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DIRECCIÓN DE NUEVAS CREACIONES
PRESENTACIÓN DE OPOSICIÓN

1. Oposición a solicitud de:

- ☒ Patente de invención
☐ Registro de Diseño Industrial
☐ Patente de Modelo de Utilidad
☐ Esquema de Trazado de Circuitos Integrados

Número de expediente: 11-165-084

Solicitante: BOEHRINGER INGELHEIM VETMEDICA, GMBH.

Apoderado: CARLOS REINALDO OLARTE GARCIA

Título de la Nueva Creación: SOLUCION BEBIBLE FARMACEUTICA DE TELMISARTAN.

Gaceta: 647 de 29 de junio de 2012, No. de publicación 844

2. Datos del Opositor

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☒ Persona Jurídica

TECNOQUIMICAS S.A.

Nombre o denominación / Razón social completa

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En caso de haber presentado poder general para asuntos que se adelanten ante la Delegatura de Propiedad Industrial, sírvase indicar el número de su radicación

6. Fundamentos de la oposición

Causal: Incumplimiento de requisitos de patentabilidad (Título II, Capítulo I, Decisión 486 de 2000)

Justificación: VER ANEXO

Prórroga:

SI

☒

NO

☐

7. Anexos

☒

Comprobante de pago de la tasa para la presentación de la solicitud No. _____ Fecha: _____

☒

Poder, si fuera el caso con el que se acredita la representación.

☒

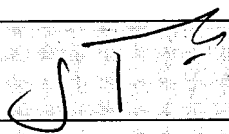
Pruebas de los fundamentos de la oposición

☒

Copias para traslado 10 folios

8. Firma

JOSÉ LUIS REYES VILLAMIZAR



Nombre y apellidos

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C.C.

T.P.

Señor

SUPERINTENDENTE DE INDUSTRIA Y COMERCIO

E. S. D.

REF: EXPEDIENTE 11-165-084

TÍTULO SOLICITADO: “SOLUCIÓN BEBIBLE FARMACÉUTICA DE TELMISARTAN”

PUBLICACIÓN: Gaceta 647 de 29 de Junio de 2012, N° de publicación 844.

PRIORIDAD: EP 09160771.3 de 20/05/2009

SOLICITANTE: BOHERINGER INGELHEIM VETMEDICA, GMBH

APODERADO: CARLOS R. OLARTE

TRÁMITE: PRESENTACIÓN DE OPOSICIÓN

JOSÉ LUIS REYES VILLAMIZAR, mayor de edad, identificado como aparece al pie de mi firma, abogado en ejercicio, titular de la tarjeta profesional número 44655 del Consejo Superior de la Judicatura, obrando en calidad de apoderado de la sociedad **TECNOQUÍMICAS S.A.**, en ejercicio de lo dispuesto por el artículo 42 de la Decisión 486 de 2000, muy respetuosamente me permito formular la siguiente

I. PETICIÓN

Sírvase negar el beneficio patentario a la solicitud contenida en el expediente **11-165-084**, por no cumplir con lo dispuesto en la Decisión 486 de 2000, con base en los fundamentos que se expondrán a continuación.

II. LEGÍTIMO INTERÉS

Asiste a **TECNOQUÍMICAS S.A.**, legítimo interés para presentar esta oposición, pues la eventual concesión de la solicitud restringiría injustificadamente el empleo de ciertas sustancias, derivados y procesos que a nuestro juicio carecen de nivel inventivo, en detrimento de sus legítimos intereses comerciales. De igual manera mis clientes están interesados, por su misma condición de industrias farmacéuticas, en evitar la concesión de privilegios de patente que incumplan los requisitos materiales de patentabilidad establecidos en las normas vigentes, y que supongan un riesgo para la libre competencia.

III. FUNDAMENTOS DE LA OPOSICIÓN

La solicitud en trámite 11-165-084, que se refiere a una solución farmacéutica para beber con un pH de 10 o superior que contiene un antagonista de la angiotensina II, preferiblemente Telmisartán, y excipientes para mejorar el sabor y prolongar la vida útil de la composición como alcoholes de azúcares, no reúne los requisitos necesarios para otorgársele el privilegio de patente de invención, como se demuestra a través de los siguientes argumentos:

- Claridad, Concisión y Soporte en la descripción

En primer lugar, las composiciones reclamadas no presentan claridad en lo que se pretende reclamar dando paso a un alto número de compuestos no sustentados y sobre los que no se permite definir el alcance de las composiciones.

Por ejemplo, se observa que el solicitante reclama en su reivindicación principal una composición que contiene: "un antagonista del receptor de angiotensina II" y "uno o mas azucares-alcoholes hasta una concentración de 40% a 70% (de preferencia 60%-70%)".

De esta forma se observa que la solicitud no es concisa en tanto NO presenta cual es el elemento activo dentro de la composición, sino que menciona un grupo farmacológico completo como lo es un "*antagonista del receptor de angiotensina II*", el cual abarca un gran número de elementos activos, le resta concisión a la

materia reclamada por el Solicitante y caracteriza la composición por su función antagonista.

Por otro lado, en la descripción, los ejemplos presentados solamente soportan las composiciones para las cuales se tiene como ingrediente activo el Telmisartán (ejemplos 1 a 8), por consiguiente, no existe en la descripción información que soporte la totalidad de las composiciones reclamadas en la reivindicación principal de la presente solicitud de patente, convirtiendo la materia reclamada en una extrapolación irrazonable de ingredientes activos.

Adicionalmente, la solicitud carece de claridad y de concisión por que además presenta términos que no son claros desde el léxico técnico, de esta forma la expresión “azúcares-alcoholes” es imprecisa y abarca un gran número de alcoholes que caben dentro de esta descripción, pero no se demuestra que cualquier alcohol incluido puedan tener el mismo comportamiento.

Lo expresado anteriormente se observa claramente en los ejemplos 1 a 8, donde los alcoholes empleados son exclusivamente manitol, xilitol y sorbitol, donde no se observan otros alcoholes que sean incluidos dentro de estas composiciones. Por estas razones, la materia reclamada por la solicitud no presenta soporte ni comprobación de su efecto técnico por lo que no puede ser objeto de patente.

Ahora bien, el Solicitante no está definiendo claramente la composición en la reivindicación 1 dado que no está presentando los porcentajes de cada uno de los componentes, ni los componentes que pueden llegar a ser parte de la composición allí mencionada.

En este mismo aspecto, la característica de los azúcares antes de entrar a la solución no hace parte de las características técnicas esenciales de la solución final, sino más bien hace parte del método por medio del cual se puede obtener dicha composición o solución. Se llama la atención del examinador sobre esta característica mencionada en la reivindicación 1, dado que no obedece a caracterización con claridad de los componentes y/o composiciones que buscan ser patentadas.

Por otra parte, existe materia (ver reivindicación 9) que se reclama de un grupo de alcoholes, ente los cuales incluye isomalt y eritrita los cuales no poseen soporte en la descripción y no son términos claros que los identifique completamente.

Otros desaciertos de la solicitud incluyen aquellos presentes en la reivindicación 18 que no cumplen con los requisitos de concisión y claridad pues presenta un recipiente que no tiene relación alguna con las características técnicas esenciales de la composición reclamada por el solicitante en la reivindicación principal.

En conclusión, la solicitud en estudio no puede tener lugar a patente debido a que no define los límites de las reclamaciones, extrapola irracionalmente los compuestos sin obedecer a los requisitos de soporte en la descripción y presenta imprecisiones técnicas que no permiten definir el alcance de lo reivindicado.

Hacemos énfasis especialmente en la reivindicación 18 que parece relacionarse con otro tipo de invención dado que no se refiere a una característica técnica estructural que haga parte de la composición sino a un recipiente, lo cual no se considera al campo de la Química Farmacéutica.

Objeciones a la Novedad

A pesar de haber descrito la forma como la solicitud no cumple con los requisitos de la Decisión 486 de la Comunidad Andina de Naciones, se observa que la composición solicitada ya había sido revelada en el estado de la técnica por el documento US2007/026026 (2007-02-01).

En este documento se presentan composiciones líquidas de Losartán con excipientes para lograr un pH mayor de 9 (página 13, reivindicación 1), mas específicamente presenta un pH entre 7 y 10 (página 13, reivindicación 2).

Adicionalmente, en la figura 5 de la muestra la estabilidad de la composición de Losartán en soluciones de glicol, glicerina y xilitol o cual demuestra que los “alcoholes-azucares” ya habían sido empleados en otras composiciones anteriores a las acá reclamadas, dando buenos resultados y pH entre 7 y 10.

Como se observa en el siguiente extracto de la solicitud, la invención buscaba también proveer composiciones líquidas con Losartán, un antagonista del receptor de la angiotensina al igual que el Telmisartán ¹(ver nota al pie).

"[0042] The present invention provides oral liquid compositions that include Losartán, or a pharmaceutically acceptable salt or metabolite thereof, and at least one pharmaceutically acceptable carrier in an amount sufficient to provide a pH of about 6 or higher. As used herein, "oral liquid composition(s)" include emulsions, solutions, suspensions, syrups and elixirs, but do not include solid dosage forms that include minor amounts of liquids therein, such as capsules or tablets. Preferably, "oral liquid composition(s)" mean Losartán, or a pharmaceutically acceptable salt or metabolite thereof, in solution."

Así mismo, la anterioridad ya contemplaba la inclusión en su composición de alcoholes azucarados como el manitol:

*"[0055] A sweetening agent, such as one or more of sorbitol, saccharin, sucralose, sodium saccharin, xylitol, sucrose, aspartame, fructose, neotame, sodium saccharate, glycyrrhizin dipotassium, acesulfame K, **mannitol**, propylene glycol, invert sugar, and mixtures thereof, can be added to modify the taste of the composition. Alternatively or in addition, a viscous sweetener such as one or more of a sorbitol solution, syrup (sucrose solution) glycerin, or high-fructose corn syrup can be used and, in addition to sweetening effects, can also be useful to increase viscosity and to retard sedimentation. Preferably, the sweetening agent includes a saccharin, more preferably sodium saccharin. Such a sweetening agent, if present, will typically be present in an amount sufficient to mask the bitterness of the losartan, or salt or metabolite thereof, and preferably to also mask any other off-flavor components included in the formulation. Typical amounts of sweetening agent include about 0.05 weight percent to about 10 weight percent, preferably about 0.1 weight percent to about 5 weight percent, more preferably about 0.5 weight percent to 2 weight percent, of the total weight of the composition."*

Teniendo en cuenta la materia reclamada por la reivindicación 1 y la revelada por US2007/026026 se tiene que las características principales ya habían sido

¹ http://es.wikipedia.org/wiki/Antagonista_de_los_receptores_de_angiotensina_II

reclamadas y por consiguiente no existe novedad en las composiciones allí reivindicadas:

Características esenciales de la solicitud	US2007/026026
Solución farmacéutica con un valor de pH 10 o superior que contiene un antagonista del receptor de angiotensina II, caracterizada porque	Párrafo 42, página 3 Reivindicación 1, página 13;
Están contenidos uno o más azúcares-alcoholes hasta una concentración total de 40% a 70%,	Párrafo 55, página 5

Objeciones al Nivel inventivo

Habiendo demostrado la falta de novedad de la solicitud, existen características adicionales que, permiten demostrar la ausencia de nivel inventivo. Veamos:

La reivindicación 3, que se refiere a “ *La solución farmacéutica según la Reivindicación 1 o 2, caracterizada por que en el caso del antagonista del receptor de angiotensina II se trata de Telmisartán*”, presenta un compuesto activo ya definido en el estado de la técnica puesto que se conocían soluciones de este grupo farmacológico, de esta forma era relativamente obvio que un técnico medio en la técnica hubiera llegado a estas composiciones a partir de las enseñanzas del documento US2007/026026 , así como del documento WO2004/028505

En el caso de WO2004/028505, este documento revelaba ya composiciones de antagonistas de receptores de la angiotensina II, específicamente de Telmisartán (página 2)

[0001] *The present invention relates to new solid pharmaceutical compositions comprising the angiotensin II receptor antagonist telmisartan, e.g. in form of granules or in form of a powder, as well as solid oral formulations ready for use/ingestion, e.g. capsule and tablet formulations made from said pharmaceutical compositions. The present invention also provides methods for producing said compositions and formulations.*

Cómo se observa, el técnico medio al estar tratando de resolver el problema de proveer composiciones líquidas de antagonistas del receptor de la angiotensina ii habría encontrado en D1 y D2 las enseñanzas que le permitirían llegar a formular composiciones como las reclamadas por la presente solicitud, en la cuales se busca estabilidad y formulaciones adecuadas para el Telmisartán dada su sensibilidad frente al pH como se observa en el siguiente extracto de la publicación WO2004/028505:

[0003] Telmisartan is generally manufactured and supplied in the free acid form. As disclosed in WO 00/43370, crystalline telmisartan exists in two polymorphic forms having different melting points. Under the influence of heat and humidity, the lower melting polymorph B transforms irreversibly into the higher melting polymorph A. Both forms are characterized by a very poor solubility in aqueous systems at the physiological pH range of the gastrointestinal tract of between pH 1 to 7.

[0004] Telmisartan is obtainable on the market under the trade name Micardis®. Starting from the free acid form Telmisartan as introduced to the market is manufactured using an expensive spray-drying process. WO 00/27397 discloses additional spray-dried granules comprising telmisartan, and tablets comprising these granules. Due to the poor solubility of the free acid form preparation of alternative telmisartan formulation is difficult.

BRIEF SUMMARY OF THE INVENTION

[0005] There is a clear need to provide alternative solid oral formulations of Telmisartan which can be prepared using less complicated and expensive processes and fulfill all prerequisites for pharmaceutical use, i.e. long-lasting stability of the formulation under different climatic conditions and sufficient solubility of the active substance for sufficient gastrointestinal absorption in the slightly acidic and neutral pH region.

En conclusión, el técnico medio enfrentado al problema de proveer composiciones líquidas estables para la administración de Telmisartán y teniendo en cuenta el problema de estabilidad y de sensibilidad al pH de este activo, habría encontrado en el documento US2007/026026 la información que le permite comprender que este activo también puede estar en forma líquida teniendo en cuenta las características de los excipientes allí también reveladas, y por su parte la anterioridad WO2004/028505 muestra los problemas en las formulaciones con

Telmisartán, y al combinar las enseñanzas de los dos documentos habría podido llegar a la formulación de la solución de Telmisartán (como se muestra en WO2004/028505) con alcoholes como el manitol, el sorbitol o el xilitol (como se muestra en US2007/026026).

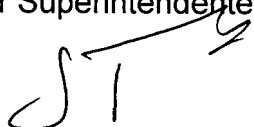
Por todo lo expresado anteriormente, la solicitud en estudio no cumple con los requisitos mínimos de patentabilidad, y mucho menos con Novedad y Nivel Inventivo, por lo que no merece el beneficio de Patente.

IV PRUEBAS

Ruego que se tenga como tal, sin perjuicio de las que puedan presentarse al vencimiento de la prórroga solicitada, y de aquellas que el Despacho considere oficiosamente, las siguientes:

- Publicación internacional US 2007/0026026, Feb. 1, 2007, ORAL LIQUID LOSARTAN COMPOSITIONS, página 3, 5, 13
- Publicación internacional WO2004/028505, Sep 12, 2007, SOLID PHARMACEUTICAL FORMULATIONS COMPRISING TELMISARTAN, páginas 1 a 5

Señor Superintendente,



JOSÉ LUIS REYES VILLAMIZAR

C.C. 79.152.473 de Usaquén
T.P.A. 44.655 de C.S.J.



US 20070026026A1

(19) **United States**

(12) **Patent Application Publication**

Delmarre et al.

(10) **Pub. No.: US 2007/0026026 A1**

(43) **Pub. Date: Feb. 1, 2007**

(54) **ORAL LIQUID LOSARTAN COMPOSITIONS**

Related U.S. Application Data

(76) Inventors: **David Delmarre**, Vernon Hills, IL (US); **Naga Mallika Surapaneni**, Mundelein, IL (US); **Carlos-Julian Sison Centeno**, Chicago, IL (US); **Meagan Erica Weldele**, Overland Parks, KS (US); **Danchen Gao**, Chicago, IL (US)

(60) Provisional application No. 60/703,866, filed on Aug. 1, 2005.

Publication Classification

(51) **Int. Cl.**
A61K 31/4184 (2007.01)
A61K 9/00 (2006.01)
(52) **U.S. Cl.** **424/400; 514/381**

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(57) **ABSTRACT**

The present invention is directed to improved oral liquid compositions that include losartan, or a pharmaceutically acceptable salt or metabolite thereof, and at least one pharmaceutically acceptable carrier in an amount sufficient to provide a pH of about 6 or higher. Processes of preparing such compositions and methods of administering such compositions are also included.

(21) Appl. No.: **11/493,801**
(22) Filed: **Jul. 27, 2006**

embodiment, the phosphate salt concentration is about 80 mM to 120 mM. The losartan, or salt or metabolite thereof, is typically present in an amount of about 1 to 50 mg/mL of the composition.

[0024] In a preferred embodiment, the losartan, or salt or metabolite thereof, is present in an amount of about 8 mg/mL to 20 mg/mL of the composition, and the pharmaceutically acceptable carrier includes a glycol present in an amount of about 5 percent to 25 percent (v/v), glycerin present in an amount of about 20 percent to 40 percent (v/v), a sweetening agent present in an amount of about 0.5 percent to 2 percent (w/v), and a buffering agent present in an amount of about 40 percent to 60 percent (v/v).

[0025] Advantageously, the composition is at least substantially stable. In one embodiment, the degradation of losartan over a period of less than two months is no more than about 1 percent to 2 percent (w/w) at 50° C. In a preferred embodiment, the liquid compositions are substantially stable.

[0026] In an exemplary embodiment, the composition is in solution form.

[0027] The present invention further relates to an oral liquid composition that includes losartan, or a pharmaceutically acceptable salt or metabolite thereof, at least one of propylene glycol or glycerin, along with a sucralose or saccharin-containing component and a phosphate-containing buffer that includes sodium phosphate, potassium phosphate, or a mixture thereof, in an amount sufficient to provide a pH of about 6 or higher.

[0028] The present invention also encompasses stable oral liquid losartan compositions that include losartan or a pharmaceutically acceptable salt or metabolite thereof, a solubilizing agent, a sweetening agent, and a buffering agent, present in an amount sufficient to provide a pH of about 6 or higher over an extended period of time to minimize degradation of the losartan component.

[0029] The present invention additionally includes oral liquid compositions that include solutions of losartan, or a pharmaceutically acceptable salt or metabolite thereof, propylene glycol, glycerin, saccharin sodium, and potassium phosphate buffer, each in an amount sufficient to provide a pH of about 6 or higher.

[0030] The present invention also relates to a method of preparing an oral liquid losartan composition. The method includes dissolving an amount of losartan, or a pharmaceutically acceptable salt or metabolite thereof, into at least one liquid adjuvant to form a liquid losartan solution, and combining the liquid losartan solution with one or more additional pharmaceutically acceptable carriers sufficient to provide a pH of about 6 or higher to form the oral liquid losartan composition. Preferably, the at least one liquid adjuvant includes a buffering agent. The oral liquid losartan composition is typically a clear solution.

[0031] Furthermore, the present invention relates to a method of preventing, treating, or managing hypertension, congestive heart failure, diabetic nephropathy or myocardial infarction in a mammal. The method includes administering to the mammal an effective amount of an oral liquid losartan composition that includes losartan, or a pharmaceutically acceptable salt or metabolite thereof, and at least one phar-

maceutically acceptable carrier, wherein the oral liquid losartan composition has a pH of about 6 or higher.

[0032] In one embodiment, the composition is administered once or twice a day. In another embodiment, the total daily dose of losartan is from about 25 mg to 100 mg.

[0033] The method preferably also includes administering at least one other therapeutic agent in association with the losartan. The other therapeutic agent(s) typically include another hypertensive agent. The at least one other hypertensive agent generally includes an angiotensin II antagonist, angiotensin converting enzyme inhibitor, or a neutral endopeptidase/angiotensin converting enzyme inhibitor, or a combination thereof.

BRIEF DESCRIPTION OF THE DRAWINGS

[0034] Further features and advantages of the invention can be ascertained from the detailed description that is provided below in connection with the following drawing(s):

[0035] FIG. 1 is a graph showing the solubility profile of losartan as a function of pH;

[0036] FIG. 2 is a graph showing the stability (measured by percent active) of losartan with different buffers at different times;

[0037] FIG. 3 is a graph showing the effect of different concentrations of propylene glycol on the stability of losartan;

[0038] FIG. 4 is a graph showing the stability of losartan (measured by percent active) with different excipient combinations as a function of time;

[0039] FIG. 5 is a graph showing the stability of losartan (measured by percent active) in solutions of propylene glycol, glycerin, and xylitol;

[0040] FIG. 6 is a graph showing the stability of losartan (measured by percent active) with different concentrations of glycerin and at different pHs; and

[0041] FIG. 7 is a graph showing the percent recovery of losartan at different temperatures in different containers.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0042] The present invention provides oral liquid compositions that include losartan, or a pharmaceutically acceptable salt or metabolite thereof, and at least one pharmaceutically acceptable carrier in an amount sufficient to provide a pH of about 6 or higher. As used herein, "oral liquid composition(s)" include emulsions, solutions, suspensions, syrups and elixirs, but do not include solid dosage forms that include minor amounts of liquids therein, such as capsules or tablets. Preferably, "oral liquid composition(s)" mean losartan, or a pharmaceutically acceptable salt or metabolite thereof, in solution.

[0043] The present liquid dosage forms provide certain advantages over the solid forms conventionally available. For example, liquid dosage forms are much easier to swallow and typically do not require separate water to administer. Patient compliance is also easier to facilitate with the flavoring and colorant agents that are typically included in

together form about 0.25 weight percent to about 15 weight percent, preferably about 0.4 weight percent to about 10 weight percent, and more preferably about 0.5 weight percent to about 5 weight percent, of the total weight of the composition.

[0054] A thickening agent or viscosity-enhancing agent can be included to generally improve the mouth-feel of the composition and/or to help coat the lining of the gastrointestinal tract. While any suitable thickening agent can be included in the compositions of the present invention, a preferred thickening agent, when used, includes one or more of acacia, alginic acid bentonite, carbomer, carboxymethyl-cellulose calcium or sodium, cetostearyl alcohol, methyl cellulose, ethylcellulose, glycerin, gelatin guar gum, hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropyl methyl cellulose, maltodextrin, polyvinyl alcohol, povidone, propylene carbonate, propylene glycol alginate, sodium alginate, sodium starch glycolate, starch tragacanth, and xanthan gum. Such a thickening agent, if present, will typically form about 0.1 weight percent to 20 weight percent, preferably about 0.3 weight percent to about 15 weight percent, and more preferably about 0.5 weight percent to 4 weight percent, of the total weight of the composition.

[0055] A sweetening agent, such as one or more of sorbitol, saccharin, sucralose, sodium saccharin, xylitol, sucrose, aspartame, fructose, neotame, sodium saccharate, glycyrrhizin dipotassium, acesulfame K, mannitol, propylene glycol, invert sugar, and mixtures thereof, can be added to modify the taste of the composition. Alternatively or in addition, a viscous sweetener such as one or more of a sorbitol solution, syrup (sucrose solution) glycerin, or high-fructose corn syrup can be used and, in addition to sweetening effects, can also be useful to increase viscosity and to retard sedimentation. Preferably, the sweetening agent includes a saccharin, more preferably sodium saccharin. Such a sweetening agent, if present, will typically be present in an amount sufficient to mask the bitterness of the losartan, or salt or metabolite thereof, and preferably to also mask any other off-flavor components included in the formulation. Typical amounts of sweetening agent include about 0.05 weight percent to about 10 weight percent, preferably about 0.1 weight percent to about 5 weight percent, more preferably about 0.5 weight percent to 2 weight percent, of the total weight of the composition.

[0056] A flavoring agent can enhance patient compliance by making the composition more palatable, particularly in the case of the imbibable compositions of the present invention. The flavoring agent is typically selected in type and amount to decrease or eliminate any bitter taste, i.e., a taste mask, that would otherwise be detectable by the patient to whom the compositions are administered. Examples of a suitable flavoring agent, when used, includes one or more of aspartame, saccharin, menthol, peppermint, anise, and any fruit flavor, such as one or more of grapefruit, orange, lemon, lime, mango, strawberry, pineapple, or cherry; or a combination thereof. A flavoring agent including grapefruit has been found to work especially well according to the invention. The flavoring agent, if present, will typically form about 0.01 weight percent to about 15 weight percent, preferably about 0.5 weight percent to about 10 weight percent, and more preferably about 0.1 weight percent to about 5 weight percent, of the total weight of the composition.

[0057] A colorant agent, when included, can provide the compositions with a more aesthetic and/or distinctive appearance. Colorant agents suitable for inclusion in the present invention include one or more water-soluble synthetic organic food additives (e.g., food dyes such as food red dye Nos. 2 and 3, food yellow dye Nos. 4 and 5 and food blue dye Nos. 1 and 2), water-insoluble lake dyes (e.g., aluminum salts of the above water-soluble synthetic organic food additives, etc.), and natural pigments (e.g., beta-carotene, chlorophyll, iron oxide red, etc.). Suitable colorants include D&C Red No. 33, FD&C Red No. 3, FD&C Red No. 40, D&C Yellow No. 10, and C Yellow No. 6. Such a colorant agent, if present, will typically form about 0.001 weight percent to about 1 weight percent, preferably about 0.005 weight percent to about 0.5 weight percent, and more preferably about 0.0075 weight percent to about 0.25 weight percent, of the total weight of the composition.

[0058] Examples of a suitable preservative component, when used, includes sodium benzoate, butylated hydroxy toluene, butylated hydroxyanisole, ethylenediamine tetraacetic acid, paraoxybenzoic acid esters, chlorobutanol, benzyl alcohol, phenylethylalcohol, dehydroacetic acid, sorbic acid, benzalkonium chloride, benzethonium chloride, phenol, phenylmercuric nitrate, thimerosal, and mixtures thereof. A preservative can be added to the compositions at levels safe for ingestion to improve storage stability. A preservative component, if present, will typically form about 0.01 weight percent to about 5 weight percent, preferably about 0.05 weight percent to about 3 weight percent, and more preferably about 0.1 weight percent to about 2 weight percent, of the total weight of the composition.

[0059] The buffering agent preferably included in the liquid compositions can include a buffer solution of one or more gluconate, lactate, citrate, acetate, phosphate, and/or carbonate salts. In addition to providing the about 6 pH or greater, the buffering agent can also modulate drug solubility. Preferably, the buffering agent includes a phosphate, more preferably a potassium phosphate or sodium phosphate buffering agent. Such a buffering agent, if present, will typically form about 10 weight percent to about 80 weight percent, preferably about 30 weight percent to about 70 weight percent, and more preferably about 40 weight percent to about 60 weight percent, of the total weight of the composition.

[0060] Solubilizing and emulsifying agents are used to facilitate more uniform dispersion of an active ingredient or other excipient that is not generally soluble in the liquid carrier. Examples of a suitable emulsifying agent, if used, includes, for example, gelatin, egg yolk, casein, cholesterol, acacia, tragacanth, chondrus, pectin, methyl cellulose, carbomer, cetostearyl alcohol, cetyl alcohol, and mixtures thereof. Examples of a suitable solubilizing agent include glycol, glycerin, D-mannitol, trehalose, benzyl benzoate, ethanol, trisaminomethane, cholesterol, triethanolamine, sodium carbonate, sodium citrate, sodium salicylate, sodium acetate, and mixtures thereof. Preferably, the solubilizing agent includes a glycol. Preferred glycols include polyethylene glycol or propylene glycol, or both. The glycol can also act as a stabilizing agent. The solubilizing or emulsifying agent is/are generally present in an amount sufficient to dissolve or disperse the losartan, or salt or metabolite thereof, in the carrier. Typical amounts are from about 1 weight percent to about 80 weight percent, preferably about

container. One sample of each container (except for the stainless steel container) was then stored at 50° C., another one at 40° C. and finally the last sample at room temperature (RT). The stainless steel container was left at room temperature. Samples from each container were then analyzed by HPLC at different times. Table 8 displays the percentage of losartan potassium as a function of time in different containers. The margin of error in the data of the table below is ±0.5%.

TABLE 8					
	Temperature (° C.)	0 hours	72 hours	312 hours	1008 hours
Glass Bottle	RT	99.82	99.92	99.80	99.70
Glass Bottle	50	99.82	99.95	99.80	99.90
Glass Bottle	40	99.82	99.92	99.92	99.90
HDPE	RT	99.82	99.92	99.78	99.90
HDPE	50	99.82	99.92	99.80	99.90
HDPE	40	99.82	99.92	99.83	99.90
Brown Glass Bottle	RT	99.82	99.92	99.83	99.90
Brown Glass Bottle	50	99.82	99.92	99.83	99.90
Brown Glass Bottle	40	99.82	99.92	99.83	99.90
Stainless Steel	RT	99.82	99.92	99.83	99.90

[0134] As demonstrated by the data above, the oral liquid losartan composition is stable as a function of time in all the different containers with minimal degradation observed after 1008 hours at room temperature, 40° C. and 50° C. These results demonstrate the superior stability of the losartan potassium in solution and confirm the conclusions of the other studies according to the invention.

[0135] To further confirm these results, the percent recovery of losartan potassium was also measured as a function of time in the different containers. Table 9 and FIG. 7 summarize the results obtained. The margin of error in the data in this table is ±2%.

TABLE 9					
	Temperature (° C.)	0 hour	72 hours	312 hours	1008 hours
Glass Bottle	RT	100.00	99.52	99.85	99.04
Glass Bottle	50	100.00	99.93	100.19	99.28
Glass Bottle	40	100.00	99.78	99.91	99.27
HDPE	RT	100.00	100.38	100.42	99.07
HDPE	50	100.00	100.05	100.16	100.22
HDPE	40	100.00	99.51	99.94	99.83
Brown Glass Bottle	RT	100.00	100.00	100.32	99.33
Brown Glass Bottle	50	100.00	100.07	100.38	101.04

TABLE 9-continued					
	Temperature (° C.)	0 hour	72 hours	312 hours	1008 hours
Brown Glass Bottle	40	100.00	99.77	100.17	99.15
Stainless Steel	RT	100.00	100.07	100.31	99.49

[0136] Small variations in the percentage of recovery as a function of time were observed in the different containers. In each container at room temperature, there was a small decrease in the recovery percentage of losartan potassium. At less than 1 percent, the decrease, however, was very small. Accordingly, glass bottles, plastic HDPE containers, brown glass bottles, and stainless steel containers are all suitable containers for holding the oral liquid losartan compositions and do not significantly decrease their stability. The preferred form of packaging the liquid formulations of the invention is in PET, HDPE, clear or a brown glass bottle, preferably in a HDPE container.

[0137] Although preferred embodiments of the invention have been described in the foregoing description, it will be understood that the invention is not limited to the specific embodiments disclosed herein but is capable of numerous modifications by one of ordinary skill in the art. It will be understood that the materials used and the chemical or pharmaceutical details may be slightly different or modified from the descriptions herein without departing from the methods and compositions disclosed and taught by the present invention.

- What is claimed is:
1. An oral liquid composition comprising losartan, or a pharmaceutically acceptable salt or metabolite thereof, and at least one pharmaceutically acceptable carrier in an amount sufficient to provide a pH of about 6 or higher.
 2. The composition of claim 1, wherein the pH is about 7 to 10.
 3. The composition of claim 2, wherein the pH is about 7.4 to 8.6.
 4. The composition of claim 1, wherein the at least one pharmaceutically acceptable carrier comprises one or more of a wetting agent, surfactant component, stabilizing agent, solubilizing agent, thickening agent, sweetening agent, flavoring agent, perfuming agent, colorant agent, preservative agent, or buffering agent.
 5. The composition of claim 4, wherein the carrier comprises one or more of a solubilizing agent, a stabilizing agent, a sweetening agent, a flavoring agent effective to mask a bitter taste, or a buffering agent.
 6. The composition of claim 5, wherein the carrier comprises a glycol or glycerin, the sweetening agent comprises a sucralose or saccharin-containing component, and the buffering agent comprises a phosphate-containing buffer.
 7. The composition of claim 5, wherein the flavoring agent is present and comprises grapefruit, orange, lemon, lime, mango, strawberry, pineapple, cherry, or a combination thereof.
 8. The composition of claim 6, wherein the phosphate-containing buffer comprises sodium phosphate, potassium phosphate, or mixtures thereof.

9. The composition of claim 8, wherein the concentration of phosphate salt in the buffering agent is from about 5 mM to 150 mM.
10. The composition of claim 9, wherein the phosphate salt concentration is about 80 mM to 120 mM.
11. The composition of claim 5 wherein the solubilizing agent is present in an amount of about 1 percent to 50 percent (v/v).
12. The composition of claim 5, wherein the sweetening agent is present in an amount of about 0.05 percent to 5 percent (w/v).
13. The composition of claim 5, wherein the buffering agent is present in an amount of about 30 percent to 70 percent (v/v).
14. The composition of claim 6, wherein the glycol is present in amount of about 1 percent to 40 percent (v/v), and the glycerin is present in an amount of about 5 percent to 50 percent (v/v).
15. The composition of claim 1, wherein the losartan, or salt or metabolite thereof, is present in an amount of about 1 to 50 mg/mL of the composition.
16. The composition of claim 1, wherein the losartan, or salt or metabolite thereof, is present in an amount of about 8 mg/mL to 20 mg/mL of the composition, and the pharmaceutically acceptable carrier comprises a glycol present in an amount of about 5 percent to 25 percent (v/v), glycerin present in an amount of about 20 percent to 40 percent (v/v), a sweetening agent present in an amount of about 0.5 percent to 2 percent (w/v), and a buffering agent present in an amount of about 40 percent to 60 percent (v/v).
17. The composition of claim 1, wherein the composition is at least substantially stable.
18. The composition of claim 1, wherein degradation of losartan over a period of less than two months is no more than about 1 percent to 2 percent (w/w) at 50° C.
19. The composition of claim 1, which is in solution form.
20. An oral liquid composition comprising losartan, or a pharmaceutically acceptable salt or metabolite thereof, and at least one of propylene glycol or glycerin, along with a sucralose or saccharin-containing component and a phosphate-containing buffer comprising sodium phosphate, potassium phosphate, or a mixture thereof, in an amount sufficient to provide a pH of about 6 or higher.
21. A stable oral liquid losartan composition comprising:
losartan or a pharmaceutically acceptable salt or metabolite thereof;

- a solubilizing agent;
a sweetening agent; and
a buffering agent, present in an amount sufficient to provide a pH of about 6 or higher over an extended period of time to minimize degradation of the losartan.
22. A oral liquid composition comprising a solution of losartan, or a pharmaceutically acceptable salt or metabolite thereof, propylene glycol, glycerin, saccharin sodium, and potassium phosphate buffer, each in an amount sufficient to provide a pH of about 6 or higher.
23. A method of preparing an oral liquid losartan composition which comprises:
dissolving an amount of losartan, or a pharmaceutically acceptable salt or metabolite thereof, into at least one liquid adjuvant to form a liquid losartan solution; and
combining the liquid losartan solution with one or more additional pharmaceutically acceptable carriers sufficient to provide a pH of about 6 or higher to form the oral liquid losartan composition.
24. The method of claim 23, wherein the at least one liquid adjuvant comprises a buffering agent.
25. The method of claim 23, wherein the oral liquid losartan composition is a clear solution.
26. A method of preventing, treating, or managing hypertension, congestive heart failure, diabetic nephropathy or myocardial infarction in a mammal which comprises administering to the mammal an effective amount of an oral liquid losartan composition comprising losartan, or a pharmaceutically acceptable salt or metabolite thereof, and at least one pharmaceutically acceptable carrier, wherein the oral liquid losartan composition has a pH of about 6 or higher.
27. The method of claim 26, wherein the composition is administered once or twice a day.
28. The method of claim 26, wherein the total daily dose of losartan is between about 25 mg to 100 mg.
29. The method of claim 26, which further comprises administering at least one other therapeutic agent.
30. The method of claim 29, wherein the at least one other therapeutic agent is at least one other hypertensive agent.
31. The method of claim 30, wherein the at least one other hypertensive agent comprises an angiotensin II antagonist, angiotensin converting enzyme inhibitor, or a neutral endopeptidase/angiotensin converting enzyme inhibitor.

* * * * *

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(54) Title: SOLID PHARMACEUTICAL FORMULATIONS COMPRISING TELMISARTAN

(57) Abstract: The invention relates to new solid pharmaceutical compositions comprising the angiotensin II receptor antagonist telmisartan, a basic agent, a surfactant or emulsifier and a water-soluble diluent, e.g. in form of granules or in form of a powder, as well as solid oral formulations ready for use/ingestion, e.g. capsule and tablet formulations made from said pharmaceutical compositions, and methods for producing said compositions and formulations making use of a fluid-bed granulation process or of a spray-drying process.

WO 2004/028505 A1

SOLID PHARMACEUTICAL FORMULATIONS COMPRISING TELMISARTAN

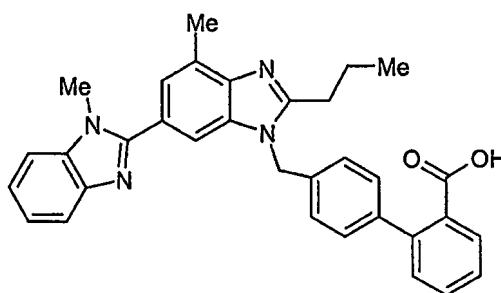
FIELD OF THE INVENTION

5

The present invention relates to new solid pharmaceutical compositions comprising the angiotensin II receptor antagonist telmisartan, e.g. in form of granules or in form of a powder, as well as solid oral formulations ready for use/ingestion, e.g. capsule and tablet formulations made from said pharmaceutical compositions. The present
10 invention also provides methods for producing said compositions and formulations.

BACKGROUND OF THE INVENTION

INN Telmisartan is an angiotensin II receptor antagonist developed for the treatment
15 of hypertension and other medical indications as disclosed in EP-A-502314. Its chemical name is 4'-[2-n-propyl-4-methyl-6-(1-methylbenzimidazol-2-yl)-benzimidazol-1-ylmethyl]-biphenyl-2-carboxylic acid having the following structure:



20

Telmisartan is generally manufactured and supplied in the free acid form. As disclosed in WO 00/43370, crystalline telmisartan exists in two polymorphic forms having different melting points. Under the influence of heat and humidity, the lower melting polymorph B transforms irreversibly into the higher melting polymorph A.
25 Both forms are characterized by a very poor solubility in aqueous systems at the physiological pH range of the gastro-intestinal tract of between pH 1 to 7.

Telmisartan is obtainable on the market under the trade name Micardis®. Starting from the free acid form Telmisartan as introduced to the market is manufactured using an expensive spray-drying process. Due to the poor solubility of the free acid form preparation of alternative telmisartan formulation is difficult.

5

BRIEF SUMMARY OF THE INVENTION

There is a clear need to provide alternative solid oral formulations of Telmisartan which can be prepared using less complicated and expensive processes and fulfill all prerequisites for pharmaceutical use, i.e. long-lasting stability of the formulation under different climatic conditions and sufficient solubility of the active substance for sufficient gastrointestinal absorption in the slightly acidic and neutral pH region.

10

It is a first object of the invention to provide said alternative solid pharmaceutical compositions comprising telmisartan, e.g. in form of granules or a powder, in a form allowing that the active compound is released with sufficient solubility for gastrointestinal absorption in the slightly acidic and neutral pH region from said compositions and formulations.

15

Preferably, the formulations should have immediate release characteristics and a dissolution showing no essential pH dependency within the physiological relevant pH interval of the gastrointestinal tract.

20

It is a second object of the invention to provide further solid oral formulations ready for use/ingestion, e.g. capsule and tablet formulations, made from said pharmaceutical compositions mentioned under the first aspect of the invention.

25

A third object of the invention relates to methods for producing said compositions and formulations mentioned hereinbefore.

DETAILED DESCRIPTION OF THE INVENTION

First object of the invention (pharmaceutical composition)

Surprisingly it has been found that the solubility of telmisartan can be raised by a factor of several hundreds by a pharmaceutical composition comprising 3 to 50 wt.% of telmisartan dispersed in a dissolving matrix comprising

(a) a basic agent in a molar ratio of basic agent : telmisartan = 1:1 to 10:1,

(b) a surfactant or emulsifier in an amount of about 1 to 20 wt.% of the final composition ,

(c) 25 to 70 wt.% of a water-soluble diluent, and

(d) optionally 0 to 20 wt.% of further excipients and/or adjuvants,

the sum of all components adding to 100%.

The term "dissolving tablet matrix" refers to a pharmaceutical tablet base formulation having immediate release (fast dissolution) characteristics that readily dissolves in a physiological aqueous medium.

Specific examples of suitable basic agents are alkali metal hydroxides such as NaOH and KOH; furthermore NaHCO_3 , KHCO_3 , Na_2CO_3 , K_2CO_3 , Na_2HPO_4 , K_2HPO_4 ; basic amino acids such as arginine; and meglumine (N-methyl-D-glucamine).

The surfactants and emulsifiers may be ionic or non-ionic, the latter being preferred. Specific examples of surfactants and emulsifiers are such as poloxamers or pluronics, polyethylene glycols, polyethylene glycol monostearate, polysorbates, sodium lauryl sulfate, polyethoxylated and hydrogenated castor oil etc.

With regard to the poloxamers or pluronics suitable as non-ionic surfactants and emulsifiers is referred to the definition given in The Merck Index, 12th edition, 1996 being herewith incorporated by reference. Suitable poloxamers may have an average

mol weight of about 2000 to 12000, preferably 4000 to 10000, more preferred 6000 to 10000, most preferred 8000 to 9000. Examples for specific poloxamers are poloxamer 182LF, poloxamer 331 and poloxamer 188.

5 Specific examples of suitable water-soluble diluents are carbohydrates such as monosaccharides like glucose; oligosaccharides like sucrose; and sugar alcohols like erythritol, sorbitol, mannitol, dulcitol, ribitol and xylitol. Mannitol, erythritol, sorbitol and sucrose are preferred diluents.

10 The other excipients and/or adjuvants are, for instance, selected from binders, carriers, lubricants, flow control agents, crystallization retarders, solubilizers and coloring agents.

The binder may be selected from the group of dry binders and/or the group of wet
15 granulation binders, depending on the manufacturing process chosen for the pharmaceutical composition. Suitable dry binders are, e.g., cellulose powder, crystalline cellulose, microcrystalline cellulose or light anhydrous silicic acid. Specific examples of wet granulation binders are corn starch, polyvinyl pyrrolidone (Povidone), vinylpyrrolidone-vinylacetate copolymer (Copovidone) and cellulose
20 derivatives like hydroxymethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose and hydroxypropylmethylcellulose.

Suitable disintegrants are, e.g., sodium starch glycolate, Crospovidon, Croscarmellose, sodium carboxymethylcellulose and dried corn starch.

25

The other excipients and adjuvants, if used, are preferably selected from diluents and carriers such as cellulose powder, crystalline cellulose or microcrystalline cellulose, cellulose derivatives like hydroxymethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose and hydroxy-propylmethylcellulose, dibasic calcium
30 phosphate, corn starch, pregelatinized starch, polyvinyl pyrrolidone (Povidone) etc.; lubricants such as stearic acid, magnesium stearate, sodium stearyl fumarate, glycerol tribehenate, etc.; flow control agents such as colloidal silica, light anhydrous silicic acid, crystalline cellulose, talc, etc.; crystallization retarders such as Povidone,

etc.; coloring agents, including dyes and pigments such as Iron Oxide Red or Yellow, titanium dioxide, talc, etc.; and mixtures of two or more of these excipients and/or adjuvants.

5 The pharmaceutical compositions according to the present invention provide improved solubilization of the poorly water-soluble telmisartan of up to a concentration of more than 4.4 mg/100mL, thereby facilitating dissolution of the drug at a physiological pH level, and also provides for immediate release from the fast disintegrating matrix.

10

The presence of component (b), a surfactant or emulsifier, is essential to achieve a substantially improved dissolution of the active ingredient as well as for the use of a simplified manufacture process such as fluid-bed granulation instead of spray-drying for preparing the solid pharmaceutical compositions according to the invention.

15

In a preferred embodiment the pharmaceutical composition according to the invention comprises 10 to 35 wt.% of telmisartan dispersed in a dissolving matrix comprising

20

(a) a basic agent, in a molar ratio of basic agent : telmisartan = 1.5:1 to 5:1,

(b) a non-ionic surfactant or emulsifier, in an amount of about 1 to 10 wt.% of the final composition,

25

(c) 35 to 60 wt.% of a water-soluble diluent, and

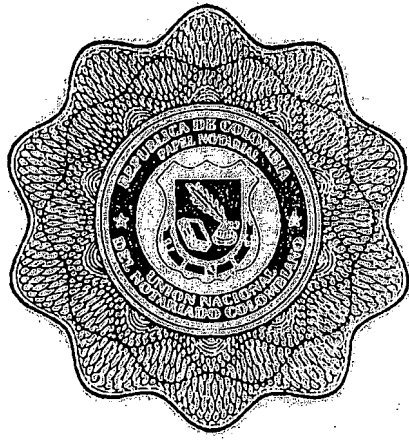
(d) optionally 0 to 20 wt.% of further excipients and/or adjuvants,

the sum of all components adding to 100%.

30

All specified components (a) to (d) mentioned hereinbefore may be used in the preferred embodiment, whereas

AA 328677 NOTARIA TERCERA ENCOLOMIA



ESCRITURA NUMERO CUATRO MIL QUINIENTOS -
TREINTA Y NUEVE (No.4.539) -----
En la ciudad de Cali, Capital del Depar-
tamento del Valle del Cauca, República de
Colombia, a los VEINTITRES (23) días -
del mes de OCTUBRE del año DOS MIL UNO --

(2.001), ante mi, JORGE ENRIQUE CAICEDO ZAMORANO, Notario
T E R C E R O (3o.) del Círculo de Cali, - - - - -
- - - - -
- - - - -
compareció JUAN MANUEL BARBERI OSPINA mayor de edad, vecino de Cali,
identificado con la cédula de ciudadanía número 14.949.561 de Cali, y dijo: ----
PRIMERO.- Que obra en su carácter de Representante Legal de en nombre y
representación de TECNOQUIMICAS S.A. sociedad comercial organizada y existente
conforme a las leyes colombianas, con domicilio y sede principal en Cali constituida
mediante escritura pública número 2670 de la Notaría Segunda de Cali de fecha 12 de
junio de 1957, reformada en distintas oportunidades, según consta en el certificado
expedido por la Cámara de Comercio de Cali -----
SEGUNDO: Que en tal carácter, por este público instrumento, concede Poder Especial
pero amplio y suficiente a JOSE LUIS REYES VILLAMIZAR, mayor de edad, vecino de
Bogotá, identificado con C.C. # 79.152.473 de Isaquén, abogado en ejercicio, portador
de la T.P 44655 del C.S.de la J., domiciliado en Bogotá, D.C., República de Colombia
con dirección carrera 7 No. 88.23 oficina 205, de la misma ciudad, como su representante
con poder especial, amplio y suficiente, para obtener la protección de nuestra propiedad
industrial y contra la competencia desleal, a cuyo efecto lo autorizo, para que nos
represente ante cualesquiera entidad o persona, ejerzan o no jurisdicción, especialmente
ante las del orden administrativo, contencioso-administrativo y judicial, en todo lo
concerniente a los siguientes asuntos: a) Obtención, formulación de observaciones y
oposición a patentes de invención, modelos y dibujos industriales y el registro de
licencias de uso de esos derechos; b) Las acciones de oposición, cancelación, nulidad,
medidas cautelares, concesión de licencias y en general los procesos civiles, penales,
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diferente naturaleza; acciones y procesos que promovamos o se nos promuevan; y c) para

Como Notario Vermitres de este Círculo
hago constar que esta fotocopia coincide
con su fotocopia autentica que se tiene
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13 AGO 2007
WILLY ALEXANDER
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4539
0523

LUZ MERY CORREA
ELABORACION DE ESCRITURAS
Notaría 3ª de Cali

que en todos los asuntos arriba determinados, , tanto en los términos señalados por los artículos 42 y complementarios de la Decisión 486 de la Comunidad Andina como del artículo 70 del C.P.C pueda sustituir este mandato, transigir, conciliar, admitir los hechos del proceso, desistir, cancelar, recibir, renunciar, y ratificar los actos de agentes oficiosos y ceder a título gratuito y/o oneroso, licenciar, inscribir contratos de cesión y de licencia, inscripción de prendas, levantamiento de prendas, inscribir derechos de retención y en general todos los asuntos que se deban tramitar ante la Superintendencia de Industria y Comercio.-----

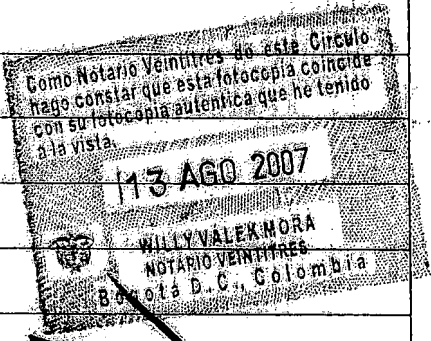
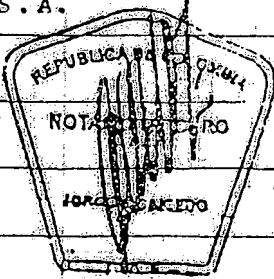
Leído el presente instrumento al otorgante, lo aprobó y en constancia firma conmigo el Notario de todo lo cual doy fe.-----

Se agregan comprobantes. Derechos \$30.000.00 Decreto 1681 de Septiembre 16 de 1996. Reformado mediante Resolución No.5839 de Diciembre 27 del año 2.000 y Decreto 1326 de Julio 06 del año 2.001. Se corrió en la hoja número AA 3286877. ENMENDADO "OCTUBRE" VALE.

91 *Juan m Barberi*

JUAN MANUEL BARBERI OSPINA

En rep. de TECNOQUIMICAS S.A.



El Notario Tercero de Cali
Dr. JORGE ENRIQUE CAICEDO ZAMORANO

23

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1	50005-01-04	PRESENTACION DE OBSERVACIONES A SOLICITUDES	12	MARCAS Y LEMAS COMERCIALES	315.000.00
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					\$315.000.00
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SON: **TRESCIENTOSQUINCE MIL PESOS MONEDA CORRIENTE***					
Responsable: _____					
Recibo de Caja Aplicado al Expediente No. _____					
SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO  No. 11-165084- -00007-0000 Fecha: 2012-09-27 16:54:36 Dep. 2020 DIR.NUEVASCR Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI Act. 400 OPOSIOBSERVTER Folios: 24					
Sede Centro: Carrera 13 No. 27 - 00 Pisos 3,4,5 y 10 Bogotá, D.C.- Colombia					
Web: www.sic.gov.co e-mai: info@sic.gov.co Conmutador: (571) 5870000 Fax: (571) 5870284 Línea: 018000-910165 Call Center: (571) 6513240					
Septiembre 27 de 2012 - 16:03:04					

24

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
NIT : 800.176.089-2
- / -



RECIBO DE CAJA

No. 12 - 0099317

Bogotá D.C., Septiembre 27 de 2012 - 16:03:03

RECIBIDO DE : REYES Y REYES ABOGADOS NI 900.048.328

*** Soporte del Pago ***

TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PAGO	VR. PAGO
CONSIGNACION	BANCO DE BOGOTA	062754387	200604272	27/09/2012	830.000.00

*** Conceptos Pagados ***

CANT.	RENTISTICO	CONCEPTO	Vr.UNDITARIO	Vr.CONCEPTO
1	50005-01-08	PRORROGA DE TERMINOS	100.000.00	100.000.00
		1609 S.DISTINTIVOS PRORROGA DE TERMINOS O PLAZO ADICIONAL		\$100.000.00
				=====

SON: **CIEN MIL PESOS MONEDA CORRIENTE***

Responsable _____

Recibó de Caja Aplicado al Expediente No. _____

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 11-165084- -00007-0000

Fecha: 2012-09-27 16:54:36 Dep. 2020 DIR.NUEVASCR
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Septiembre 27 de 2012 - 16:03:04