

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIVISION DE NUEVAS CREACIONES

2020
Bogotá, D.C.,

Abogado
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Apoderado
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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 03-095323- -00010-0000

Fecha: 2007-07-04 15:16:15 Dep. 2020 DIR.NUEVASCR
Tra. 11 PATENTEIYII Eve: 379 FASENACIONALII
Act. 519 TRASLADOINFORME Folios: 1

ASUNTO

Radicación 03 95323
Trámite 002
Evento 001
Actuación 430
Oficio
Folios 006

07923

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

1. Documentos estudiados

- 1.1. Descripción: Folios 45 - 83
Folios 256 - 281 (modificaciones)
- 1.2. Reivindicaciones: Folios 282 - 287
- 1.3. Prioridad: Presentada en Estados Unidos el 31.05.01, bajo el número 60/294845

2. Objeto de la invención

- Título de la solicitud: Composiciones de timolol y de lípido hipotensivas y los métodos para utilizarlas.

Según las reivindicaciones 1-16 se provee una composición farmacéutica que comprende un componente de timolol y un componente lípido hipotensor de fórmula (I), cuyos sustituyentes se revelan en la descripción. Dichas composiciones son utilizadas para tratar la hipertensión ocular.

El problema planteado en esta solicitud es la necesidad de una composición efectiva para el tratamiento de la hipertensión ocular con menos efectos secundarios que los conocidos en el estado de la técnica.

Para solucionar este problema técnico la solicitud en estudio proporciona una composición que comprende timolol y un componente lípido hipotensor (prostaglandinas) de fórmula (I).

- Clasificación Internacional de Patentes A 61 K 31/5575

3. De la solicitud de Patente

3.1. Reivindicaciones (artículo 30 D 486)

- Las reivindicaciones 2-5 se relacionan con un efecto terapéutico relativo (“produce al menos un efecto secundario reducido relativo a...), lo cual no limita ni especifica las características técnicas de la composición que se pretende proteger
- La reivindicación 6 caracteriza a una composición por su efecto farmacológico, lo cual no es correcto. Se le recuerda al solicitante que una composición farmacéutica se debe caracterizar por sus componentes específicos y la proporción de los mismos para que se puedan diferenciar claramente de aquellos que se encuentran en el estado de la técnica.

4. Determinación del Estado de la Técnica

Considerando que la fecha de presentación de la primera solicitud de patente de la cual se reivindica prioridad es 31.05.01, se buscaron documentos del estado de la técnica relacionados, con fecha de publicación anterior a esta.

Nº	Documento	Título	Fecha de Publicación
D1	EP 0286903	“Uso de una prostaglandina en combinación con un agente bloqueador adrenérgico para la reducción de la presión intraocular”	19.10.88

5. Análisis de patentabilidad (artículo 14 D486)

5.1. Nivel inventivo (artículo 18 D486).

El documento EP 0286903 enseña un método y una composición que comprende la combinación de:

- Un bloqueador adrenérgico, como el maleato de timolol
- Una prostaglandina o un derivado de ésta.

Teniendo en cuenta el objeto de la solicitud, el cual es proveer composiciones que comprenden timolol y una prostaglandina para el tratamiento de la hipertensión ocular, es una derivación evidente del estado de la técnica, debido a que una persona versada en la materia tomaría las enseñanzas del documento citado y cambiaría las prostaglandinas usadas allí por las de la presente solicitud, esperando que dicha combinación serviría para el tratamiento de la hipertensión ocular.

Finalmente no se demuestran ventajas de las composiciones de la presente solicitud en comparación con las del estado de la técnica.

Por todo lo anterior, se podría afectar el nivel inventivo de la presente solicitud.

6. Conclusión:

Los requisitos de patentabilidad de la presente solicitud se encuentran afectados así:

Nº	Documento Nº	Reivindicaciones Afectadas	Requisito que Afecta
D1	EP 0286903	1-16	Nivel Inventivo

En cumplimiento del artículo 45 de la Decisión 486 de la Comisión de la Comunidad Andina, se le indica que debe dar respuesta dentro del término de sesenta 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 5 del título primero de la Circular Única Nº 10 de 2001.


Clara de Jaimes
Jefe de División de Nuevas Creaciones (e)

El anterior requerimiento fue notificado por fijación en lista, de fecha 5 JUL. 2007

CONCEPTO TECNICO No. 0965	EXAMINADOR TECNICO Código No.202024
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(19)



Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Publication number:

0 286 903
A1

(12)

EUROPEAN PATENT APPLICATION

(21) Application number: 88104999.3

(51) Int. Cl. 4: **A61K 31/557**, **/(A61K31/557,**
31:535),(A61K31/557,31:135)

(22) Date of filing: 28.03.88

(30) Priority: 03.04.87 US 34484

(43) Date of publication of application:
19.10.88 Bulletin 88/42

(84) Designated Contracting States:
AT BE CH DE ES FR GB GR IT LI LU NL SE

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(54) Use of a prostaglandin in combination with an adrenergic blocking agent for reduction of
intraocular pressure.

(57) This invention provides a method for treating
ocular hypertension or glaucoma in a subject's eye.
The method comprises contacting the surface of the
eye with an effective intraocular pressure reducing
amount of a mixture of an adrenergic blocking agent
and a prostaglandin or prostaglandin derivative in an
ophthalmically compatible carrier, so as to reduce
the intraocular pressure of the eye and maintain
such reduced intraocular pressure.

This invention also provides a composition for
topical treatment of ocular hypertension or glaucoma
in the eye of a subject. The composition comprises
an effective intraocular pressure reducing amount of
a mixture of an adrenergic blocking agent and a
prostaglandin or prostaglandin derivative in an oph-
thalmically compatible carrier.

EP 0 286 903 A1

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cle. In some cases of glaucoma, when flow through the trabecular meshwork is reduced to the point when it cannot be effectively increased by pilocarpine, pilocarpine can have only a very small additional beneficial effect or may have an adverse rather than a beneficial effect by reducing the remaining outflow channels through the ciliary muscle. Therefore, a combination drug, or drug regimen, that acts by decreasing aqueous humor secretion, such as an adrenergic blocking agent and a PG would be ideal, provided that the adrenergic blocking agent can be shown not to block the ocular hypotensive effects of PGs.

In the medical treatment of glaucoma, combination therapy, therefore, is commonly required since in many cases effective intraocular pressure control cannot be maintained with a single drug. The experiments set forth herein establish that the use of a combination of an adrenergic blocking agent and a PG have a great advantage from a physiological point of view, since they show that adrenergic blocking agents do not block the ocular hypotensive effect of a PG and since these blocking agents act by reducing the secretion of aqueous humor whereas PGs, as stated above, act by increasing uveoscleral outflow. In addition, using a combination of an adrenergic blocking agent and a prostaglandin, each of them in a concentration lower than would be required if used separately in the treatment of ocular hypertension and glaucoma, would yield a significant reduction in the occurrence of such side effects as ocular discomfort, irritative responses, conjunctival hyperemia, and cardiovascular response.

Summary of The Invention

This invention provides a method for treating ocular hypertension or glaucoma in a subject's eye. The method comprises contacting the surface of the eye with a composition comprising an effective intraocular pressure reducing amount of a mixture of an adrenergic blocking agent and a prostaglandin or prostaglandin derivative in an ophthalmically compatible carrier, so as to reduce the intraocular pressure of the eye and maintain such reduced intraocular pressure.

The invention also provides a composition for topical treatment of ocular hypertension or glaucoma. The composition comprises an effective intraocular pressure reducing amount of a mixture of an adrenergic blocking agent and a prostaglandin or prostaglandin derivative in an ophthalmically compatible carrier.

Moreover, this invention provides a method for treating ocular hypertension or glaucoma in a primate subject's eye which comprises contacting the

surface of the eye with a composition comprising an effective intraocular pressure reducing amount of a mixture of levobunolol hydrochloride and PGF_{2α}-1-isopropyl ester dissolved in an ophthalmically compatible carrier, so as to reduce the intraocular pressure of the eye and maintain such reduced intraocular pressure.

This invention further provides a composition for the topical treatment of ocular hypertension or glaucoma which comprises an effective intraocular pressure reducing amount of a mixture of levobunolol hydrochloride and PGF_{2α}-1-isopropyl ester dissolved in an ophthalmically compatible carrier.

Brief Description Of The Figures

Figure 1 This figure shows the effect of a 2% timolol solution and a combination of a 2% timolol solution and 0.5 g PGF_{2α}-1-isopropyl ester on the intraocular pressure in cat eyes. Application of 0.5 μg PGF_{2α}-1-isopropyl ester to eyes already treated with a 2% timolol solution caused a significant further drop in intraocular pressure within one hour.

Figure 2 This figure shows the ocular hypotensive effect of a solution containing both timolol (at a concentration of 2.0%) and PGF_{2α}-1-isopropyl ester (at a final concentration of 0.002%) on cat eyes as compared to the ocular hypotensive effect of timolol applied by itself.

Figure 3 This figure shows the ocular hypotensive effect of PGF_{2α}-1-isopropyl ester on cat eyes pretreated 2 hrs earlier with an 0.5% solution of betaxolol.

Figure 4 This figure shows the ocular hypotensive effect of PGF_{2α}-1-isopropyl ester on cat eyes pretreated 2 hrs earlier with an 0.5% solution of levobunolol.

Detailed Description Of The Invention

This invention provides a method for treating ocular hypertension or glaucoma in a subject's eye. The method comprises contacting the surface of the eye with a composition comprising an effective intraocular pressure reducing amount of a mixture of an adrenergic blocking agent and a prostaglandin or prostaglandin derivative in an ophthalmically compatible carrier, so as to reduce the intraocular pressure of the eye and maintain such reduced intraocular pressure. In the preferred embodiment, the subject is a primate, particularly a human being.

Although any adrenergic blocking agent may be employed in the practice of this invention, the

preferred adrenergic blocking agent is a beta blocker. The presently preferred beta blockers are timolol maleate, betaxolol hydrochloride, and levobunolol hydrochloride. Furthermore, while any prostaglandin or prostaglandin derivative may be employed in the practice of this invention, the presently preferred prostaglandin or prostaglandin derivative is of one of the A, E or F type. Of these types, PGF_{2α} or a PGF_{2α} derivative are particularly useful, specifically PGF_{2α}-1-isopropyl ester.

Additionally, a range of concentrations of adrenergic blocking agents may be employed in the practice of the invention. However, the preferred amount present in the mixture is from about 0.01 μg to about 1,000 μg, specifically from about 5 μg to about 500 μg.

The presently preferred effective amount of prostaglandin or prostaglandin derivative present in the mixture is from about 0.01 μg to about 1,000 μg, specifically from about 0.1 μg to about 50 μg.

The ophthalmically compatible carrier may be any well known carrier. Presently preferred for use in the practice of this invention are aqueous solutions, such as a saline solution containing an ophthalmically compatible preservative, a surfactant, and an agent, such as a soluble polymer, to increase the viscosity of the solution. In a preferred embodiment, the mixture is dissolved in the ophthalmically compatible carrier.

Various regimens may be employed for treating ocular hypertension or glaucoma in the subject's eye. In the preferred embodiment, the treatment comprises contacting the surface of the eye, i.e., the cornea, periodically, preferably at least daily, with an effective amount of a mixture of an adrenergic blocking agent and a prostaglandin or prostaglandin derivative to reduce intraocular pressure.

This invention further provides composition for topical treatment of ocular hypertension or glaucoma in a subject's eye. The composition comprises an effective intra-ocular pressure reducing amount of a mixture of an adrenergic blocking agent and a prostaglandin or a prostaglandin derivative in an ophthalmically compatible carrier.

In a preferred embodiment, the adrenergic blocking agent present in the composition is a beta blocker and the prostaglandin or prostaglandin derivative present in the composition is of the A, E or F type. The presently preferred beta blockers are timolol maleate, betaxolol hydrochloride, and levobunolol hydrochloride. The presently preferred prostaglandin or prostaglandin derivative is PGF_{2α} or a PGF_{2α} derivative, specifically, PGF_{2α}-1-isopropyl ester.

The presently preferred effective amount of adrenergic blocking agent present in the composition is from about 0.01 μg to about 1,000 μg,

specifically from about 5 μg to about 500 μg.

The presently preferred effective amount of prostaglandin or prostaglandin derivative present in the composition is from about 0.01 μg to about 1,000 μg, specifically from about 0.1 μg to about 50 μg.

The ophthalmically compatible carrier may be any well known carrier. Presently preferred for use in the practice of this invention are aqueous solutions, such as a saline solution containing an ophthalmically compatible preservative, a surfactant and an agent, such as a soluble polymer, to increase the viscosity of the solution. In a preferred embodiment, the mixture is dissolved in the ophthalmically compatible carrier.

This invention also provides a method for treating ocular hypertension or glaucoma in a primate subject's eye. The method comprises contacting the surface of the eye with a composition comprising an effective intraocular pressure reducing amount of a mixture of levobunolol and PGF_{2α}-1-isopropyl ester dissolved in an ophthalmically compatible carrier, so as to reduce the intraocular pressure of the eye and maintain such reduced intraocular pressure.

This invention further provides a composition for the topical treatment of ocular hypertension or glaucoma comprising an effective intraocular pressure reducing amount of a mixture of levobunolol hydrochloride and PGF_{2α}-1-isopropyl ester dissolved in an ophthalmically compatible carrier.

Finally, this invention provides a method for treating ocular hypertension or glaucoma in a subject's eye. The method comprises separately contacting the surface of the eye with an intraocular pressure reducing amount of an adrenergic blocking agent and of a prostaglandin or prostaglandin derivative, each in an ophthalmically compatible carrier, so as to reduce the intraocular pressure of the eye and maintain such reduced intraocular pressure.

EXPERIMENTAL RESULTS

Materials

The following materials used in the practice of this invention may be obtained from commercial sources: timolol maleate, (as Timoptic™ from Merck Sharp & Dohme Division of Merck & Co. Inc., West Point, PA), betaxolol hydrochloride (as Betoptic from Alcon Laboratories, Fort Worth, Texas), and levobunolol HCl (as Betagan™ from Allergan America, Hormigueros, Puerto Rico).