Clarke, Modet & C°
COLOMBIA

ESCOBAR - URIBE ASOCIADOS
Intellectual Property

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2585/P.

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIVISION DE NUEVAS CREACIONES
E. S. D.

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
No 03-065794- -00009-0000
Fecha: 2007-03-15 18:43:08 Dep: 2020 NUECREACIONES
Tip: 2 PATENTES Eve: 1 REGDEPOSITO
Act: 457 SOLIC.PRORROGA Folios: 2

Re: Expediente No. **03-065.794**
Solicitud de Patente a nombre de
McNeil-PPC, Inc.

Yo, JIMENA ESCOBAR URIBE, identificada como aparece al pie de mi firma, domiciliada en la carrera 11 No. 86-53, piso 6, obrando como apoderada en este negocio, atentamente solicito a usted se sirva conceder una prórroga de 30 días para dar respuesta al oficio No. 3435 notificado por fijación en lista el 15 de marzo de 2007, relacionado con la solicitud de patente que se está tramitando bajo el expediente de la referencia.

Acompaño el recibo No. 07 - 23,997 de 23 de marzo de 2007, correspondiente a la tasa de la prórroga del término.

Señor Superintendente,

JIMENA ESCOBAR URIBE
C.C. 39.779.452 de Usaquen
T.P. 68.228
Cod. 5376
EUA/ra.

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2585

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

NIT : 800176089-2

RECIBO OFICIAL DE CAJA : 07 - 23,997
FECHA : MARZO 23 DE 2007

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

No 03-065794- -00009-0000

Fecha 2007-03-13 16:43:08 Dep 2020 NUECREACIONES
Usuario PATENTES Evento REGDEPOSITO
Actuación SOLIC PRORROGA Folios 2

***** C O N S I G N A C I O N *****

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PGO	Vr. PAGO
ESCOBAR URIBE ASOCIADOS	CONSIGNACION	BANCO POPULAR	050-00110-6	63066250	22/03/2007	6,644,000.00

***** C O N C E P T O *****

CANT.	RENTISTICO	CONCEPTO	TOTAL CONCEPTO
1	50005-01-08 PRORROGA DE TERMINOS	31 PRORROGA DE TERMINOS	72,000.00
		TOTAL : $	72,000.00

SON: SETENTA Y DOS MIL PESOS

RESPONSABLE : _____

RECIBO DE CAJA APLICADO AL EXPEDIENTE No._____

Clarke, Modet & Cº
COLOMBIA

ESCOBAR - URIBE ASOCIADOS
Intellectual Property

2585/P

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIVISION DE NUEVAS CREACIONES
E. S. D.

Re: Expediente No. **03065794**
Solicitud de patente a nombre de
McNeil-PPC, Inc.

Yo, JIMENA ESCOBAR URIBE, identificada como aparece al pie de mi firma, domiciliada en la carrera 11 No. 86-53, Piso 6, obrando como apoderada de la sociedad **McNeil-PPC, Inc.**, domiciliada en Skillman, New Jersey, Estados Unidos de América, solicitante de la patente de la referencia, en respuesta al oficio No. 3435 notificado por fijación en lista el 15 de marzo de 2007, relacionado con el concepto técnico de fondo No. 407, me permito manifestar lo siguiente:

1. Con fundamento en la facultad que confiere el artículo 34 de la Decisión 486 al solicitante para modificar la solicitud de patente en cualquier momento del trámite, presento junto con este memorial de nuevo el capítulo reivindicatorio en el cual se realizó la reforma en el orden de aparición de las reivindicaciones dentro del mismo con el propósito de brindarle un sentido más organizado en la secuencia. Las modificaciones fueron las siguientes:

1.1.1 La antigua reivindicación 15 se renumeró como la nueva reivindicación 13.

1.1.2 La antigua reivindicación 16 se renumeró como la nueva reivindicación 14.

1.1.3 La antigua reivindicación 24 se renumeró como la nueva reivindicación 15.

1.1.4 La antigua reivindicación 16 se renumeró como la nueva reivindicación 16.

1.1.5 La antigua reivindicación 13 se renumeró como la nueva reivindicación 17.

1.1.6 La antigua reivindicación 14 se renumeró como la nueva reivindicación 18 y se modificó su dependencia.

1.1.7 La antigua reivindicación 18 se renumeró como la nueva reivindicación 19.

1.1.8 La antigua reivindicación 19 se renumeró como la nueva reivindicación 20.

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1.1.9 La antigua reivindicación 20 se renumeró como la nueva reivindicación 21 y se modificó su dependencia.

1.1.10 La antigua reivindicación 21 se renumeró como la nueva reivindicación 22 y se modificó su dependencia.

1.1.11 La antigua reivindicación 22 se renumeró como la nueva reivindicación 23 y se modificó su dependencia.

1.1.13 La antigua reivindicación 23 se renumeró como la nueva reivindicación 24 y se modificó su dependencia.

1.1.14 La antigua reivindicación 26 se renumeró como la nueva reivindicación 25.

1.1.15 La antigua reivindicación 17 se renumeró como la nueva reivindicación 26 y además en dicha reivindicación se cambió la expresión "***condiciones suficientes***" por la expresión "***temperatura y presión ambiente***", el sustento para esta modificación se encuentra en la página 26 línea 20 hasta la línea 1 de la página 27 de la memoria descriptiva.

Sobre este particular me permito manifestar que el capítulo reivindicatorio presentado con este memorial no amplía de ninguna manera la materia de la invención en estudio y las modificaciones se realizaron con el fin de dar cabal cumplimiento a las objeciones respecto a los artículos 28 y 30 de la Decisión 486.

Para este efecto, me permito acompañar el recibo No.07-51,462 de 27 de junio de 2007 con el cual queda cubierta la tasa correspondiente a la modificación de una solicitud de patente en cuanto a sus reivindicaciones.

2. Claridad de la Solicitud

2.1 Respecto a la antigua reivindicación 16, me permito decir que la misma ya se había redactado de tal manera que la expresión "*satisface los requerimientos de disolución de la USP*" hiciera parte del preámbulo y no de la parte caracterizante de la reivindicación. En este sentido, me permito decir que una persona versada en la materia entiende que dicha característica o condición no sólo la puede cumplir la tableta de la presente invención sino cualquier tableta y en consecuencia dicha reivindicación es clara, ya que está caracterizada no por la expresión en cuestión sino porque comprende una cantidad efectiva de un ingrediente farmacéutico activo de acuerdo con la invención.

2.2 En cuanto a la antigua reivindicación 17 (nueva reivindicación 26), me permito manifestar que la objeción de claridad queda cabalmente superada, toda vez que se reemplazó el término ambiguo "***condiciones suficientes***" por la expresión "***temperatura y presión ambiente***", cuyo sustento está ubicado en la página 26 línea 20 hasta la línea 1 de la página 27 de la descripción.

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3. Nivel Inventivo

En el oficio No. 3435, el examinador continúa estableciendo que: *"El documento del Estado de la Técnica más próximo es D2 que enseña una forma de dosis farmacéutica que comprende un núcleo y un recubrimiento que comprende: (a) formador de película (polímero de ácido acrílico como Eudragit L30D) y (c) plastificante (PEG).*
La única diferencia con D2 es que esta solicitud menciona expresamente el ***parabeno****. Pero este no parece conceder un efecto técnico inesperado a la forma farmacéutica.*
El mencionar ahora la inclusión del ***parabeno*** *en la composición de esta anterioridad, para lograr así la composición reivindicada, era evidente para un experto en la materia, enfrentado al Problema Técnico planteado en esta solicitud: La necesidad de una forma farmacéutica con un recubrimiento con resistencia, plasticidad, dureza, espesor adecuados que se adhieran bien al sustrato, con dispersión uniforme de color y apariencia estética sin rugosidad, con brillo y espesor uniforme y que evite la contaminación microbiana.*
El hecho de incluir ***parabeno*** *que es un preservante conocido en la técnica (ver D3 Pág. 2241 donde se explica que toda forma farmacéutica líquida o semisólida necesita incluir un preservante tal como parabeno que es éster metílico o propílico del ácido p-hidroxibenzóico) en la composición de recubrimiento de D2, con el fin de evitar la contaminación microbiológica, es evidente para un experto en la materia. Por lo cual no hay nivel inventivo en las reivindicaciones 1-12, 15, 18-25, 13-14 y 26."*
Si se hubiese demostrado que la inclusión de ***parabeno*** *tiene efectos superiores en comparación con las formas farmacéuticas de la técnica, se podría considerar que hay nivel inventivo. Pero no es así.*

El método de hacer tabletas recubiertas que consiste en recubrirlas por inmersión (reivindicación 17) es obvio a partir de D1 que enseña el método de hacer capletas recubiertas que consiste en recubrirlas por inmersión, donde la figura 2 presenta la forma como se sostiene la tableta y se sumerge en el material de recubrimiento y se explica que después de dejar secar, se recubre con otra capa y luego se realiza el mismo proceso con el otro extremo de la capleta que aún no ha sido recubierto, por lo cual no tiene nivel inventivo.

Respuesta a los Argumentos del solicitante
Inatención a los argumentos del solicitante se hacen las siguientes aclaraciones:
1. Dice el solicitante que adjunta un nuevo capítulo reivindicatorio. Se aclara al solicitante que se acepta el nuevo capítulo de los folios 154-160.
2. Dice el solicitante que D1 no afecta el nivel inventivo de esta solicitud porque incluye un recubrimiento de gelatina. Y que el recubrimiento con gelatina tiene la desventaja de ser aplicado por aspersión y ser susceptible de contaminación microbiana.
Se aclara al solicitante que D1 si afecta el nivel inventivo de esta solicitud justamente porque aunque incluye un recubrimiento de gelatina, este no se aplica por aspersión, sino por inmersión. De manera que para una persona conocedora de la materia era obvio aplicarlo con composiciones como las que se enseñan previamente en D2.
3. Dice el solicitante que D2 no afecta el nivel inventivo de esta solicitud aunque menciona un recubrimiento que comprende: (a) formador de película... y (c) plastificante (PEG), porque no menciona el parabeno como plastificante.
Se reitera al solicitante que incluir el ***parabeno*** *(que en un preservante conocido en la técnica) en la composición de esta anterioridad, para lograr así la composición reivindicada, era evidente*

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para un experto en la materia, enfrentado al Problema Técnico planteado en esta solicitud: la necesidad de uniforma farmacéutica con un recubrimiento con resistencia, plasticidad, dureza, espesor adecuados que se adhieran bien al sustrato, con dispersión uniforme de color y apariencia estética sin rugosidad, con brillo y espesor uniforme y que evite la contaminación microbiana."

En primer lugar, respecto a la afectación del nivel inventivo de la antigua reivindicación 17 (nueva reivindicación 26) con las enseñanzas del documento US 4,820,524, me permito decir que el uso de gelatina como un material de recubrimiento farmacéutico presentaba desventajas y limitaciones que incluían la posibilidad de disminuir la velocidad de disolución luego de almacenamiento prolongado, esto debido al entrelazamiento de la gelatina. Adicionalmente también presentaba posible contaminación microbiana de la solución de gelatina durante el procesamiento y por último, tiempos de procesamiento prolongados debido a requerimientos de secado extenso.

Si a lo anteriormente mencionado se agregan las desventajas de costos relacionados con la energía implicada en los recubrimientos de gelatina, la cual tiende a ser alta, toda vez que el material de gelatina debía ser aplicado a los substratos a una temperatura elevada de por lo menos 40°C para mantener la fluidez de la gelatina, mientras que los substratos se mantenían a 50 °C para minimizar el crecimiento microbiano, se puede decir que las soluciones de recubrimiento que contenían gelatina resultaban ser bastantes dispendiosas al momento de la fabricación de los recubrimientos en capletas.

En este sentido, el documento D1 en su columna 3, líneas 6 a 9 revela o sugiere que la gelatina debe ser pre-tratada con agua en un horno para cocción a presión a una temperatura de 120 a 140°F (48.8 a 60°C) durante un período de 30 a 40 minutos a fin de reducir las propiedades adhesivas de la gelatina para permitir el recubrimiento de la tableta. Aún más, en la columna 8 entre las líneas 63 a 68 de D1 se sugiere que la mezcla de gelatina debe poseer un valor de viscosidad de 500 cp a una temperatura de operación de 130°F (54.4°C).

Esta información le estaría indicando a la persona versada en la materia que el proceso revelado en D1, se debe realizar a **temperaturas más altas que la temperatura ambiente** con el ánimo de mantener condiciones aptas para evitar la contaminación microbiana y conservar propiedades deseadas en la mezcla de gelatina y condiciones de mayor presión en pre-tratamiento de la solución de gelatina.

Por el contrario, el método para preparar tabletas recubiertas de acuerdo con la invención en estudio comprende recubrir por inmersión tabletas con la dispersión acuosa a una **temperatura y presión ambientes** para formar un recubrimiento sobre la tableta. Esto no habría sido susceptible de derivación evidente por parte de una persona versada en la materia justo antes de la fecha de prioridad de esta solicitud, es decir, antes del 2 de agosto de 2002, toda vez que la técnica anterior enseñaba un método para el recubrimiento de capletas con **composiciones de gelatina a temperaturas por encima de la temperatura ambiente y con pre-tratamientos en hornos de cocción a presión** para alcanzar propiedades deseables en la composición de gelatina.

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En consecuencia, el método revelado en la presente invención ahora especificado para una **temperatura y presión ambiente**, no habría sido evidente para una persona versada en la materia a partir de lo revelado en D1, toda vez que dicha anterioridad sugiere un **método a temperaturas más altas que la ambiente y con pre-tratamiento a alta presión**. Así las cosas, la nueva reivindicación 26 sí posee altura inventiva sobre lo revelado en D1.

De otra parte, el examinador establece que las antiguas reivindicaciones 1 a 12, 15, 18 a 25, 13 a 14 y 26 carecían de nivel inventivo en vista de la combinación de los documentos D2 y D3.

Sobre este particular, me permito decir que existían desventajas asociadas con la inmersión de tabletas o cápsulas en un sistema de recubrimiento que careciera de gelatina, toda vez que resultaban recubrimientos con escasas propiedades físicas adecuadas, por ejemplo resistencia a la tensión, plasticidad, dureza y espesor.

Si bien se sabía que la inclusión de plastificantes podía mejorar las propiedades de plasticidad de los recubrimientos, dichos sistemas de recubrimiento sin gelatina por lo general resultaban inconvenientes para las tabletas, toda vez que terminaban siendo **recubrimientos blandos, pegajosos y sin una dureza suficiente** para mantener su forma o suavidad durante su manipulación.

Además, muchas composiciones que no son de gelatina no se adherían al substrato de tableta en una cantidad suficiente para recubrir uniformemente la tableta después de una sola inmersión. Es así que muchas composiciones que no eran de gelatina carecían de las propiedades reológicas suficientes necesarias para mantener una dispersión de color uniforme durante todo el proceso de inmersión y secado.

En este sentido, se habían hecho intentos para mejorar las propiedades reológicas de estas composiciones, por ejemplo mediante **el aumento de su contenido de sólidos para incrementar la viscosidad**. Sin embargo, con frecuencia dichas composiciones resultaban inconvenientemente en una estética de recubrimiento indeseable, como rugosidad de superficie, disminución de brillo, y un grosor no uniforme del recubrimiento.

En este orden de ideas, la superación de estas desventajas mediante las composiciones de la presente invención se constituye en un hecho importante y contribuyente al campo técnico, toda vez que se logra producir un material de recubrimiento, en particular un material de recubrimiento por inmersión, que no solo promueve una forma de dosis elegante, brillante, de alto lustre, preferida por el consumidor, y similar a las formas recubiertas con gelatina, sino que supera las limitaciones acarreadas por la presencia de la gelatina en las composiciones de recubrimiento de la técnica anterior.

Ahora bien, el examinador establece que el incluir parabeno el cual es un preservante conocido en la técnica como lo indica D3 en la composición de recubrimiento de D2 con el fin de evitar la contaminación microbiológica, era evidente para un versado en la materia.

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Sobre este particular, me permito manifestar que como se demostró en mi memorial anterior, la referencia D2 revela o sugiere un proceso para producir una tableta que contiene S-ibuprofeno, que permite la rápida liberación del ingrediente activo. De hecho, D2 trata sobre el problema de la **poca fluidez de la mezcla en polvo durante la etapa de compresión** cuando la mezcla contiene el ingrediente activo S-ibuprofeno.

D2 sugiere que para lograr tabletas de ibuprofeno que sean de fácil liberación y que puedan ser preparadas con facilidad a gran escala, la mezcla debe ser combinada con un aglutinante seco para que las tabletas presenten ventajas durante la compresión.

Así las cosas, D2 no se está enfocado al problema de encontrar recubrimientos con resistencia, plasticidad, dureza y espesor adecuados que sean susceptibles de adherirse de manera eficaz al sustrato mediante un proceso de aplicación por inmersión.

Si a lo anterior se suma el hecho de que la referencia D3 (Remington Farmacia) enseña que el parabeno es un conservador para una forma farmacéutica líquida o semisólida a fin de evitar el crecimiento de hongos, se puede constatar que la combinación de estas dos anterioridades **no llevaría de manera evidente a una persona medianamente versada en la técnica** a la materia objeto de la solicitud en estudio, toda vez que D2 no se refiere a un problema similar y D3 enseña parabenos como conservadores.

En este sentido, se podría decir que la persona versada en la materia no encontraría evidente la incorporación de parabeno como un **plastificante** en composiciones para recubrimiento exentas de gelatina, toda vez que pensaría que el parabeno sólo se podría emplear para **evitar el crecimiento de hongos en composiciones que tuvieran gelatina que sería un medio apropiado para el crecimiento de hongos y bacterias** y no vería necesaria la participación de parabeno en composiciones que no presentaran gelatina.

Aún más, como se expuso más arriba, en la técnica anterior se había tratado de mejorar las características reológicas de composiciones de recubrimiento que carecían de gelatina mediante el aumento de su contenido de sólidos para incrementar la viscosidad. En este sentido, me permito dirigir la atención del examinador a los cuadros A y B ubicados en la página 36 de la descripción:

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Cuadro A

Composición acuosa de dispersión de recubrimiento de inmersión

Ingrediente	**Cantidad (g)**
Cloruro de poli(acrilato de etilo, metacrilato de metilo)trimetilamonioetilo metacrilato, de Rohm Pharma bajo la marca "Eudragit RL30D" * (dispersión al 30%)	100.0*
Metilparabeno	5.0
Polivinilpirrolidona de BASF Aktiengesellschaft bajo la marca "K-90"	12.0
Agua	60.0
Colorante rojo # 55	1.0
Laca roja # 40	0.5
PEG 400	4.0
Peso de solución total	182.5
Sólidos en solución de recubrimiento	**52.5 g (28.78%)**

Cuadro B

Composición acuosa en dispersión del recubrimiento de inmersión

Ingrediente	**Cantidad (g)**
Cloruro de poli(acrilato de etilo, metacrilato de metilo)trimetilamonioetilo metacrilato, de Rohm Pharma bajo la marca "Eudragit RL30D" (*dispersión al 30%)	100.0*
Metilparabeno	5.0
Polivinilpirrolidona de BASF Aktiengesellschaft bajo la marca "K-90"	12.0
Agua	110
Color amarillo "Opatint"® de Colorcon, Inc.	3.0
PEG 400	4.0
Peso de solución total	234
Sólidos en solución de recubrimiento	**54 g (23.07%)**

En dichos cuadros se puede apreciar como el porcentaje de sólidos en la solución de recubrimiento de la presente invención no pasan del 29%, lo cual resulta ser sorprendente debido a que no hay necesidad de aumentar la viscosidad de las composiciones a fin de obtener propiedades reológicas deseables ya que gracias a la presencia del parabeno como un **plastificante primario** se logran dichas

propiedades en las composiciones de recubrimiento de la presente invención que carecen de gelatina.

Así las cosas, me permito decir que ni el método para preparar las tableas recubiertas por inmersión ni las composiciones de recubrimiento de la presente solicitud podrían ser derivadas de manera evidente por una persona versada en la materia a partir de los documentos citados por ese despacho.

De hecho, la única manera mediante la cual se llegaría a las composiciones de la invención en cuestión sería a través de un enfoque de tipo hindsight, el cual no es permitido al momento de juzgar la altura inventiva de una patente.

Sobre este particular, atentamente me permito dirigir la atención del examinador al *Manual para el Examen de Solicitudes de Patentes de Invención en las Oficinas de Propiedad Industrial de los Países de la Comunidad Andina*, principalmente al numeral 10.2 que versa sobre el método para la evaluación del nivel inventivo, en especial a la página 78 donde se manifiesta que "*se debe tener en cuenta que la búsqueda de anterioridades se efectúa a* ***posteriori*** *tomando como punto de partida la misma invención. Por lo tanto el* ***examinador debe realizar un esfuerzo intelectual*** *de colocarse en la situación que ha tenido que afrontar el técnico con conocimientos medios en la materia en un momento en que la invención no era conocida, es decir antes de la invención.*" (Resaltado fuera de texto).

En efecto, el examinador no está enfocando su análisis en el momento en el que el inventor plantea un problema con el fin de solucionar fallas técnicas existentes en los productos convencionales, sino en el momento de la solución dada al problema planteado. En este instante para el examinador puede resultar "obvio" que el objeto de la presente solicitud se derive de manera evidente de la materia objeto de los documentos citados como referencia, sin dar mayor importancia al trabajo desplegado y a la capacidad inventiva del solicitante para lograr llegar a la solución del problema planteado.

Lo anterior significa que el examinador no ha realizado su análisis partiendo del problema mismo que existía en la técnica en el momento en que **el inventor dirige todos sus esfuerzos para encontrar una solución técnica, sino que enfoca su estudio en el momento en que el problema ya está resuelto**. El examinador debe brindar más importancia al problema técnico planteado y a los medios realizados para llegar a la solución propuesta al momento de enfocar su análisis, en lugar de limitarse a la simple comparación de las características técnicas del producto objeto de la patente solicitada con las características de las referencias citadas.

De esta manera, para que el examinador desvirtúe la invención por falta de altura inventiva, debe enfocar primero su atención en la comprensión del problema planteado y la solución suministrada en ese momento por el inventor y no incurrir en el error de analizar o considerar el problema **después** de que este ha sido resuelto.

En este orden de ideas, la persona versada en la materia llegaría al objeto de la solicitud en estudio a través de estos documentos (D1 a D3) **únicamente teniendo en cuenta la manera como se soluciona** el problema antes planteado mediante esta invención. Esta forma de análisis es perceptible en los argumentos del examinador, quien sin hacer un esfuerzo intelectual por colocarse en el momento justo antes de la presentación de esta solicitud, hace referencia al libro Remington Farmacia (D3) como documento relevante en combinación con D2, arguyendo que D3 enseña los parabenos como conservadores, pero sin contemplar que D3 falla en sugerir o enseñar que pudieran participar dichos parabenos como plastificantes primarios, mediante los cuales se lograran composiciones de recubrimiento con propiedades deseables, como sí lo hace la invención en estudio.

En conclusión, me permito decir que la presente invención cumple con los requisitos de patentabilidad, principalmente con lo que respecta al nivel inventivo y así las cosas, ruego a ese despacho aceptar la argumentación presentada y conceder finalmente el beneficio de patente de invención a la solicitud en estudio.

Señor Superintendente,

JIMENA ESCOBAR URIBE

C.C. 39.779.452 de Usaquen

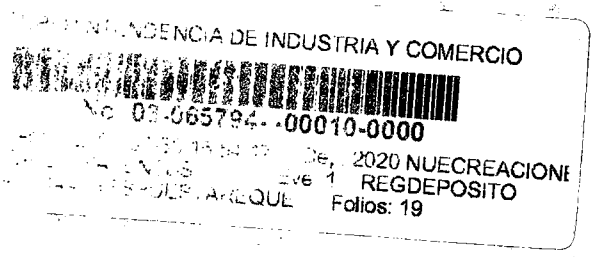
T.P. 68.228

EUA/ml.

3585 182

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

NIT : 800176089-2



[redacted]IBO OFICIAL DE CAJA : 07 - 51,462
[redacted]CHA : JUNIO 27 DE 2007

***** C O N S I G N A C I O N *****

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PGO	Vr. PAGO
CLARKE MODET Y CO. COLOMB	CONSIGNACION	BANCO POPULAR	050-00110-6	66415409	26/06/2007	9,193,000.00

***** C O N C E P T O *****

[redacted]T.	RENTISTICO	CONCEPTO	TOTAL CONCEPTO
1	50005-01-03 CAMBIO DE MODALIDAD Y MODIFICA	12 MARCAS Y LEMAS COMERCIALES	99,000.00
		TOTAL :	$ 99,000.00

SON: NOVENTA Y NUEVE MIL PESOS

RESPONSABLE : _____

RECIBO DE CAJA APLICADO AL EXPEDIENTE No._____

10

REIVINDICACIONES

1.- Una forma de dosis farmacéutica que comprende

a) un núcleo que tiene una superficie; y

b) una composición formadora de película que cubre al menos una porción de la superficie, dicha composición formadora de película comprende, en base al peso total de sólidos secos de la composición:

(a) de 10 por ciento a 70 por ciento de un formador de película comprendido de un polímero o copolímero de ácido acrílico o un derivado del mismo, o una mezcla del polímero o copolímero de ácido acrílico o un derivado del mismo;

(b) de 2 por ciento a 20 por ciento de un plastificante primario comprendido de un parabeno; y

(c) de 1 por ciento a 50 por ciento de un plastificante secundario seleccionado del grupo que consiste de polivinilpirrolidona, polietilenglicol 300, polietilenglicol 400, sales farmacéuticamente aceptables de los mismos y sus mezclas.

2.- La forma de dosis farmacéutica de conformidad con la reivindicación 1, caracterizada además porque el formador de película se selecciona del grupo que consiste de:

a) un polímero o copolímero de ácido metacrílico o un derivado del mismo; y

(b) mezclas del polímero o copolímero de ácido metacrílico o su derivado.

3.- La forma de dosis farmacéutica de conformidad con la reivindicación 1, caracterizada además porque el formador de película es copolímero de metacrilato de amonio.

4.- La forma de dosis farmacéutica de conformidad con la reivindicación 1, caracterizada además porque el formador de película se selecciona del grupo que consiste de:

a) poli(acrilato de etilo, metacrilato de metilo, cloruro de trimetilamonioetilo metacrilato) en una relación en peso de 1:2:0.1;

b) poli(ácido metacrílico, metacrilato de metilo) en una relación en peso de 1:2;

c) poli(ácido metacrílico, metacrilato de metilo) en una relación en peso de 1:1;

d) copolímeros de los mismos; y

e) mezclas de los mismos.

5.- La forma de dosis farmacéutica de conformidad con la reivindicación 1, caracterizada además porque el formador de película se selecciona del grupo que consiste de:

a) poli(acrilato de etilo, metacrilato de metilo, cloruro de trimetilamonioetilo metacrilato);

b) poli(ácido metacrílico, acrilato de etilo);

c) poli(acrilato de etilo, metacrilato de metilo);

d) poli(acrilato de etilo, metacrilato de metilo)cloruro de trimetilamonioetilo metacrilato);

e) copolímeros de los mismos; y

f) mezclas de los mismos.

6.- La forma de dosis farmacéutica de conformidad con la reivindicación 1, caracterizada además porque el parabeno se selecciona del grupo que consiste de metilparabeno, etilparabeno, propilparabeno, butilparabeno, sales farmacéuticamente aceptables de los mismos, y mezclas de los mismos.

7.- La forma de dosis farmacéutica de conformidad con la reivindicación 1, caracterizada además porque el plastificante secundario es polivinilpirrolidona.

8.- La forma de dosis farmacéutica de conformidad con la reivindicación 1, caracterizada además porque está sustancialmente libre de gelatina.

9.- La forma de dosis farmacéutica de conformidad con la reivindicación 1, caracterizada además porque comprende, en base al peso seco total de la composición, de 0 por ciento a 14 por ciento de un agente colorante.

10.- La forma de dosis farmacéutica de conformidad con la reivindicación 9, caracterizada además porque el agente colorante se selecciona del grupo que consiste de colorantes azo, colorantes de quinoftalona, colorantes de trifenilmetano, colorantes de xanteno, colorantes indigoides, óxidos de hierro, hidróxidos de hierro, dióxido de titanio, colorantes naturales, y mezclas de los mismos.

11.- La forma de dosis farmacéutica de conformidad con la reivindicación 1, caracterizada además porque comprende una pluralidad de recubrimientos exteriores, en donde por lo menos una primera porción de la forma de dosis está comprendida de un primer recubrimiento exterior, y por lo menos una segunda porción de la forma de dosis está comprendida de un segundo recubrimiento exterior.

12.- La forma de dosis farmacéutica de conformidad con la reivindicación 11, caracterizada además porque el segundo recubrimiento exterior es visualmente distinto del primer recubrimiento exterior.

13.- Una forma de dosis farmacéutica de conformidad con la reivindicación 1 en la forma de una tableta o capleta.

14.- La forma de dosis farmacéutica que cumple con los requerimientos de disolución de la USP para formas de liberación inmediata de ingrediente farmacéutico activo de conformidad con la reivindicación 1, caracterizada porque comprende una cantidad efectiva de un ingrediente farmacéutico activo.

15.- La forma de dosis farmacéutica de conformidad con la reivindicación 1, caracterizada además porque el formador de película es una mezcla que comprende un polímero o copolímero de ácido acrílico o un derivado del mismo.

16.- La forma de dosis farmacéutica de conformidad con la reivindicación 1, caracterizada además porque el formador de película es un

copolímero que comprende un polímero o copolímero de ácido acrílico o un derivado del mismo.

17.- Una forma de dosis farmacéutica que comprende un núcleo, una subcapa de recubrimiento que cubre sustancialmente dicho núcleo, y un recubrimiento exterior que cubre sustancialmente dicha subcapa, en donde el recubrimiento exterior está comprendido de la composición formadora de película comprendida, en base al peso total de sólidos secos de la composición, de:

(a) de 10 por ciento a 70 por ciento de un formador de película comprendido de un polímero o copolímero de ácido acrílico o un derivado del mismo, o una mezcla del polímero o copolímero de ácido acrílico o un derivado del mismo;

(b) de 2 por ciento a 20 por ciento de un plastificante primario comprendido de un parabeno; y

(c) de 1 por ciento a 50 por ciento de un plastificante secundario seleccionado del grupo que consiste de polivinilpirrolidona, polietilenglicol 300, polietilenglicol 400, sales farmacéuticamente aceptables de los mismos y sus mezclas.

18.- La forma de dosis recubierta de conformidad con la reivindicación 17, caracterizada además porque la subcapa de recubrimiento se selecciona del grupo que consiste de éteres de celulosa, plastificantes, policarbohidratos, pigmentos, opacantes y mezclas de los mismos.

19.- Una forma de dosis farmacéutica que comprende un núcleo

y un recubrimiento, dicho recubrimiento cubriendo por lo menos una porción de dicho núcleo, en donde el recubrimiento comprende:

a) de 40 por ciento a 65 por ciento de un formador de película comprendido de un polímero o copolímero de ácido acrílico o un derivado del mismo, o una mezcla del polímero o copolímero de ácido acrílico o un derivado del mismo;

b) de 5 por ciento a 15 por ciento de un plastificante primario comprendido de un parabeno; y

c) de 15 por ciento a 35 por ciento de un plastificante secundario seleccionado del grupo que consiste de polivinilpirrolidona, polietilenglicol 300, polietilenglicol 400, sales farmacéuticamente aceptables de los mismos y sus mezclas.

20.- Una forma de dosis farmacéutica, que comprende:

a) un núcleo que tiene un primer extremo y un segundo extremo;

b) una primera capa de recubrimiento que tiene una primera distinción visual provista sobre dicho primer extremo de dicho núcleo de tableta; y

c) una segunda capa de recubrimiento que tiene una segunda distinción visual sobre dicho segundo extremo de dicho núcleo de tableta;

en donde por lo menos una de la primera capa de recubrimiento y la segunda capa de recubrimiento está comprendida en base al peso total de sólidos secos de la composición :

(a) de 10 por ciento a 70 por ciento de un formador de película

comprendido de un polímero o copolímero de ácido acrílico o un derivado del mismo, o mezclas del polímero o copolímero de ácido acrílico o derivados de los mismos;

(b) de 2 por ciento a 20 por ciento de un plastificante primario comprendido de un parabeno; y

(c) de 1 por ciento a 50 por ciento de un plastificante secundario seleccionado del grupo que consiste de polivinilpirrolidona, polietilenglicol 300, polietilenglicol 400, sales farmacéuticamente aceptables de los mismos y sus mezclas.

21.- La forma de dosis farmacéutica de conformidad con la reivindicación 20, caracterizado además porque la segunda distinción visual es visualmente diferente de dicha primera distinción visual.

22.- La forma de dosis farmacéutica de conformidad con la reivindicación 21, caracterizado además porque la primera distinción visual es de un primer color, y la segunda distinción visual es de un segundo color.

23.- La forma de dosis farmacéutica de conformidad con la reivindicación 20, caracterizado además porque comprende una subcapa de recubrimiento que cubre sustancialmente dicho núcleo; dicha subcapa de recubrimiento estando provista entre dicho núcleo y dicha primera capa de recubrimiento y dicha segunda capa de recubrimiento.

24.- La forma de dosis farmacéutica de conformidad con la reivindicación 23, caracterizado además porque la subcapa de recubrimiento se selecciona del grupo que consiste de éteres de celulosa, plastificantes,

policarbohidratos, pigmentos, opacantes, y mezclas de los mismos.

25.- Una composición formadora de película que comprende un núcleo y un recubrimiento, dicho recubrimiento recubre al menos una porción del núcleo, en donde el recubrimiento comprende, en base al peso total de sólidos secos del recubrimiento:

(a) de 10 por ciento a 70 por ciento de un formador de película comprendido de un polímero o copolímero de ácido acrílico o un derivado del mismo, o una mezcla del polímero o copolímero de ácido acrílico o un derivado del mismo; y

(b) de 3 por ciento a 70 por ciento de un plastificante seleccionado del grupo que consiste de triacetina, monolglicérido acetilado, aceite de colza, aceite de oliva, aceite de ajonjolí, acetiltributil citrato, glicerina sorbitol, dietiloxalato, dietilmalato, dietil fumarato, dietil succinato, dietilmalonato, dioctilftalato, dibutilsuccinato, trietilcitrato, tributilcitrato, glicerotributirato, propolenglicol, polietilen glicoles, aceite de ricino hidrogenado, ácidos grasos, glicéridos y triglicéridos sustituidos, metil parabeno, etil parabeno, propil parabeno, butil parabeno, polivinilpirrolidona, polietilenglicol 300, polietilen glicol 400, y sales farmacéuticamente aceptables y mezclas de los mismos.

26.-Un método para preparar tabletas recubiertas, que comprende recubrir por inmersión tabletas con la dispersión acuosa a temperatura y presión ambientes para formar un recubrimiento sobre la tableta, dicha dispersión acuosa comprendida en base al peso total de la

dispersión:

(a) de 10 por ciento a 70 por ciento de un formador de película comprendido de un polímero o copolímero de ácido acrílico o un derivado del mismo, o mezclas del polímero o copolímero de ácido acrílico o derivados de los mismos;

(b) de 1 por ciento a 40 por ciento de un plastificante primario comprendido de un parabeno; y

(c) de 5 por ciento a 20 por ciento de un plastificante secundario seleccionado del grupo que consiste de polivinilpirrolidona, polietilenglicol 300, polietilenglicol 400, sales farmacéuticamente aceptables de los mismos y sus mezclas; y

(d) de 5 por ciento a 30 por ciento de agua.

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United States Patent [19]

Berta

[11] **Patent Number: 4,820,524**

[45] **Date of Patent: Apr. 11, 1989**

[54] **GELATIN COATED CAPLETS AND PROCESS FOR MAKING SAME**

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[73] Assignee: **McNeilab, Inc., Spring House, Pa.**

[21] Appl. No.: **16,914**

[22] Filed: **Feb. 20, 1987**

[51] **Int. Cl.**[4] **A61K 45/00**

[52] **U.S. Cl.** **424/474**; 424/463; 424/475; 427/3

[58] **Field of Search** 424/460, 463, 474, 475, 424/454; 427/3; 206/528; 220/8, 20; 604/890.1

[56] **References Cited**

U.S. PATENT DOCUMENTS

599,865	3/1898	Richards .	
671,804	4/1901	Metcalf .	
724,436	4/1903	Clark .	
1,872,190	8/1932	Sindl	425/272
3,045,641	7/1962	Oddo	118/16
3,185,626	5/1965	Baker	167/82
3,228,789	1/1966	Glassman	117/118
3,436,453	4/1969	Vinunt, Jr. et al.	424/463
3,896,762	7/1975	Banker	118/30
4,238,510	12/1980	Cherukuri .	
4,562,024	12/1985	Rogerson	264/117
4,585,764	4/1986	Bailey	514/163
4,590,183	5/1986	Bailey	514/163
4,684,516	8/1987	Bhutani	427/3
4,713,248	12/1987	Kjorn et al.	424/468
4,716,042	12/1987	Blank et al.	424/474

FOREIGN PATENT DOCUMENTS

52-041213	3/1977	Japan .
65009994	7/1984	Japan .
65009992	7/1984	Japan .
60-084215	5/1985	Japan .
69027916	7/1985	Japan .
69026677	7/1985	Japan .

OTHER PUBLICATIONS

Stedman's Medical Dictionary, Anderson Publ. Co., 5th ed., Williams and Wilkins, Baltimore, MD (1982) p. 1377.

Lackman, *The Theory and Practice of Industrial Pharmacy*, Liberman and King, pp. 389–398 (1970).

Glatt Air Techniques Trade Literature for GC–1000, Ramsey, N.J.

Remington's Practice of Pharmcy, Martin & Cook, 17th Ed., pp. 1625–1630.

Cherry–Burrell Trade Literature for 950 Hard Gelatin Capsule Machine, Cedar Rapids, IA.

Vector/Freund Trade Literature for Hi–Coaters System, Marion, IA.

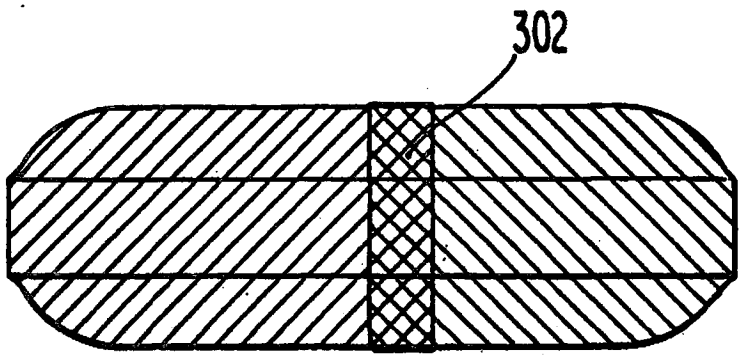
C. G. Richardson, Franciscus Pill Coater, Int'l. Pharm. Abs., 28:90–91, pp. 70–86 (Oct. 1986).

Primary Examiner—Ellis P. Robinson
Assistant Examiner—P. J. Ryan
Attorney, Agent, or Firm—Joseph F. Shirtz

[57] **ABSTRACT**

A novel capsule-like medicament, method for producing such medicaments and apparatus are disclosed. The method provides a procedure for coating solid cores, such as caplets, with gelatinous coatings to produce a shiny, capsule-like medicament. Such medicaments are achieved by individually dipping and drying first one end, and then the other end, of each caplet to provide a coating which is smoother and easier to swallow than an uncoated caplet. The production of these capsule-like medicaments is readily facilitated by simple and inexpensive modifications which can be made to existing empty gelatin capsule making equipment.

7 Claims, 5 Drawing Sheets



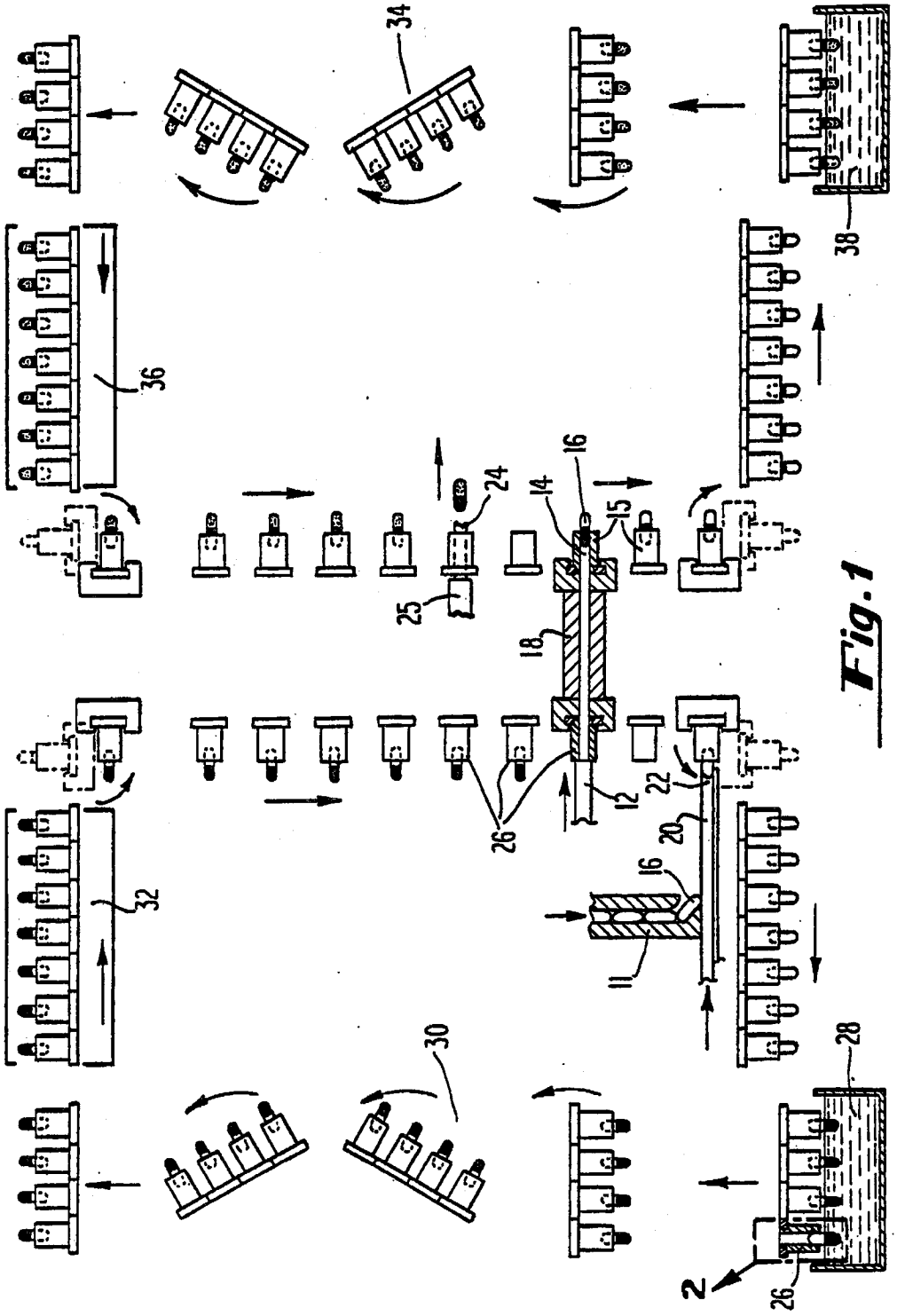


Fig. 1

GELATIN COATED CAPLETS AND PROCESS FOR MAKING SAME

FIELD OF THE INVENTION

This invention relates to coated medicaments and processes for providing gelatinous coverings for such medicaments. This invention is also directed to novel apparatus for producing such medicaments.

BACKGROUND OF THE INVENTION

Until recently, the pharmaceutical industry has relied upon empty gelatin capsules for the encapsulation of medicinal agents as a popular method for administering drugs. Hard capsules are not new. As early as 1848, Murdock introduced the two-piece, hard gelatin capsule. Capsules are tasteless, easily administered and easily filled either extemporaneously or in large quantities commercially. Many patients find it easier to swallow capsules than tablets, therefore preferring to take this form whenever possible. This preference has prompted pharmaceutical manufacturers to market certain products in capsule form even though they are also available in tablet form.

Empty gelatin capsules are typically made from gelatin-glycerin, pure gelatin, starch or sugar gelatin, or other soluble gelatin combinations. See *Remington's Practice of Pharmacy*, Martin & Cook, 17th edition, pp. 1625–1630, which is herein incorporated by reference. Capsules serve as adequate housings for powders, masses, liquids, pellets and oils and offer improved palatability and convenience.

Generally, empty hard gelatin capsules are manufactured using automated equipment. This equipment employs rows of stainless steel pins, mounted on bars or plates, which are dipped into a gelatin solution maintained at a uniform temperature and fluidity. The pins are then withdrawn from the gelatin solution, are rotated and then inserted into drying kilns through which a strong blast of filtered air with controlled humidity is forced. A crude capsule half is thus formed over each pin during drying. Each capsule half is then stripped, trimmed to uniform length, filled and joined to an appropriate mating half. Such hard capsule making systems are sold by Cherry-Burrell of Cedar Rapids, Iowa.

During most of this century, empty gelatin capsules were a popular dosage form for prescription and over-the-counter (OTC) drugs. However, in the early 1980's there was an unexpected increase in tampering with the contents of those capsules, resulting in several widely publicized deaths. This curtailed consumer demand for these products, caused ubiquitous concern regarding safety among those in the pharmaceutical community, and idled much of the industry's hard capsule making equipment. Improved gelatin capsules and tamper-resistant packaging were then developed, but were expensive to produce and were not foolproof.

Once the threat of capsule tampering was recognized, many manufacturers withdrew their capsule products from the market, often replacing them with solid, oblong-shaped medicaments referred to commonly as caplets. Caplets are solid oblong tablets which are sometimes coated with material such as cellulose. Typically, this coating is applied using coating-pan systems such as the "Vector-Freund Hi-Coaters", sold by Vector Corporation, 675 44th Street, Marion, Iowa, or the "GC-1000" sold by Glatt Air Techniques, 20 Spear Road, Ramsey, N.J.

A coating-pan system has a perforated pan or a drum which revolves in a manner similar to a standard clothes dryer. The system includes an air-atomization, spray gun which is inserted into the center of the drum for spraying a fine mist of coating material. A batch of solid medicaments or caplets is typically introduced into the cylindrical pan, wherein said batch is caused to tumble. The tumbling action tends to smooth out some of the rough edges on the caplets prior to coating with organic or aqueous film solutions which may contain solid additives. Coating pans generally produce consistent coating thicknesses and weights but are capable of providing only one color coating. Coatings produced by this method are often thin, offering poor coverage of medicament imperfections and rough edges not removed by the tumbling operation. Unless time is taken to build up a thicker coat, defects on the solid core result in a medicament that does not exhibit a pleasing appearance and may be perceived as being harder to swallow. Moreover, coating abrasion occurring during tumbling produces a surface finish on these medicaments that fails to exhibit the shiny surface that consumers and those in the art have associated with ease of swallowability. Applicant has pan coated caplets with gelatin on an experimental basis and has measured coating thicknesses of only about 6 mils. Moreover, these pan coated gelatin caplets were not observed to be as shiny as caplets coated by a dipping process.

Swallowability, the ability to pass through the fauces, pharnyx and esophagus into the stomach, is dependent on the physical characteristics of the medicament as well as psychological factors. See *Stedman's Medical Dictionary*, Anderson Publishing Co., 5th edition, p.1377, which page is herein incorporated by reference. Physical characteristics, such as medicament shape, size and surface finish, can be correlated with esophageal adherence and swallowability. With respect to psychological factors, swallowing is normally volitional in adults, and muscular contractions of the throat are understood to be under the control of the individual at a subconscious level. See *Stedman's*, at 1377. Consumer surveys suggest that a shiny, capsule-like appearance has a special appeal to users as being easier to swallow. In addition, surveys indicate that consumers perceive capsule products to be more effective, thereby adding a possible additional placebo factor to their actual effectiveness.

Solid medicaments comprising gelatin in their coatings have been taught in a number of abstracts. The abstract of J. A. Glassman, U.S. Pat. No. 3,228,786, for instance, is directed to peroral capsules and tablets and a method for manufacturing same. Glassman discloses delayed release, compartmental medicaments with gelatin coatings, and includes treatments for tablets or pellet coatings. The abstract of Japanese Pat. No. 52041213, assigned to Freund Industry Ltd., discloses a process for coating tablets with a solution containing gelatin as a film-forming agent. The abstract of Japanese Pat. No. 69027916, assigned to Sankyo Co. Ltd., is directed to gelatin coated tablets and a process for making same. The process of this patent includes feeding raw tablets at continuous intervals into a support. The tablets are immersed in a coating solution which can comprise gelatin. They are then recovered and held on a holder. Excess coating solution deposited at the lower surface of the tablet is removed by an eliminating plate, and

finally the tablet is released into a cooling solution from which it is recovered and dried to produce a *seamless* coated tablet. The abstract of Japanese Pat. No. 65009992, assigned to Konishi, is directed to a film-coating method using gelatin for coating tablets in a coating pan. The gelatin described in this abstract is pre-treated with water in a pressure-cooker at a 120°–140° F. for 30–40 minutes to reduce the adhesive properties of the gelatin to allow coating of the tablet. The abstract of Japanese Pat. No. 65009994, also assigned to Konishi, is directed to coating tablets in a coating pan with an emulsion including a mixture of hot water, gelatin, a surface active agent and a member selected from a group consisting of fats and oils, paraffin and wax. The use of the emulsion described in this patent abstract allows tablets to be coated with gelatin in the same manner as coating tablets with sugar. See also the abstract of an article by Richardson entitled "Franciscus Pill Coater", *Pharm. Hist.*, 28: 90–91 (2)1986. This abstract is directed to the Franciscus Pill Coater, one of the later refinements of the gelatin-coated process that appealed to the practicing pharmacists in the 19th century. Other abstracts also disclosing coatings for solid medicaments comprising gelatin include those for: Japanese Pat. No. 60084215, assigned to Shinetsu Chemical Industries, U.S. Pat. No. 4,238,510, assigned to Lifesavers, Inc., and Japanese Pat. No. 69026677, assigned to Daiichi Seiyaku Co. Ltd.

Several patents have disclosed the concept of coating pills by dipping half the surface of the pill at a time. Richards, U.S. Pat. No. 599,865 is directed to a process and apparatus for dipping pills wherein an adhesive bearing bar is used to hold the pills before dipping them into gelatin. This process requires great care in maintaining the consistency of the adhesive material, i.e. wax, so that each pill will adhere to the dipping-bar. The specification of Richards also warns that great care must be taken not to dip the pills so deep as to get any of the gelatin upon the wax, which may ruin its adhesive capacity. The method of Richards additionally is labor intensive, and therefore, is more expensive by today's standards. Clark, U.S. Pat. No. 724,436, is directed to a pill coating machine that employs pill-bars having a series of perforations for receiving pills. Each perforation is adapted for suction, whereby the pill is held in position during the dipping operation. Banker, U.S. Pat. No. 3,896,762, discloses a rotary immersion coating that similarly employs suction to hold solid medicaments prior to passing these medicaments through a coating bath. While Clark and Banker provide apparatus for holding and dipping medicaments, neither discloses that the final product will exhibit a capsule-like appearance with or without a seam. Moreover, applicant has tested vacuum holding apparatus and has discovered that the suction tends to attract some of the gelatin into the holder, producing an irregular seam. Vacuum holding systems such as these also require significant power consumption, are often complicated and uncertain in their action, and necessitate expensive and sensitive vacuum equipment. Finally Oddo, U.S. Pat. No. 3,045,641, discloses apparatus for color-coding tablets that utilizes a rotating resilient roller impregnated with a coating substance, whereby tablets are passed beneath the roller on a conveyor and are deeply impressed into the resilient roller surface. This patent does not disclose the use of gelatin or the use of a dipping process to produce a thick capsule-like coating.

Although these gelatin coated medicaments and processes have achieved some commercial success in the marketplace, a need remains for a coated medicament which is at least as tamper-resistant as a caplet while providing the ease of swallowability of a capsule. There is also a need for a less expensive medicament coating method capable of producing a multi-colored, capsule-like coating which is perceived by the consuming public to be more effective.

SUMMARY OF THE INVENTION

The present invention provides a novel method for coating solid cores, such as caplets, with gelatinous coatings to produce simulated capsule-like medicaments. Such capsule-like medicaments are achieved by individually dipping and drawing first one end and then the other end of each caplet to provide a medicament which is observed to be similar to a regular capsule. The production of such capsules is readily facilitated by simple and inexpensive modifications which may be made to existing, hard capsule, production equipment or by similarly designed newer equipment. In particular, the preferred apparatus of the present invention replaces the prior art steel pins of a standard capsule production machine with novel caplet holding means having caplet channels therein for receiving, individually gripping and transferring caplets during various stages of the herein described coating process. Also included, are novel caplet designs which readily facilitate the method of this invention. As a result, novel capsule-like medicaments are provided having smooth, relatively thick, shiny, multi-colored gelatinous coatings thereon. These medicaments are pleasing to the eye, and should be perceived by consumers as easier to swallow and more effective than prior art caplet medicaments, while providing much greater tamper resistance than conventional capsules.

It is, therefore, an object of this invention to provide a simulated, capsule-like medicament having a gelatinous coating capable of being provided in two or more colors.

It is another object of this invention to provide a simulated, capsule-like medicament that is tamper-resistant.

It is another object of this invention to provide a simulated, capsule-like medicament that provides greater ease in swallowing and is perceived to be more effective than pan-coated pharmaceutical equivalents.

It is still another object of this invention to provide a novel and less expensive method and apparatus for adapting existing hard capsule equipment for manufacturing gelatin coated caplets.

It is still another object of this invention to provide a heavy layer of gelatin as a single coating to cover imperfections inherent on the caplet core.

With these and other objects in view, which will become apparent to one skilled in the art as the description proceeds, this invention resides in the novel construction, combination, arrangements of parts and methods substantially as hereinafter described and more particularly defined by the attached claims.

BRIEF DESCRIPTION OF THE DRAWINGS

The accompanying drawings illustrate a complete embodiment of the invention according to the best mode so far devised for the practical application of the principles thereof, and in which:

FIG. 1 is a diagrammatic view of the manufacturing sequence for providing a gelatin coating on caplets illustrating how the caplets are inserted, how the gelatinous coating is applied to the first and second ends of the caplet, and how the caplets are dried and ejected;

FIG. 1A is a partial diagrammatic view of an alternative manufacturing sequence illustrating an alternative transferring method.

FIG. 1B is a partial diagrammatic view of an alternative manufacturing sequence illustrating an alternative holding means and transferring method.

FIG. 2 is an enlarged detail of a cross-sectional view of the holding means 26 of FIG. 1 with a caplet being dipped in a gelatinous material, said caplet being retained by "O"-rings 100 and 102;

FIG. 3 is an enlarged detail of a transverse cross-sectional view of an alternate holding means illustrating a flat spring 202;

FIG. 4 is an enlarged detail of a longitudinal cross-sectional view of a caplet being retained by flat spring 202 of FIG. 3, taken through line 4—4;

FIG. 5 is an enlarged detail of a transverse cross-sectional view of an alternative holding means embodiment illustrating a spring retention means 200;

FIG. 6 is an enlarged top view of an uncoated caplet;

FIG. 7 is an enlarged detail of a transverse view of the caplet of FIG. 6;

FIGS. 8*a–d* are enlarged details of transverse views of caplets illustrating various coating patterns.

FIG. 9 is an enlarged longitudinal view of an alternative shape for an uncoated caplet.

FIG. 10 is an enlarged detail of a transverse view of the caplet of FIG. 9.

FIGS. 11(*a*) and (*b*) are enlarged details of the longitudinal cross-section views of the alternative holding means of FIG. 1B showing how the ends of the caplet are held.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides a novel method for coating caplets with gelatinous coatings to produce simulated capsule-like medicaments. The subject method may be performed by modifying existing machines originally intended to fabricate empty gelatin capsules or by newer similarly designed apparatus.

The novel process of this invention comprises the steps of providing a holding means having a caplet channel defined therein and inserting a first end of a caplet into said caplet channel while leaving the second end of the caplet exposed. The holding means is then manipulated relative to a bath of gelatinous coating to dip the second exposed end of each caplet into that bath. The resulting gelatinous coating on the second exposed end of the caplet is then permitted, and preferably caused, to dry to form a coated end. During the drying process the caplet may be rotated to assist in uniformly distributing gelatin during drying. Once dry, the coated (second) end of the caplet is then displaced through the caplet channel to expose its uncoated first end. A gelatinous coating is then applied to the uncoated first end of said caplet. The coating applied to the first end of the caplet is then permitted (or preferably caused) to dry, again with rotation if desired for the purpose of spreading the coating evenly. In accordance with the preferred embodiment method, the baths of gelatinous coating into which the caplet ends are dipped may be of different colors, to thereby create a simulated 2-piece capsule look to the finished caplets with seams about their transverse axes.

A substantial advantage of the present invention is that existing hard capsule manufacturing may be readily adapted for the purpose of producing the coated caplet products of the present invention. In the preferred embodiment apparatus of the present invention, the conventional bars of such machines having stainless steel capsule-forming protuberances mounted thereon are replaced with bars having a plurality of cylindrical holding means mounted thereon. Each holding means receives, retains and facilitates the transfer of an individual caplet. The apparatus is fitted with a caplet feeder to feed caplets into each holding means. The holding means may, for example, be a cylinder which is open at both ends and which comprises a retaining means, such as "O"-rings or a spring biased retainer for the purpose of holding each caplet in position during the dipping process. The feeding means is preferably associated with an inserting means, which may be a simple channel and plunger assembly, for inserting a first end of each caplet into an appropriate holding means. The feeding means ensures that each caplet is inserted a sufficient distance to cause the second end of the caplet to appropriately protrude therefrom during the upcoming dipping process. Once each bar is loaded with caplets, it then proceeds to a dip station where the gelatinous coating is applied to the exposed ends of the caplets protruding therefrom, whereupon the bar is rotated through a first drying means for permitting the gelatinous coating to dry to form a coated second end. In a preferred embodiment apparatus, the second gripping means also comprise substantially cylindrical holders which are open at both ends, having central bores defined therethrough. In this embodiment, these second holders are axially aligned with the bores of the first holders, at the transfer positions, whereupon a plunger or other means is used to displace the half-coated caplets through and out of the "backs" of the first holders and into the "backs" of the second holders, and then through the second holders until the remaining uncoated ends of the caplets are exposed for subsequent dipping. The dipping and drying processes are then repeated (preferably with a different colored gelatinous coating), whereupon a caplet ejection means pushes the caplets out of the second holders.

In another preferred embodiment, the "fronts" of the second holder means are aligned with the "fronts" of the first holder means, whereupon the caplets are mechanically transferred from the first to the second holders without the need for an additional alignment device. In still another embodiment, a single holding means is used for dipping both ends of the caplet, whereby, after dipping the second end, the caplet is transferred through this single holding means to expose the uncoated first end. This holder is then shifted to the second gelatinous coating bath which preferably contains a different color gelatin for dipping the first end of the caplet.

The subject apparatus and method may be further understood with reference to the figures. FIG. 1 illustrates, diagrammatically, the preferred method and apparatus for dipping solid caplets into a gelatinous material embodying the teachings of this invention. A holding means is first provided having a caplet channel 106 defined therein, which can take any form having a cross-section sized to slidably mate with said caplet 16. The caplet 16 having a first and second end, 110 and 104

of FIG. 2, is inserted using inserting means 20 into said caplet channel 106 while leaving the second end of the caplet 104 exposed. Next, a gelatinous coating, known to those in the pharmaceutical arts, is applied by first application means 28 to the exposed second end 104 of the caplet. The extent to which the second end 104 can be coated is dependant upon the desired color configuration and "seam" requirements. The half-coated caplet is then dried using the first drying means 30 and 32 which permits the gelatinous coating on the second end 104 to dry, forming a coated second end. The caplet 16 is then displaced through said caplet channel 106 to expose the first end 110 preferably using a gripping means illustrated in the embodiment of FIG. 1 as transfer means 12, alignment means 18 and second holding means 15. The caplet 16 is then coated with a gelatinous material on its first end 110 by second application means 38 which is then dried by second drying means 34 and 36, resulting in a dry caplet substantially covered in gelatin. Accordingly, this invention provides novel means for providing simple and inexpensive modifications to existing hard capsule equipment to manufacture simulated capsule-like medicaments. This invention teaches preferred process sequences that supplement and partially replace otherwise standard empty gelatin capsule techniques and parameters that are known to the art. For example, gelatin materials used for the coatings of this invention may be any of the well known types utilized in the art of manufacturing empty capsules and coated medicaments.

Referring again to FIG. 1, the caplet 16 is fed into inserting means 20 by feeder 11. The feeder 11 preferably comprises a chute attached to a reservoir. Alternatively, mechanical means or pneumatic means may be developed for this purpose. In one embodiment, a 20–40 wide channel vibrational feeder has been deemed useful. It is expected that those in the art could readily adapt current automation technology to develop a means for feeding caplets into inserting means 20 of this invention. In the preferred embodiment, plungers displace caplets into each of a series of molding means spaced apart along a bar mount, shown in end cross section in FIG. 1, i.e., holding means 26. Each caplet 16 is then inserted into a first holding means 26 using plunger 20. Both the first and second holding means 26 and 15 are preferably cylindrical, having caplet channels 106 having a cross-section sized to slidably mate with the caplet 16 to permit passage of the caplet 16. However, in the embodiment of FIG. 1A, these channels, or more preferably, bores, can extend through the holding means with one cross-section sized to slidably mate with caplet and another cross-section sized to receive only a plunging means. This design is made possible due to the fact that the caplets can be transferred without displacing them through the entire length of the holding means in the method embodiment of FIG. 1A.

Included with one holding means embodiment of this invention, are retaining means for retaining the caplet at least during the first gelatinous coating application step. As shown by the embodiments found in FIGS. 2–5, the retaining means can comprise a plurality of recessed rubber "O"-rings 100 and 102, a flat spring 202 fixed by pin 204 and having convex side facing the caplet, or a resilient spring 200. As shown in FIG. 3 the flat spring 202 may be extended to enable external manipulation of the retaining means. The choice of retaining means is not critical and any known securing or resilient device may be used. However, it is important that the retaining means provide enough clearance to pass the gelatin coated end, yet securely hold the uncoated end.

Inserting means 20 preferably comprises a plunging means having at least an end portion 22 disposed to abut the caplet 16 to effect displacement of the caplet 16 into the bore 106 of the first holding means 26.

In a preferred embodiment, a plurality of holding means are mounted on a fixture which can be transferred by the mechanical pushing means of a hard gelatin capsule assembly line. In such an embodiment, inserting means 20 has multiple plunging means having a plurality of end portions 22 disposed to abut multiple caplets to effect displacement thereof into the fixture. In one embodiment, 10 to 50 holding means, preferably 20 to 40, and most preferably 30 holding means are attached to the fixture. A plurality of said fixtures can be fed into a conventional hard-capsule manufacturing assembly which can accommodate about 1500 to 1800 fixtures at a time.

The caplet coating process of FIG. 1 next applies a gelatinous coating to the second exposed end 104 of said caplet 16. A first application means 28 is employed for this purpose. In the preferred embodiment of this invention, groups of 4 or more fixtures are fed into a dipping means and vertically lowered into a gelatinous material such as methyl cellulose, calcium alginate or gelatin. The depth of the dip is preferably cam-regulated to the desired capsule size, color scheme, and "seam" requirements. As indicated in FIGS. 8*a–d*, the color scheme can be bifurcated as depicted by caplet coatings 304 and 306, and a seam 302 or 300 can be provided by overlapping the gelatinous coatings on the first and second ends 110 and 104.

The coatings on the first and second ends 110 and 104 of the caplet, when preferably dipped in gelatin can include plasticizers such as glycerin or sorbitol, water, preservatives, coloring agents, and opacifying agents. See *Remington's Practice of Pharmacy*, pages 1625 to 1630. The preferred gelatin solution should be maintained at a uniform temperature and a constant degree of fluidity. If the gelatin solution varies in viscosity, it will correspondingly decrease or increase the thickness of the coating. Acceptable gelatin compositions can contain small amounts of methyl cellulose, polyvinyl alcohols, and denatured gelatins to modify their solubility or produce a enteric effect. Common sources of gelatin contemplated by this invention include animal bones, hide portions and frozen pork skin. Grades of gelatin that are appropriate for this invention include pharmaceutical grade, food grade, Type A and Type B. Although the coatings herein provided can be made from any of these sources or grades, those learned in the art of capsule making are aware that the usual practice is to use a mixture of grades and sources as dictated by availability and cost considerations. Differences in the physical properties of finished capsules as a function of the type of gelatin used are slight. Reference may also be made to "The Theory and Practice of Industrial Pharmacy," by Lackman, Liberman and King (1970) pages 389–398, published by Lea and Febiger, Philadelphia, Pa., said pages being hereby incorporated by reference. In a preferred embodiment of this invention, a gelatin mixture is prepared using 40% by weight bone (150 bloom), 20% by weight hyde (245 bloom) and 40% pork skin (270 bloom). This mixture has a viscosity of 500 cp as measured on a Brookfield Chromatograph, at an operating temperature of 130° F.

Gelatin coated caplets can be supplied in a variety of shapes and sizes, from 000, the largest size which can be swallowed, to 5, which is the smallest. Larger sizes can also be made available for use in veterinary medicine. FIGS. 6, 7, 9 and 10 illustrate two of the preferred shapes for caplets. FIGS. 6 and 7, show in top and transverse views respectively, an oblong caplet having a raised portion circumscribing its perimeter. FIGS. 9 and 10 illustrate in longitudinal and transverse views another preferred embodiment having a cylindrical center portion and rounded ends having a transverse diameter slightly less than that of the cylindrical center portion. These novel caplet designs facilitate the dipping method herein provided since they are easily held by the above retaining means and can be manufactured using conventional compression molding equipment.

From the foregoing it can be realized that this invention provides a simulated capsule-like medicament, a method for manufacturing this medicament, and apparatus used in the method. The advantages over the prior art are: increased tamper-resistance over hollow capsules, increased swallowability over pan-coated medicaments, variable color scheme capability not available with pan-coated medicaments, less expensive operating costs and a greater perception by the consuming public that gelatin coated caplets are more effective. Although various embodiments have been illustrated, this was for the purpose of describing, but not limiting, the invention. Various modifications, which will become apparent to one skilled in the art, are within the scope of this invention described in the attached claims.

I claim:

1. A simulated capsule-like medicament comprising:
(a) A solid caplet having a first and a second end, said caplet comprising a generally cylindrical shape;
(b) A first gelatinous coating of a first color provided on said second end of said caplet;
(c) A second gelatinous coating, of a color different from said first color, provided on said first end of said caplet, partially overlapping said first gelatinous coating and forming a seam circumscribing said medicament at about a midway point of a longitudinal axis of said medicament to form a simulated capsule-like medicament.

2. The medicament of claim 1 wherein said caplet ends are coated in a red and white gelatinous material.

3. The medicament of claim 1 wherein said caplet is pre-coated to reduce absorption of moisture and said gelatinous coatings by said caplet.

4. The medicament of claim 1 wherein said first and second gelatinous coatings are provided in thicknesses of about 5 to 40 mils.

5. The medicament of claim 1 wherein said caplet comprises a width and a length, wherein said length is at least 2.5 times the width.

6. The medicament of claim 1 wherein said first and second gelatinous coatings are provided in thicknesses of about 15–25 mils.

7. The medicament of claim 1 wherein said first and second gelatinous coatings comprise gelatin.

* * * * *

Coloring can be added to the coatings to produce opaque or transparent colors such as red, white, pink, green, reddish brown, blue, yellow and black. Colored medicaments are necessary to give a specialty product a distinctive appearance. Titanium dioxide is often added to the gelatin to form white medicaments, or to make an opaque colored coating.

Still referring to FIG. 1, after coating the second end 104, the gelatinous coating is permitted to dry to form a coated second end. It is important to the teachings of this invention that the caplet 16 is permitted to dry without contacting other objects, thus producing a shiny, simulated capsule-like finish on said caplet. In the preferred embodiment, a group of fixtures is raised from the gelatin and elevated to the first drying means, comprising rotating means 30 and kiln means 32. Preferably, the caplets are rotated to distribute the coating on the caplet. In a most preferred apparatus, the fixtures are automatically revolved after dipping to spread the gelatin more evenly over the caplet ends and eliminate excess accrual at the ends. See Sindl, U.S. Pat. No. 1,872,190, which is herein incorporated by reference. The caplets are then fed into a kiln drying means 32. Preferably, 5–60 fixtures containing caplets enter the drying kiln, where they move under drying ducts. Air volume, temperature and humidity are controlled in the kiln and are set to conventional process parameters known to those in the industry.

When the gelatinous coating on the second end 104 of the caplet is dry, it is displaced through the caplet channel 106 to expose the first end 110 using a gripping means illustrated in the embodiment of FIG. 1 as transfer means 12, alignment means 18 and second holding means 15. In one preferred embodiment, the transfer means 12 comprises an end portion 14 disposed to abut said caplet to effect displacement of said caplet from a the first holding means 26 to the second holding means 15. The caplet is then preferably displaced through the caplet channel or bore 106 of the first holding means 26, through the alignment means 18 and into said second holding means 15 to expose the uncoated first end 110 of the caplet 16.

Alternatively, as depicted in FIG. 1A, when the gelatinous coating on the second end 104 is dry, it can be displaced through the caplet channel 106 to expose the first end 110 by transferring the caplet from the "front" of a first holding means to the "front" of a second holding means, thus eliminating the need for alignment means 18 of FIG. 1. It is also envisioned that a single holding means 210 like the one illustrated in FIGS. 11(*a*) and (*b*) could replace the use of the two holding means 26 and 15 of FIGS. 1 and 1A by providing for the displacement of the caplet through a central bore 201. Three "O"-rings 203, 205 and 207 are shown in FIGS. 11(*a*) and (*b*) for retaining the caplet during the process of coating the second and first ends 104 and 110 using a single holding means 210. However, other retaining means, as previously described for the holding means 26 and 15 of FIG. 1, may also be employed for this purpose. As illustrated, in the embodiment of FIG. 1B, by transferring bars containing a plurality of holding means 210 from the left side of the diagrammatic view of the process of FIG. 1 to the right side, the need for a second holding means is eliminated.

After displacing the caplet through the caplet channel 106, the protruding first end is ready for the application of a gelatinous coating which is illustrated on the right side of FIG. 1. As indicated in the above preferred embodiments, groups of 4 or more fixtures can be fed into a dipping means 38 and vertically lowered into a gelatinous material, preferably containing a different color dye or pigment for providing a distinctive apearance. As indicated in FIG. 8, a seam 300 or 302 can now be provided by overlapping the dried coating on the second end 104. Through careful selection of gelatin color schemes, the seam can exhibit a different color than the ends of the caplet, i.e., green and yellow coatings on the ends can be overlapped to form a blue seam. The gelatinous coating on the first end is then permitted to dry without contacting other objects, as previously described for the second end 104. Separate rotating means 34 and kiln means 36 are illustrated in FIG. 1 for drying the coating on the first end. However, those in the art may find it convenient to use the same drying apparatus used in drying the second end 104.

Finally, the caplet may be ejected from the second holder means 15 after the first end 110 is dry. Removal of the coated caplet 16 can be effected by ejection means 25 which preferably is similar in structure to inserting means 20 and transfer means 12, in that it comprises an end portion disposed to abut said caplet. Removing the caplet can be accomplished by plunging horizontally as in FIGS. 1 and 1A or by plunging the caplet out of the holding means vertically as in FIG. 1B. The ejected caplet, now coated in gelatinous material, is then ready for printing and packaging.

In view of the above it is expected that a novel, simulated capsule-like medicament can be produced. The gelatin coated medicament of this invention which can be produced by the above method comprises a solid caplet having a first and a second end, wherein a first gelatinous coating is provided on said second end, and a second gelatinous coating is provided on said first end of the caplet. The caplet generally is at least 2.5 times longer than it is wide, and ideally comprises a cylindrical shape. The first and second gelatinous coatings substantially cover the caplet to form a simulated capsule-like medicament with a seam about a transverse axis of the medicament. As previously discussed, the first and second ends 110 and 104 of the caplet can be coated with gelatinous coatings of different colors to provide a distinctive appearance for specialty products. A preferred color scheme for the medicament of this invention includes a caplet which is coated in a red and white gelatinous material. It has been discovered that absorption of the gelatinous coating or the moisture in the gelatinous coating by the solid caplet may be reduced by applying a conventional precoat sealant to caplet prior to dipping into a gelatinous material. See Baker, U.S. Pat. No. 3,185,626, which is herein incorporated by reference. Without a precoat sealant, it is possible that some of the gelatinous coating or moisture in the coating would seep into the caplet, resulting in a duller surface. The gelatinous coatings of this invention are generally provided in substantially uniform thicknesses of about 5 to 40 mils, preferably about 10 to 30 mils, and most preferably from 15 to 25 mils. However, it may be understood by those familiar with coating processes that the coating thickness may be varied to provide a smoother, easier to swallow, caplet.

Gelatin coated caplets have been produced using the above method, wherein the second applied gelatinous coating partially overlaps the first applied gelatinous coating forming a capsule-like seam circumscribing the medicament at about a midway point of a longitudinal access of the medicament.

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US006165513A

United States Patent [19]

Dansereau et al.

[11] **Patent Number: 6,165,513**

[45] **Date of Patent: Dec. 26, 2000**

[54] **FILM-COATED TABLET FOR IMPROVED UPPER GASTROINTESTINAL TRACT SAFETY**

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[73] Assignee: **The Procter & Gamble Co.**, Cincinnati, Ohio

[21] Appl. No.: **09/095,322**

[22] Filed: **Jun. 10, 1998**

Related U.S. Application Data

[60] Provisional application No. 60/049,306, Jun. 11, 1997.

[51] **Int. Cl.**[7] **A61K 9/16**; A61K 9/50

[52] **U.S. Cl.** **424/490**; 424/451; 424/456; 424/457; 424/461; 424/464; 424/468; 424/474; 424/475; 424/486; 424/489; 514/108; 514/960; 514/961; 514/962; 514/963; 514/964

[58] **Field of Search** 424/451, 456, 424/457, 461, 464, 468, 474, 475, 486, 489, 490; 514/108, 960–964

[56] **References Cited**

U.S. PATENT DOCUMENTS

4,302,440	11/1981	John et al.	424/35
5,096,717	3/1992	Wirth et al.	424/490
5,146,730	9/1992	Sadek et al.	53/454
5,431,920	7/1995	Bechard	424/480
5,622,721	4/1997	Dansereau et al.	424/490
5,658,589	8/1997	Parekh et al.	424/463

FOREIGN PATENT DOCUMENTS

0 377 439	1/1990	European Pat. Off. .
86 22 513	12/1986	Germany .
WO 94/12200	6/1994	WIPO .
WO 97/09967	3/1997	WIPO .
196 15 812	10/1997	WIPO .
WO 97/39755A1	10/1997	WIPO .

OTHER PUBLICATIONS

Seitz, J.A., Mehta, S.P., Yeager, J.L., "Table Coating", *The Theory and Practice of Industrial Pharmacy*, 3rd Edition, pp. 346–373, (1986).

Primary Examiner—Bennett Celsa
Attorney, Agent, or Firm—James C. Kellerman; Mary Pat McMahon

[57] **ABSTRACT**

A novel oral dosage to be delivered to the stomach comprising a safe and effective amount of an active ingredient selected from the group consisting of emepronium bromidebromide, doxycycline, and other tetracyclines/antibiotics, iron preparations, quinidine, nonsteroidal anti-inflammatory drugs, alprenolol, ascorbic acid, captopril, theophylline, zidovoudine (AZT), bisphosphonates and mixtures thereof and pharmaceutically-acceptable excipients, wherein said oral dosage form is a generally oval form and film coated to facilitate rapid esophageal transit and avoid irritation in the mouth, buccal cavity, pharynx, and esophagus.

10 Claims, 1 Drawing Sheet

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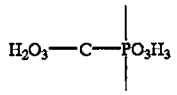
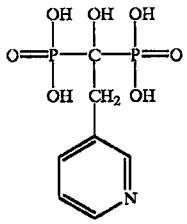
ment of a hyperosmolar solution which causes mucosal desiccation. Preferred actives are selected from the group consisting of emperonium bormide, doxycycline, and other tetracyclines/antibiotics, iron preparations, potassium chloride, quinidine, nonsteroidal anti-inflammatory drugs, alprenolol, ascorbic acid, captopril, theophylline, zidovoudine (AZT) and bisphosphonates. More preferred actives are risedronate, alendronate and pamidronate, most preferred is risedronate.

The disphosphonates of the present invention are structural variations of the geminal grouping:



The term "risedronate", as used herein, denotes the disphosphonate compound 3-pyridyl-1-hydroxyethylidene-1,1-bisphosphonic acid and has the following structure:



The compound risedronate is further described in U.S. Pat. No. 5,583,122, Benedict et al., assigned to the Procter & Gamble Co., issued Dec. 10, 1996, and "An American Conference, Bisphosphonates: Current Status and future Prospects, The Royal College of Physicians, London, England, May 21–22, 1990, organized by IBC Technical Services, both references hereby are incorporated by reference.

The term "risedronate active ingredient" includes risedronate, risedronate salts, and risedronate esters, or any mixture thereof. Any pharmaceutically-acceptable, non-toxic salt or ester of risedronate may be used as the risedronate active ingredient in the novel oral dosage forms of the present invention. The salts of risedronate may be acid addition salts, in particular the hydrochloride, but any pharmaceutically-acceptable, non-toxic organic or inorganic acid salt may be used. In addition, salts formed with the phosphonic acid group may be used, including, but not limited to alkali metal salts (K, Na) and alkaline earth metal salts (Ca, Mg) the Ca and Na salts being preferred.

Particularly, other esters of risedronate which are suitable for use as the active ingredient herein are straight chain or branched chain C_1–C_{18} alkyl esters, including, but not limited to, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, amyl, hexyl, heptyl, octyl, nonyl, decyl, lauryl, myristyl, cetyl, and stearyl; straight chain or branched C_2–C_{18} alkenyl, esters, including but not limited to vinyl, alkyl, undecenyl, and linolenyl; C_3–C_8 cycloalkyl esters, including, but not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl; aryl ester, including, but not limited to phenyl, toluyl, xylyl, and naphthyl; alicyclic esters, including, but not limited to, menthyl; and aralkyl esters, including, but not limited to benzyl, and phenethyl.

The term "alendronate" as used herein, denotes the disphosphate compound 4-amino-1-hydroxybutylidene-1,1-bisphosphonic acid and its pharmaceutically-acceptable salts, i.e. monosodium trihydrate. The compound alendronate is further described in U.S. Pat. Nos. 4,922,007 and 5,019,651 both issued to Merck and both hereby incorporated by reference.

Generally speaking, the proper selection of the active ingredient depends on the selected type of formulation, the disease pattern, especially the site and type of the disease, and the desired release of the active ingredient. In addition, the physical and chemical characteristics of the active ingredient must be taken into account when selecting suitable pharmaceutically-acceptable excipients for use in the novel dosage forms containing the active ingredient.

The effective oral dose of the active ingredient depends on the extent of the disease. For examples, for adults the amount of risedronate usually amounts to from about 1 mg to about 40 mg daily, preferably from about 1 mg to about 30 mg daily. When the dose is to be administered continuously, the preferred dose is from 1–15 mg/day, preferably from 1–10 mg/day. When the dose is to be administered cyclically, the dose is preferably from 5–40 mg/day, preferably from 10–30 mg/day.

B. Site of Delivery of the Active Ingredient

A human or other mammal suffering from various diseases or disorders can be successfully treated by the delivery of the novel dosage form containing the active ingredient to the stomach of said human or other mammal. The novel oral generally oval shaped, film coated dosage forms described herein facilitate rapid transit through the esophagus thus effectively delivering the dosage form to the stomach and avoiding or minimizing the undesired release of risedronate in the mouth, pharynx and/or the esophagus thereby prohibiting the erosion, ulceration or other like irritation of the epithelial or mucosal layers of these tissues. The term "gastrointestinal tract" as used herein relates to the alimentary canal, i.e., that musculo-membranous tube about thirty feet in length, extending from the mouth to the anus. The term "upper gastrointestinal tract" as used herein means the buccal cavity, the pharynx, the esophagus, and the stomach. The term "lower gastrointestinal tract" as used herein means the small intestine, and the large intestine.

The term "buccal cavity" means the mouth or oral cavity and is lined with a mucous membrane which is continuous with the integument of the lips and with the mucous lining of the pharynx.

The term "pharynx" relates to the part of the upper gastrointestinal tract which is placed behind the nose, mouth and larynx. It is a mucomembraneous tube about 4 inches in length and posteriority with the esophagus and is composed of a mucous coat, a fibrous coat, and a muscular coat.

The term "esophagus" as used herein is a muscular canal about nine inches long extending from the pharynx to the stomach. The esophagus has three coats; and internal mucous coat surrounding the lumen, a middle aveolar coat and an external muscular coat.

The term "stomach" as used herein means that part of the gastrointestinal tract between the esophagus and the small intestine.

C. The Film Coating

The term "film-coated" as used herein relates to a mixture of pharmaceutically-acceptable excipients which is applied to, combined with, mixed with or otherwise added to the active ingredients. The said coating may be applied to a

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compressed tablet, beads, granules, or particles of active ingredient that are compressed into tablets. The coating chosen must be compatible with the particular active ingredient selected.

Accordingly, the said film coating is preferably applied to a compressed tablet which contains particles or granules of active ingredient; however, in the event the particles or granules are themselves film-coated before being compressed into a tablet, then the film coating of the compressed tablet itself is optional. Because of their film coating, these novel dosage forms will avoid the undesirable delivery of the active ingredient to the mucosal and epithelial tissues of the upper gastrointestinal tract, especially the mouth, pharynx and esophagus. Said coating also achieves the delivery of the active to the stomach which can be manipulated by one skilled in the art by choosing the excipients which make up the coating, its type, and/or its thickness.

Preferred polymers for film-coating are soluble at pH of from about 1.2 to about 5. Particularly preferred polymers are selected from the group consisting of hydroxypropylmethylcellulose (HPMC) alone and/or in combination with hydroxypropylcellulose (HPC), carboxymethylcellulose, methylcellulose, ethylcellulose, acrylic resins, and polyvinylpyrrolidone and gelatin or other commercially available film-coating preparations such as Dri-Klear, manufactured by Crompton & Knowles Corp., Mahwah, N.J. or Opadry manufactured by Colorcon, West Point Pa. Particularly preferred are HPMC, HPC, Dri-Klear and Opadry. The lower viscosity LIPMC's grades, E-5 and the E-15 are the preferred grades and the most preferred is the E-5 grade. The preferred concentration of the polymer in the coating suspension is controlled to yield a viscosity of between 50–250 cps.

The amount of coating deposited on the tablet is usually in the range of from about 2% to about 5% weight gain with a preferred weight gain of about 3%. The coating can, and usually will, contain a plasticizer. The preferred plasticizers are polyethylene glycol and polypropylene glycol and the most preferred plasticizer is polyethylene glycol. The preferred amount of plasticizer is from about 15% to about 40% with respect to the film-forming polymer, with the most preferred level of about 20%. Dyes or pigments may also be added to provide the required opacity and color to the film-coating. The preferred level of the pigment is from about 10% to about 40% with respect to the film-forming polymer, with the most preferred level of from about 20% to about 30%. Other additives may be added to minimize foam or to facilitate spraying of the solution on the tablets.

D. Novel Generally Oval Shaped, Film Coated Oral Dosage Forms for Delivery of the Active Ingredient Containing Dosage Form to the Stomach

As stated hereinabove, the present invention is directed to novel generally oval shaped, film-coated oral dosage forms of an active ingredient to effect delivery to the stomach of a human or other mammal. The novel generally oval shaped, film-coated dosage form facilitates rapid transit through the upper gastrointestinal tract and avoids the delivery of the active ingredient until it reaches the stomach of the individual. Upon reaching the stomach the dosage form dissolves and absorption of the active ingredient through the small and/or large intestine can be achieved. Thus, tissues of the upper gastrointestinal tract, especially the epithelial and mucosal layers of the buccal cavity, the pharynx and esophagus are spared direct contact with the active ingredient and the active ingredient is absorbed at the appropriate site. Said oral dosage form, therefore, substantially alleviates the esophagitis or esophageal irritation which occasionally occurs upon oral administration of pharmaceutical compositions containing certain active ingredients.

Accordingly, oral dosage forms suitable for use herein are generally oval shaped, preferably modified oval shape and are film coated. A modified oval dosage form is demonstrated in FIGS. **1–3**. The dosage forms are formulated with active ingredients along with suitable pharmaceutical excipients which are well-known to those skilled in the art as described hereinbelow and are formed into the appropriate shape using apparatuses and/or methods which are well-known to those skilled in the art. The generally oval tablets have the following preferred dimensions: length from about 0.23 to about 0.85 inches preferably from about 0.25 to about 0.75 inches, width from about 0.11 to about 0.4 inches preferably from about 0.15 to about 0.35 inches, and a thickness of from about 0.075 to about 0.3 inches, preferably from about 0.10 to about 0.25 inches. The modified oval tablet as shown in FIGS. **1–3** may have the following dimensions: a length of about 0.455 inches, width of about 0.225 and a thickness of approximately 0.157 inches.

The term "pharmaceutical composition" means an oral dosage form comprised of a safe and effective amount of an active ingredient and pharmaceutically-acceptable excipients. The pharmaceutical compositions described herein are comprised of from about, 0.1% to about 99%, preferably from about 0.5% to about 95% of an active ingredient, and from about 1% to about 99.9%, preferably from 5.00% to about 99.90% of pharmaceutically-acceptable excipients. For risedronate the composition comprises, preferably 0.25% to 40%, preferably from about 0.5% to about 30% of a risedronate active ingredient and from about 60% to about 97%, preferably from about 70% to about 99.5% of pharmaceutically-acceptable excipients.

The phrase "safe and effective amount", as used herein means an amount of a compound or composition high enough to significantly positively modify the symptoms and/or condition to be treated, but low enough to avoid serious side effects (at a reasonable benefit/risk ratio), within the scope of sound medical judgment. The safe and effective amount of active ingredient for use in the method of the invention herein will vary with the particular condition being treated, the age and physical condition of the patient being treated, the severity of the condition, the duration of the treatment, the nature of concurrent therapy, the particular active ingredient being employed, the particular pharmaceutically-acceptable excipients utilized, and like factors within the knowledge and expertise of the attending physician.

The term "pharmaceutically-acceptable excipients" as used herein includes any physiologically inert, pharmacologically inactive material known to one skilled in the art, which is compatible with the physical and chemical characteristics of the particular active ingredient selected for use. Pharmaceutically-acceptable excipients include, but are not limited to, polymers, resins, plasticizers, fillers, lubricants, binders, disintegrants, solvents, co-solvents, buffer systems, surfactants, preservatives sweetening agents, flavoring agents, pharmaceutical grade dyes and pigments. All or part of the pharmaceutically-acceptable excipients contained in the pharmaceutical compositions described herein is used to make the film coating which is to be utilized in the novel oral dosage forms described herein.

The term "oral dosage form" as used herein means any pharmaceutical composition intended to be administer to the

stomach of an individual via the mouth of said individual, and for purposes of the present invention, the delivered form is in the form of a modified oval tablet (preferably film coated) containing granules or particles of active ingredient.

"Film-coated oral dosage form" as used herein relates to an oral dosage form containing a pharmaceutical composition as described herein which utilizes a film coating to effect the release of the active ingredient in the stomach. The film-coated oral dosage from is a compressed tablet containing granules or particles of the active ingredient, which may be coated or uncoated.

The term "rapid esophageal transit" as used herein means the time it takes for a tablet to pass from the oropharynx to the stomach. Rapid esophageal transit would comprise of transit less than about 90 seconds, preferably from about 1 to about 60 seconds. Most preferred is less than 20 seconds when taken with 50 ml of water.

As stated hereinabove, the ultimate site of topical delivery in the stomach can be satisfactorily controlled by one skilled in the art, by manipulating any one or more of the following:

(a) The active ingredient proper;

(b) the type of the coating, and the concomitant desirable thickness and permeability (swelling properties) of said coating;

(c) the time-dependent conditions of the coating itself and/or within the coated tablet, particle, bead, or granule; and

(d) the particle size of the granulated active ingredient.

As stated hereinabove, pharmaceutically-acceptable excipients include, but are not limited to polymers, resins, plasticizers, fillers, lubricants, binders, disintegrants, solvents, cosolvents, surfactants, preservatives, sweetener agents, flavoring agents, buffer systems, pharmaceutical-grade dyes and pigments.

The preferred solvent is water.

Flavoring agents among those useful herein include those described in *Remington's Pharmaceutical Sciences,* 18th Edition, Mack Publishing Company, 1990, pp. 1288–1300, incorporated by reference herein. Dyes, or pigments among those useful herein include those described in *Handbook of Pharmaceutical Excipients,* Second Edition pp. 126–134, 1994 by the American Pharmaceutical Association & the Pharmaceutical Press, incorporated by reference herein.

Preferred co-solvents include, but are not limited to, ethanol, glycerin, propylene glycol, polyethylene glycol.

Preferred buffer systems include, but are not limited to potassium acetate, boric carbonic, phosphoric, succinic, malic, tartaric, citric, acetic, benzoic, lactic, glyceric, gluconic, glutaric and glutamic. Particularly preferred are phosphoric, tartaric, citric, and potassium acetate.

Preferred surfactants include, but are not limited to, polyoxyethylene sorbitan fatty acid esters, polyoxyethylene monoalkyl ethers, sucrose monoesters and lanolin esters and ethers.

Preferred preservatives include, but are not limited to, phenol, alkyl esters of parahydroxybenzoic acid, benzoic acid and the salts thereof, boric acid and the thereof, sorbic acid and the salts thereof, chorbutanol, benzyl alcohol, thimerosal, phenylmercuric acetate and nitrate, nitromersol, benzalkonium chloride, cetylpyridinium chloride, methyl paraben, and propyl paraben. Particularly preferred are the salts of benzoic acid, cetylpyridinium chloride, methyl paraben and propyl paraben.

Preferred sweeteners include, but are not limited to, sucrose, glucose, saccharin, and aspartame. Particularly preferred are sucrose and saccharin.

Preferred binders include, but are not limited to methycellulose, sodium carboxymethycellulose, hydroxypropylmethylcellulose, carbomer, providone, acacia, guar gum, xanthan gum and tragacanth. Particularly preferred are methycellulose, carbomer, xanthan gum, guar gum, povidone and sodium carboxymethycellulose.

Preferred fillers include, but are not limited to lactose, sucrose, maltodextrin, mannitol, starch, and microcrystalline cellulose.

Preferred plasticizers include, but are not limited to polyethylene glycol, propylene glycol, dibutyl phthalate, and castor oil, acetylated monoglycerides, and triacetin.

Preferred lubricants include, but are not limited to, magnesium stearate, stearic acid, and talc.

Preferred disintegrants include, but are not limited to, crospovidone, sodium carboxymethyl starch, sodium starch glycolate, sodium carboxymethyl cellulose, alginic acid, clays, and ion exchange resins.

Preferred polymers, include but are not limited to hydroxypropylmethylcellulose (HPMC) alone and/or in combination with hydroxypropylcellulose (HPC), carboxymethylcellulose, acrylic resins such as Eudragit® RL30D, manufactured by Rohm Pharma GmbH Weiderstadt, West Germany, methylcellulose, ethylcellulose, and polyvinylpyrrolidone or other commercially available film-coating preparations such as Dri-Klear, manufactured by Crompton & Knowles Corp., Mahwah, N.J. or Opadry manufactured by Colorcon, West Point, Pa.

Utilizing the novel oral dosage forms of the present invention, the active ingredient can be reliably delivered to the stomach thereby avoiding the undesirable exposure of the active in the mucosal and epithelial tissues of the mouth, pharynx, and/or esophagus. Said dosage forms render the active ingredient readily available for absorption from the stomach and, there is substantially no contact of the active ingredient upon the epithelial and mucosal tissues of the mouth, pharynx, or esophagus. Accordingly, the novel modified oval, film-coated oral dosage form of the present invention substantially alleviates the condition of esophagitis or esophageal irritation which occasionally results from the oral administration of a pharmaceutical composition comprising certain active ingredients.

Any film-coating which is soluble in the gastric contents pH 1.2–5 can be used in the practice of the present invention. The preferred polymer to be used as the film coating must be applied to the compressed tablet, the gelatin capsule and/or beads, particles or granules of active ingredient in a sufficient thickness so that the entire coating dissolves in the stomach. The dissolution or disintegration of the excipient coating generally does not occur until the entry of the coated dosage form into the stomach.

The following non-limiting examples serve to further illustrate the novel oral dosage forms of the present invention.

EXAMPLE I

Modified Oval, Film-Coated Risedronate Tablet

The film-coating is applied to 110 kg of risedronate core tablets each weighing 240 mg.

Component	kg/batch	mg/tablet
Risedronate sodium tablets 30 mg	110	240
Dri-Klear	2.598	5.67
Chroma-Tone White	0.701	1.53
Purified Water	30.2 kg	65.9

Dri-Klear is a mixture of HPMC, HPC, polyethylene glycol, and silicon dioxide manufactured by Crompton and Knowles, Marwah, N.J., Chroma-Tone White is a mixture of HPC and titanium dioxide manufactured by Crompton and Knowles, Marwah, N.J.

The coating suspension is prepared as follows:

1. Add the Dri-Klear to hot purified water, 60–80° C., with agitation.
2. Cool the Dri-Klear solution to 40° C. or below, with continual mixing until all the Dri-Klear is dissolved.
3. Add the Chroma-Tone White to purified water with mixing. Disperse with the use of a high shear mixer for 10–25 minutes.
4. Add the pigment suspension (step 3) to the polymer solution (step 2) and mix. Continue mixing until ready for use.
5. Load the core tablets into a 48 inch side vented coating pan.
6. Preheat the tablets until the exhaust temperature reaches approximately 35° C. and begin spraying. Apply the coating suspension using an inlet air temperature of 40–60° C. at a rate of 300–400 g/minute.
7. Cool the tablets and discharge.

EXAMPLE II

Caplet Shaped, Film-Coated Alendronate Fablet

The film-coating is applied to 100 kg of alendronate core tablets each weighing 200 mg.

Component	kg/batch	mg/tablet
Alendronate sodium tablets 10 mg	100	200.0
Opadry	5.0	10.0
Red iron oxide	0.1	0.2
Purified Water	50 kg	100

Opadry is a commercial film-coating mixture manufactured by Colorcon, West Point, Pa. The coating suspension is prepared as follows:

1. Add the Opadry to room temperature purified water with agitation.
2. Mix until all the Opadry is dissolved.
3. Add the red iron oxide to purified water with mixing. Disperse with the use of a high shear mixer for 5 minutes.
4. Add the red iron oxide suspension (step 3) to the polymer solution (step 2) and mix. Continue mixing until ready for use.
5. Load the core tablets into a 48 inch side vented coating pan.
6. Preheat the tablets until the exhaust temperature reaches approximately 40° C. and begin spraying. Apply the coating suspension using an inlet air temperature of 40–60° C. at a rate of 250–350 g/minute.
7. Cool the tablets and discharge.

EXAMPLE III

Oval Risedronate Tablets

The film-coated risedronate tablets are made by preparing granules containing the active, coating the granules, compressing into a tablet and then film-coating the tablets.

A. Preparation of the risedronate sodium granules, 212.5 kg

Component	kg/batch	mg/g (Dry basis)
Risedronate sodium	2.5	11.7
Lactose, anhydrous	100	471
Microcrystalline cellulose	100	471
Polyvinylpyrrolidone	10	47.1
Purified Water	75 kg	—

The granulation is prepared as follows:

1. Dissolve the polyvinylpyrrolidone in the purified water.
2. Mix the risedronate sodium, lactose and microcrystalline cellulose in a high shear mixer for 3 minutes.
3. Granulate the mixture with the polyvinylpyrrolidone solution with mixing over a 5 minute interval.
4. Dry the wetted mass in a fluid bed dryer at an inlet temperature of 60° C.
5. Mill the dried material using a hammer mill to achieve the desired granule size.

B. Coating of the granules and preparation of risedronate sodium tablets, 130.3 kg

Component	kg/batch	mg/tablet
Risedronate sodium granules	106.8	213.6
Hydroxypropylmethylcellulose E-15	5	10.0
Purified Water	50	100.
Crospovidone	3	6.0
Microcrystalline cellulose	15	30.0
Magnesium Stearate	0.5	1.0

The granulation is coated and compressed into tablets as follows:

1. Dissolve the hydroxypropylmethylcellulose E-15 in purified water at 60° C. with continued mixing. Cool to 30° C. and mix until dissolved.
2. Add the risedronate sodium granules to a suitable coating column.
3. Spray on the hydroxypropylmethylcellulose E-15 solution at an inlet temperature of 50° C. After coating, dry the coated granules at an inlet temperature of 60° C.
4. Transfer the coated granules to a twin shell blender and add the crospovidone and microcrystalline cellulose and mix for 5 minutes.
5. Add the magnesium stearate and mix for 3 minutes and compress into tablets on a rotary press.

C. Film-coating

Film-coating is applied to 120 kg of risedronate core tablets each weighing 260.6 mg.

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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIRECCION DE NUEVAS CREACIONES

2020
Bogotá, D.C.,

Abogado:
JIMENA ESCOBAR URIBE

ASUNTO:	Radicación No.	03 06 5794
	Trámite	002
	Evento	001
	Actuación	430
	Oficio	
	Folios	13365

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 5 a 48 como se radicó inicialmente.
Reivindicaciones:	Folios 183 a 191 como se radicó inicialmente.
Prioridad:	US10/211139 (02/08/2002)

Objeto de la Invención

Titulo de la invención: "Composiciones que forman película acrílica"

Problema Técnico Planteado: "Necesidad de un recubrimiento con resistencias, plasticidad, dureza, espesor adecuados que se adhieran bien al sustrato, con dispersión uniforme de color y apariencia estética sin rugosidad con brillo y espesor uniforme y que evite la contaminación microbiana, para sustratos tales como tabletas y cápsulas"

Solución: "Proporcionar una composición para cubrir un sustrato por inmersión compuesta por: formador de película y plastificante"

IPC: A61K9/54, A61K9/32, A61K9/48, A61K9/20

Se acepta el nuevo capítulo reivindicatorio para estudio.

Análisis de la Solicitud de Patente

Reivindicaciones (Art 30 D 486, Art 22 PCT)

Concisión: Las reivindicaciones 11 y 12 hablan acerca de recubrimientos exteriores, sin embargo no enumeran los materiales que hacen parte de este recubrimiento.

Claridad: La reivindicación 14 caracteriza la composición por que cumple con los requisitos de disolución de acuerdo a la USP. Esta característica no define a la composición. No se acepta esta reivindicación.

Determinación del Estado de la Técnica

El Estado de la Técnica se determinó con base en la fecha de presentación 2002-08-02 y se encontraron los siguientes documentos que anticipan el objeto de esta solicitud:

Item	Documento	Título	Fecha de Publicación
D1	US 4 820 524	*Gelatin coated caplets and process for making the same*	11.04.1989
D4	US6165513	*Film-coated tablet for improved upper gastrointestinal tract safety*	26.12.2000

Análisis de Patentabilidad (Art 14 D486)

Nivel Inventivo (Art18 D486)

La reivindicación 1 dice: "Una forma de dosis farmacéutica que comprende: a) un núcleo que tiene una superficie; y b) una composición formadora de película que cubre al menos una porción de la superficie, dicha composición formadora de película comprende, en base al peso total de sólidos secos de la composición: a) de 10 a 70 por ciento de un formador de película comprendido de un polímero o copolímero de ácido acrílico o un derivado del mismo, o una mezcla del polímero o copolímero de ácido acrílico o un derivado del mismo b) de 2 a 20 por ciento de un plastificante primario comprendido de un parabeno, y c) de 1 a 50 por ciento de un plastificante secundario seleccionado del grupo que consiste de polivinilpirrolidona, polietilenglicol 300, polietilenglicol 400, sales farmacéuticamente aceptables de los mismos y sus mezclas"

Estado de la Técnica más cercano: D1, enseña formas farmacéuticas recubiertas para la administración de ibuprofeno, e incluye una formulación para realizar el recubrimiento de las tabletas (portada). Además un nuevo método para cubrir núcleo sólido como las capletas con cubiertas de gelatina que además resultan en producto suave, y con apariencia coloreada (columna 4). Dice además que las cubiertas pueden contener plastificantes como glicerina, sorbitol, agua, preservativos, agentes colorantes y agentes opacantes. Además, que la solución de gelatina puede contener pequeñas cantidades de metilcelulosa, polivinilalcoholes y gelatinas denaturadas(columna 8). Así mismo, esta solicitud presenta un método para realizar una cubierta sobre una tableta por inmersión de una cubierta acuosa (columna 5)

La solicitud se diferencia de D1 en la inclusión exacta de PARABENOS a la composición del recubrimiento.

El Efecto Técnico que logra la diferencia no parece superar los resultados obtenidos por los métodos presentados por el estado del arte.

El Problema Técnico Objetivo de esta solicitud es proveer composiciones para recubrimiento resistentes a la contaminación microbiana.

D4 presenta formas farmacéuticas sólidas que han sido cubiertas con una composición formadora de película (portada) que contiene polímeros que son

solubles a pH 1.2-5. Dentro de los polímeros acá presentados se encuentran HPMC sola o en combinación con HPC, CMC, MC, etilcelulosa, resinas acrílicas y polivinilpirrolidona y gelatina (columna 5). Presenta demás que la película equivale a 2-5% del peso total de la tableta, además que la cubierta contiene un plastificante, que puede ser polietilenglicol y que va del 15 al 40% con respecto al polímero formador de película, con el nivel preferido de 20%. Además, revela que la composición formadora de película puede contener pigmentos y colorantes en un porcentaje de 10 a 40 % y otros aditivos como antiespumantes o facilitar el rocío de las tabletas. Revela además a los parabenos como preservativos de la composición (columna 8).

El experto en la materia habría sido motivado por D4 para usar un preservativo, como por ejemplo un parabeno, a manera de plastificante acorde a lo enseñado por D2 en la composición formadora de película, asimismo D4 sugiere el uso de plastificantes, como el polietilenglicol, en una proporción de 15 a 40%, y de formador de película en un porcentaje de 75 a 20 %, lo cual habría podido ser utilizado por el experto en la materia para llegar a la materia revelada por la presente solicitud en la reivindicación 1.

Adicionalmente, la persona versada en la materia habría sido sugerida por D2 a recubrir tabletas por inmersión con dispersión acuosa a temperatura y presión ambiente como se presenta en la presente solicitud en la nueva reivindicación 26.

Las demás reivindicaciones no presentan materia que hagan inventiva a la presente solicitud.

Se recomienda negar este privilegio de patente ya que no cumple con el requisito de nivel inventivo.

Conclusión

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

	Documento	Reivindicaciones afectadas	Requisito que afecta
D1	US4820524	**1-13, 15-25**	**Nivel Inventivo**
D4	US6165513	**1-13, 15-25**	**Nivel Inventivo**

Respuesta a los argumentos del solicitante

El Señor solicitante dice que D1 indica un proceso que se debe realizar a temperaturas mayores a la ambiente para evitar la contaminación microbiana y conservar las propiedades para el recubrimiento mientras el método de la solicitud recubre tabletas por inmersión con la dispersión acuosa a temperatura y presión ambientes, lo cual no es derivable de la técnica anterior. Afirma que los sistemas de recubrimiento sin gelatina carecen de las propiedades reológicas necesarias para obtener un buen resultado en términos de apariencia y que la materia de la presente invención da un resultado elegante, brillante y de alto lustre. Además, manifiesta que D2 no se enfrenta al problema de recubrimiento con características adecuadas para la forma farmacéutica y dice D3 solo sugiere a los parabenos como conservadores y no como plastificante.

Se anota que en D3 se sugería el uso de parabenos como agentes preservantes para evitar el crecimiento de microbios en las preparaciones, lo cual sugiere a la persona versada su uso en la composición para evitar la contaminación microbiana, por otro lado el documento D1 sugiere el método de recubrimiento con una composición acuosa para recubrimiento y D2 sugería uso de preservantes como plastificantes, lo cual llevaría a la persona versada a llegar a una formulación que incluyera parabeno como plastificante y con D1 habría derivado el método acá reivindicado. Respecto a las propiedades reológicas, esta habrían sido mejoradas por la adición de plastificantes como había sido sugerido por D1.

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

El anterior requerimiento fue notificado por fijación en lista, de fecha 26 NOV. 2009

CONCEPTO TECNICO NUMERO: 3632	EXAMINADOR TÉCNICO Código:202092