil monohydrate 1000 mg.
- (b) Cross-linked polyvinylpyrrolidone 200 mg.
- 20 (c) Dibasic calcium phosphate 200 mg.

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	(d)	Microcrystalline cellulose/guar gum mixture containing 26 mg. guar gum	200 mg.
	(e)	Mannitol	350 mg.
	(f)	Colloidal silicon dioxide	50 mg.
5	(g)	Magnesium stearate	27 mg.
	(h)	Aspartame	4.5 mg.
	(i)	Sodium saccharine	4.5 mg.
	(j)	Strawberry aroma	30 mg.
	(k)	Raspberry aroma	30 mg.

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

2020
Bogotá, D.C.,

Abogado:
MARGARITA CASTELLANOS ABONDANO

ASUNTO:	Radicación No.	06 12 2967
	Trámite	011
	Evento	378
	Actuación	430
	Oficio	3080
	Folios	

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

Documentos estudiados:

Descripción: Folios 27 a 39 como se radicó inicialmente.

Reivindicaciones: Folios 40 a 44 como se radicó inicialmente.

Prioridad: No reivindica. Fecha de presentación nacional: 2006.12.06

Objeto de la Invención

Titulo de la invención: "Nueva formulación farmacéutica de cefixima con mejor biodisponibilidad"

Problema Técnico Planteado: "Necesidad de una formulación de cefixima que tuviera una biodisponibilidad similar a la de la suspensión de cefixima sin la desventaja de su sabor amargo, su limitada vida de anaquel y la alta de exactitud para administrar la dosis"

Solución: "Proveer composiciones farmacéuticas con partículas de trihidrato de cefexima que tienen un tamaño de partícula medio de 20 µm a 120 µm."

IPC: A61K 9/0 AC; A61K 31/546 AC; A61P 31/0 AC

Análisis de la Solicitud de Patente

Reivindicaciones (Art 30 D 486, Art 22 PCT)

Claridad: La reivindicación 1 reclama una composición farmacéutica, pero no define claramente cuales son los componentes de dicha composición, se entiende a partir de la misma que la característica técnica esencial de la composición es que contiene trihidrato de cefixima con un tamaño de partícula promedio de 20 a 120

μm . Adicionalmente, las reivindicaciones 3, 4, 5, 6, 8 y 9 presentan términos no concisos como aproximadamente, se sugiere retirarlos del capítulo.

Por otro lado, de acuerdo a las reivindicaciones, el número de posibles combinaciones son bastantes y solamente se presentan datos de bioequivalencia para el ejemplo 3, que contiene 30% del activo.

Soporte en la descripción:

Se recuerda al solicitante, que las reivindicaciones deben ser una generalización de los ejemplos, y en este caso, los datos de biodisponibilidad solo están plasmados en la descripción para una sola composición de todas. Se sugiere limitar el alcance de la reivindicación 1.

Determinación del Estado de la Técnica

El Estado de la Técnica se determinó con base en la fecha de presentación en fase nacional: 2006.12.06 y se encontraron los siguientes documentos que anticipan el objeto de esta solicitud:

Item	Documento	Título	Fecha de Publicación
D1	US 5514383	<i>Process for the preparation of tablets of derivatives of cephalosporanic acid by direct compression</i>	May 7, 1996
D2	WO9846213	<i>Cefadroxil monohydrate tablet formulation</i>	Oct 22, 1998

Análisis de Patentabilidad (Art 14 D486)

Novedad (Art 16 D486)

La reivindicación 1 se refiere a una composición farmacéutica que contiene cefixima (folio 40).

D1 presenta formas farmacéuticas para cefalosporinas en forma de tableta (portada). En el ejemplo 1 (columna 3), revela que la cefixima usada es la trihidrato y que el tamaño de partícula (columna 4) puede variar así: 5% en partículas con un diámetro mayor a 250 μm , 55-95% diámetro entre 250 y 90 μm , 5-40% diámetro menor que 90 μm .

Características esenciales de la Solicitud	D1
	US 5514383
Composición farmacéutica que contiene cefixima	SI (columna 2, línea 30)
Tamaño de partícula medio 20-120 μm	SI (columna 4, líneas 50 a 65)
la forma del activo es trihidrato	SI (columna 3, líneas 10 a 20)

Dado que las características técnicas esenciales de la reivindicación 1 ya habían sido anticipadas por el estado del arte. Las reivindicaciones 24 y 25 revelan procesos y métodos que ya habían sido anticipados por D1 (columna 1, líneas 35 a 55). Se concluye que las reivindicaciones 1, 24 - 26 carece de novedad.

Nivel Inventivo (Art18 D486)

La reivindicación 2 adiciona como característica esencial que la composición comprende una base masticable para tableta y uno o más excipientes farmacéuticamente aceptables.

D1 revela que las formas sólidas que contienen cefixima pueden ser elaboradas por vía húmeda o por compresión directa (página 2).

La solicitud se diferencia de D1 en que la formulación contiene una base masticable para tableta.

El Efecto Técnico que logra la diferencia no es inesperado, ya que el estado del arte ya revelaba la forma de superar el problema planteado por el solicitante.

El Problema Técnico Objetivo de esta solicitud es proveer una composición farmacéutica alternativa que contenga cefixima.

D2 revela tabletas por composición directa sin cubierta que contenga cefadroxil monohidrato para masticar (portada). Una de las composiciones reveladas tiene 50% de monohidrato de cefadroxil, 10-12% de celulosa microcristalina y goma guar, 9.5-29% de PVP, 2.5-10% de dióxido de silicio coloidal, 4-19 % de fosfato de calcio dibásico, y 9-12% de manitol o malitol.

También revela el uso de aspartame, sacarina sódica y aroma de fresa, entre otros excipientes para la formulación de tabletas masticables (página 3 y 4).

Para solucionar el problema planteado, el experto en la materia habría sido sugerido por D2 para formular una tableta masticable con un activo como cefixima tal y como la revelada en D1, de manera que sería capaz de llegar al mismo resultado acá presentado.

Se concluye que las reivindicaciones 2-23 y 27 no poseen nivel inventivo.

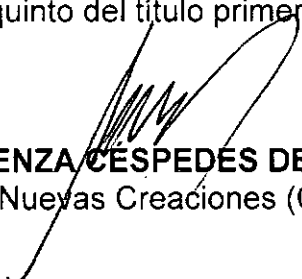
Conclusión

Los requisitos de Patentabilidad de la presente Solicitud se encuentran afectados así:

Nº	Documento	Reivindicaciones afectadas	Requisito que afecta
D1	US 5514383	1, 25-26 2-23 y 27	Novedad Nivel inventivo
D2	WO9846213	2-23 y 27	Nivel inventivo

En cumplimiento del artículo 45 de la Decisión 486 de la Comisión de la Comunidad Andina, se le indica que debe dar respuesta dentro del término de 60 días contados a partir de la fecha de notificación de la presente comunicación. En caso de no dar respuesta al presente requerimiento, o si a pesar de la respuesta subsistieran los impedimentos para la concesión, se denegará la patente.

Notifíquese el presente oficio conforme a lo dispuesto en el numeral 5.2, literal e), del capítulo quinto del título primero de la Circular Única N° 10 de 2001.


ALIX CARMENZA CÉSPEDES DE VERGEL
Directora de Nuevas Creaciones (C)

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

05 MAR. 2010

CONCEPTO TECNICO NUMERO: 559	EXAMINADOR TÉCNICO Código:202092
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