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SEÑORES

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

DIVISIÓN DE NUEVAS CREACIONES

E. S. D.

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



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Solicitud de Patente de Invención Titulada: "COMBINACIONES DE GLICOPIRROLATO Y AGONISTAS DEL ADRENOCEPTOR-BETA2"

Solicitante: NOVARTIS AG

SOLICITUD DE EXAMEN DE PATENTABILIDAD SEGÚN
EL ARTÍCULO 44 DE LA DECISION 486, GACETA No. 583

CARLOS R. OLARTE, mayor de edad y vecino de Bogotá, D.C., identificado tal como aparece al pie de mi firma, en mi condición de apoderado de la sociedad de la referencia, respetuosamente me permito solicitar que se examine si la invención reúne los requisitos de patentabilidad previstos en la misma, dando cumplimiento a lo establecido en el artículo 44 de la Decisión 486 de la comisión de la Comunidad Andina. Adjunto recibo por el monto de \$420.000 pesos para cubrir la tasa correspondiente, según la Resolución 44372 de 26 de diciembre 2007.

Atentamente,

CARLOS R. OLARTE
C.C. 79.782.747 de Bogotá
T.P. 74.295

Anexo: Recibo por \$420.000 pesos

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DIVISIÓN DE NUEVAS CREACIONES

RADICACIÓN EXPEDIENTE No. 06-113683

EL EXTRACTO DE LA PRESENTE SOLICITUD DE PATENTE DE INVENCION

FUE PUBLICADO EN LA GACETA DE PROPIEDAD INDUSTRIAL No 583 DE

FECHA 18 DE DICIEMBRE DE 2007 EL TÉRMINO HÁBIL SEÑALADO POR LA

LEY EXPIRA EL 14 DE MARZO DE 2008

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

SE PRESENTARON OPOSICIONES POR PARTE DE TERCEROS.

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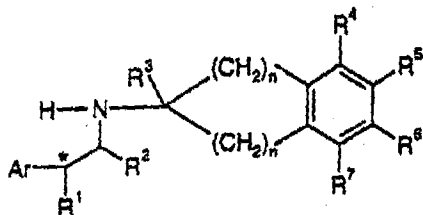
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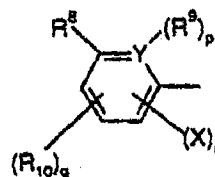
- With international search report.
- Before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments.

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: BETA2-ADRENOCEPTOR AGONISTS



(I)



(II)

(57) Abstract: Compounds of formula (I) in free or salt or solvate form, where Ar is a group of formula (II) Y is carbon or nitrogen and R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, R⁹, R¹⁰, X, n, p, q and r are as defined in the specification, their preparation and their use as pharmaceuticals, particularly for the treatment of obstructive or inflammatory airways diseases. The compounds of formula (I) in free, salt or solvate form, have β 2-adrenoreceptor agonist activity.

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Compounds of formula XVIII are novel compounds which may be prepared by reaction of a compound of formula



where Ar^1 is as hereinbefore defined and Hal is a halogen atom, preferably chlorine or bromine, with a compound of formula XVII as hereinbefore defined. The reaction may be carried out using conventional procedures, for example those described by Yoshizaki et al, J. Med. Chem (1976), 19(9), 1138-42.

Where desired, the protection of any reactive group may be carried out at any appropriate stage in the above processes. The protecting group is suitably one used conventionally in the art and may be introduced and removed using conventional procedure. For example, when a hydroxy group in Ar^1 is protected by a benzyl group, the latter may be removed by catalytic hydrogenation in the presence of palladium on charcoal using conventional procedures, such as those used hereinafter in the Examples.

Compounds of formula I in free, salt or solvate form are useful as pharmaceuticals. Accordingly the invention also provides a compound of formula I in free, salt or solvate form for use as a pharmaceutical. The compounds of formula I in free, salt or solvate form, hereinafter referred to alternatively as "agents of the invention", have good $\beta 2$ -adrenoreceptor agonist activity. The $\beta 2$ agonist activity, onset of action and duration of action of the agents of the invention may be tested using the guinea pig tracheal strip in vitro assay according to the procedure of R.A. Coleman and A.T. Nials, J.Pharmacol. Methods (1989), 21(1), 71-86. The binding potency and selectivity for the $\beta 2$ -adrenoreceptor relative to the $\beta 1$ -adrenoreceptor can be measured by a classical filtration binding assay according to the procedure of Current Protocols in Pharmacology (S.J.Enna(editor-in-chief) et al, John Wiley & Son, Inc, 1998), or by cAMP determination in cells expressing $\beta 2$ - or $\beta 1$ -adrenoceptor, according to the procedure of B. January et al, British J. Pharmacol. 123: 701-711 (1998).

The agents of the invention commonly have a rapid onset of action and have a prolonged stimulating action on the $\beta 2$ -adrenoreceptor, compounds of the Examples hereinbelow having K_i ($\beta 2$) values of the order of 0.1 to 1000 nM, having durations of action of the

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order of 1 to greater than 12 hours, and having binding selectivities for the β_2 -adrenoreceptor relative to the β_1 -adrenoreceptor from 1.5 to 500. For example, the compounds of Examples 1, 2, 4, 5, 6, 8, 27 and 29 have β_2 and β_1 binding potencies, measured by cAMP determination in cells expressing β_2 - and β_1 - adrenoreceptors, represented by EC_{50} values (β_2/β_1) (in nM) of 0.92/9.52, 0.23/1.25, 6.07/14.5, 0.79/6.10, 0.3/3.60, 0.57/8.46 and 0.012/0.5 respectively. The compounds of Examples 2, 4, 5, 27 and 29 have T(50%) times (in minutes) of >400 at 71nM concentration, 82 at 100 nM, 444 at 100nM, 222 at 1.0nM and 279 at 10nM respectively in the guinea pig tracheal strip assay, where T(50%) is the time for inhibition of contraction to decay to 50% of its maximum value.

Having regard to their β_2 agonist activity, the agents of the invention are suitable for use in the treatment of any condition which is prevented or alleviated by activation of the β_2 -adrenoreceptor. In view of their long acting selective β_2 agonist activity, the agents of the invention are useful in the relaxation of bronchial smooth muscle and the relief of bronchoconstriction. Relief of bronchoconstriction can be measured in models such as the in vivo plethysmography models of Chong et al, J. Pharmacol.Toxicol. Methods 1998, 39, 163-168, Hammelmann et al, Am. J. Respir. Crit. Care Med., 1997, 156, 766-775 and analogous models. The agents of the invention are therefore useful in the treatment of obstructive or inflammatory airways diseases. In view of their long duration of action, it is possible to administer the agents of the invention once-a-day in the treatment of such diseases. In another aspect, agents of the invention commonly exhibit characteristics indicating a low incidence of side effects commonly encountered with β_2 agonists such as tachycardia, tremor and restlessness, such agents accordingly being suitable for use in on demand (rescue) treatment as well as prophylactic treatment of obstructive or inflammatory airways diseases.

Treatment of a disease in accordance with the invention may be symptomatic or prophylactic treatment. Inflammatory or obstructive airways diseases to which the present invention is applicable include asthma of whatever type or genesis including both intrinsic (non-allergic) asthma and extrinsic (allergic) asthma. Treatment of asthma is also to be understood as embracing treatment of subjects, e.g. of less than 4 or 5 years of age, exhibiting wheezing symptoms and diagnosed or diagnosable as "wheezy infants", an established patient category of major medical concern and now often identified as incipient

or early-phase asthmatics. (For convenience this particular asthmatic condition is referred to as "wheezy-infant syndrome".)

Prophylactic efficacy in the treatment of asthma will be evidenced by reduced frequency or severity of symptomatic attack, e.g. of acute asthmatic or bronchoconstrictor attack, improvement in lung function or improved airways hyperreactivity. It may further be evidenced by reduced requirement for other, symptomatic therapy, i.e. therapy for or intended to restrict or abort symptomatic attack when it occurs, for example anti-inflammatory (e.g. corticosteroid) or bronchodilatory. Prophylactic benefit in asthma may in particular be apparent in subjects prone to "morning dipping". "Morning dipping" is a recognised asthmatic syndrome, common to a substantial percentage of asthmatics and characterised by asthma attack, e.g. between the hours of about 4 to 6 am, i.e. at a time normally substantially distant from any previously administered symptomatic asthma therapy.

Other inflammatory or obstructive airways diseases and conditions to which the present invention is applicable include adult respiratory distress syndrome (ARDS), chronic obstructive pulmonary or airways disease (COPD or COAD), including chronic bronchitis, or dyspnea associated therewith, emphysema, as well as exacerbation of airways hyperreactivity consequent to other drug therapy, in particular other inhaled drug therapy. The invention is also applicable to the treatment of bronchitis of whatever type or genesis including, e.g., acute, arachidic, catarrhal, croupus, chronic or phthinoid bronchitis. Further inflammatory or obstructive airways diseases to which the present invention is applicable include pneumoconiosis (an inflammatory, commonly occupational, disease of the lungs, frequently accompanied by airways obstruction, whether chronic or acute, and occasioned by repeated inhalation of dusts) of whatever type or genesis, including, for example, aluminosis, anthracosis, asbestosis, chalicosis, ptilosis, siderosis, silicosis, tabacosis and byssinosis.

Having regard to their β_2 agonist activity, the agents of the invention are also useful in the treatment of a condition requiring relaxation of smooth muscle of the uterus or vascular system. They are thus useful for the prevention or alleviation of premature labour pains in pregnancy. They are also useful in the treatment of chronic and acute urticaria, psoriasis, allergic conjunctivitis, actinitis, hay fever, and mastocytosis.

The agents of the invention are also useful as co-therapeutic agents for use in conjunction with anti-inflammatory or bronchodilatory drug substances, particularly in the treatment of obstructive or inflammatory airways diseases such as those mentioned hereinbefore, for example as potentiators of therapeutic activity of such drugs or as a means of reducing required dosaging or potential side effects of such drugs. An agent of the invention may be mixed with the anti-inflammatory or bronchodilatory drug in a fixed pharmaceutical composition or it may be administered separately, before, simultaneously with or after the anti-inflammatory or bronchodilatory drug. Such anti-inflammatory drugs include steroids, in particular glucocorticosteroids such as budesonide, beclamethasone, fluticasone or mometasone, and dopamine receptor agonists such as cabergoline, bromocriptine or ropinirole. Such bronchodilatory drugs include anticholinergic or antimuscarinic agents, in particular ipratropium bromide, oxitropium bromide and tiotropium bromide. Combinations of agents of the invention and steroids may be used, for example, in the treatment of COPD or, particularly, asthma. Combinations of agents of the invention and anticholinergic or antimuscarinic agents or dopamine receptor agonists may be used, for example, in the treatment of asthma or, particularly, COPD.

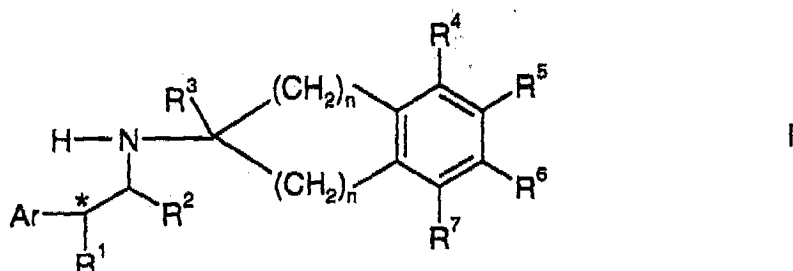
In accordance with the foregoing, the present invention also provides a method for the treatment of an obstructive or inflammatory airways disease which comprises administering to a subject, particularly a human subject, in need thereof a compound of formula I, or a pharmaceutically acceptable salt or solvate thereof, as hereinbefore described. In another aspect, the invention provides a compound of formula I, or a pharmaceutically acceptable salt or solvate thereof, as hereinbefore described for use in the preparation of a medicament for the treatment of an obstructive or inflammatory airways disease.

The agents of the invention may be administered by any appropriate route, e.g. orally, for example in the form of a tablet or capsule; parenterally, for example intravenously; topically to the skin, for example in the treatment of psoriasis; intranasally, for example in the treatment of hay fever; or, preferably, by inhalation, particularly in the treatment of obstructive or inflammatory airways diseases.

In a further aspect, the invention also provides a pharmaceutical composition comprising a compound of formula I in free form or in the form of a pharmaceutically acceptable salt or solvate thereof, optionally together with a pharmaceutically acceptable diluent or carrier therefor. Such compositions may be prepared using conventional diluents or excipients and techniques known in the galenic art. Thus oral dosage forms may include tablets and

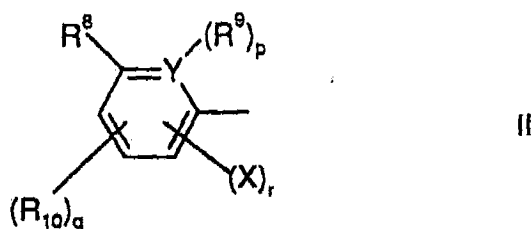
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150Claims

1. A compound of formula



in free or salt or solvate form, where

Ar is a group of formula



R^1 is hydrogen, hydroxy, or alkoxy,

R^2 and R^3 are each independently hydrogen or alkyl,

R^4 , R^5 , R^6 and R^7 are each independently hydrogen, halogen, cyano, hydroxy, alkoxy, aryl, alkyl, alkyl substituted by one or more halogen atoms or one or more hydroxy or alkoxy groups, alkyl interrupted by one or more hetero atoms, alkenyl, trialkylsilyl, carboxy, alkoxycarbonyl, or $-\text{CONR}^{11}\text{R}^{12}$, where R^{11} and R^{12} are each independently hydrogen or alkyl, or R^4 and R^5 , R^5 and R^6 , or R^6 and R^7 together with the carbon atoms to which they are attached denote a carbocyclic or heterocyclic ring,

R^8 is halogen, $-\text{OR}^{13}$, $-\text{CH}_2\text{OR}^{13}$ or $-\text{NHR}^{13}$ where R^{13} is hydrogen, alkyl, alkyl interrupted by one or more hetero atoms, $-\text{COR}^{14}$, where R^{14} is hydrogen, $-\text{N}(\text{R}^{15})\text{R}^{16}$, alkyl or alkyl interrupted by one or more hetero atoms, or aryl and R^{15} and R^{16} are each independently hydrogen, alkyl or alkyl interrupted by one or more hetero atoms, or R^{13} is $-\text{C}(=\text{NH})\text{R}^{17}$, $-\text{SOR}^{17}$ or $-\text{SO}_2\text{R}^{17}$ where R^{17} is alkyl or alkyl interrupted by one or more hetero atoms, and R^9 is hydrogen, or R^8 is $-\text{NHR}^{18}$ where $-\text{NHR}^{18}$ and R^9 , together with the carbon atoms to which they are attached, denote a 5- or 6- membered heterocycle,

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R^{10} is $-OR^{19}$ or $-NHR^{19}$ where R^{19} is hydrogen, alkyl, alkyl interrupted by one or more hetero atoms, or $-COR^{20}$, where R^{20} is $-N(R^{21})R^{22}$, alkyl or alkyl interrupted by one or more hetero atoms, or aryl, and R^{21} and R^{22} are each independently hydrogen, alkyl or alkyl interrupted by one or more hetero atoms,

X is halogen or halomethyl or alkyl,

Y is carbon or nitrogen,

n is 1 or 2,

p is zero when Y is nitrogen or 1 when Y is carbon,

q and r are each zero or 1, the sum of q+r is 1 or 2; and

the carbon atom marked with an asterisk* has the R or S configuration, or a mixture thereof, when R^1 is hydroxy or alkoxy.

2. A compound according to claim 1, in which Ar is a group of formula II in which

Y is carbon,

R^8 is $-NHR^{18}$ and $-NHR^{18}$ and R^9 together denote

a group of formula $-NH-CO-R^{23}$ where R^{23} is an alkylene, alkenylene or alkyleneoxy group,

a group of formula $-NH-SO_2-R^{24}$ where R^{24} is an alkyleneoxy group,

a group of formula $-NH-R^{25} (COOR^{26})$ where R^{25} is an alkylene or alkenylene group and R^{26} is alkyl, or

a group of formula $-NH-CO-NH-$ or $-NH-CO-S-$,

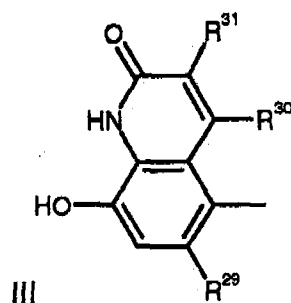
R^{10} is $-OR^{19}$, where R^{19} is as defined in claim 1,

X is alkyl,

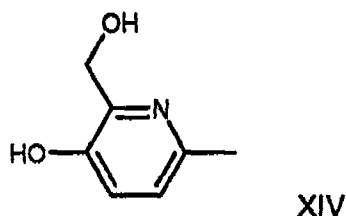
p is 1, q is 1 and r is zero or 1.

3. A compound according to claim 2, in which Ar is a group of formula III, IV, V, VI or VII

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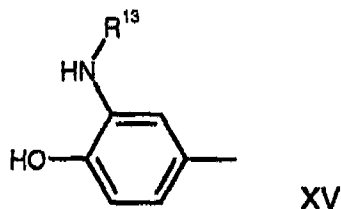


in which R^{29} , R^{30} and R^{31} are each independently hydrogen or C_1 - C_4 -alkyl

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7. A compound according to claim 1, in which Ar is a group of formula II in which Y is carbon, R^8 is $-NHR^{13}$ where R^{13} is hydrogen, C_1 - C_{10} alkyl, C_1 - C_{10} alkyl interrupted by 1 to 3 hetero atoms, $-COR^{14}$ where R^{14} is hydrogen, C_1 - C_{10} -alkyl or C_1 - C_{10} -alkyl interrupted by 1 to 3 hetero atoms, or R^{13} is $-C(=NH)R^{17}$, $-SOR^{17}$ or $-SO_2R^{17}$ where R^{17} is C_1 - C_{10} -alkyl or C_1 - C_{10} -alkyl interrupted by 1 to 3 hetero atoms, R^9 is hydrogen, R^{10} is $-OR^{18}$ where R^{18} is hydrogen, C_1 - C_4 -alkyl or C_1 - C_4 -alkoxy- C_1 - C_4 alkyl, p and q are each 1 and r is zero.

8. A compound according to claim 7, in which Ar is a group of formula XV

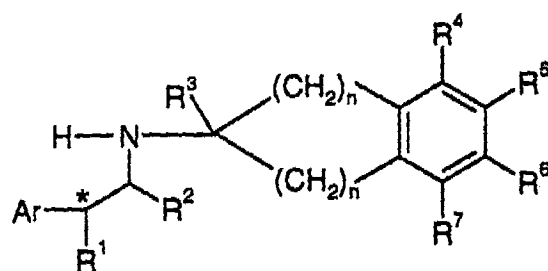


9. A compound according to any one of the preceding claims, in which R^4 , R^5 , R^6 and R^7 are each hydrogen or are such that the benzene ring to which they are attached is symmetrically substituted.

10. A compound according to claim 1, in which Ar is a group of formula III, IV, V, XII or XV, R^1 is hydroxy, R^2 and R^3 are hydrogen, and R^4 and R^7 are identical and are each hydrogen, C_1 - C_4 -alkyl or C_1 - C_4 -alkoxy, and either R^5 and R^6 are identical and are each hydrogen, C_1 - C_4 -alkyl, C_1 - C_4 -alkoxy or C_1 - C_4 -alkoxy- C_1 - C_4 -alkyl, or R^5 and R^6 together denote $-(CH_2)_4-$ or $-O(CH_2)_2O-$, in free or salt or solvate form.

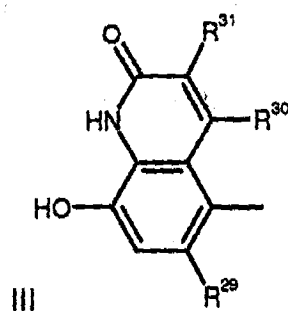
11. A compound according to claim 10, in which the carbon atom in formula I marked with an asterisk * has the R configuration.

12. A compound of formula

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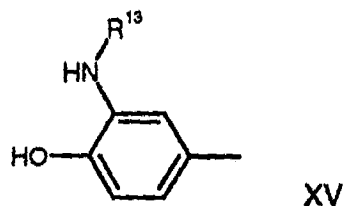
in free or salt or solvate form,

(A) wherein Ar is a group of formula



- in which R^{29} , R^{30} and R^{31} are each H, R^1 is OH, R^2 and R^3 are each H and
- (i) n is 1, and R^4 and R^7 are each $\text{CH}_3\text{O}-$ and R^5 and R^6 are each H; or
 - (ii) n is 1, and R^4 and R^7 are each H and R^5 and R^6 are each CH_3CH_2- ; or
 - (iii) n is 1, and R^4 and R^7 are each H and R^5 and R^6 are each CH_3- ; or
 - (iv) n is 1, and R^4 and R^7 are each CH_3CH_2- and R^5 and R^6 are each H; or
 - (v) n is 1, and R^4 and R^7 are each H and R^5 and R^6 together denote $-(\text{CH}_2)_4-$; or
 - (vi) n is 1, and R^4 and R^7 are each H and R^5 and R^6 together denote $-\text{O}(\text{CH}_2)_2\text{O}-$; or
 - (vii) n is 1, and R^4 and R^7 are each H and R^5 and R^6 are each $\text{CH}_3(\text{CH}_2)_3-$; or
 - (viii) n is 1, and R^4 and R^7 are each H and R^5 and R^6 are each $\text{CH}_3(\text{CH}_2)_2-$; or
 - (ix) n is 2, R^4 , R^5 , R^6 and R^7 are each H; or
 - (x) n is 1, and R^4 and R^7 are each H and R^5 and R^6 are each CH_3OCH_2- ; or

(B) wherein Ar is a group of formula



in which R^{13} is H, R^1 is OH, R^2 and R^3 are each H, R^4 and R^7 are each H and R^5 and R^6 are each H and n is 1; or

11 H CH₃CH₂ CH₃CH₂ H 341

Example 10: ¹H-NMR (d₄-MeOH) ppm: 2.78 (2H, m), 2.9 (2H, m), 3.15 (2H, m), 3.28 (6H, s), 3.7 (1H, m), 4.55 (1H, br s), 5.15 (1H, m), 6.58 (1H, d), 6.9 (1H, d), 7.11 (2H, s), 7.15 (1H, s), 8.25 (1H, s).

Example 12

8-Hydroxy-5-[1-hydroxy-2-(indan-2-ylamino)-ethyl]-1H-quinolin-2-one

Intermediate 10 (18 mg, 0.054 mmol) is dissolved in methanol (2 mL) and cooled on ice. Sodium borohydride (6 mg, 0.12 mmol) is added over 2 hours. Concentrated HCl is then added until pH reaches 1, and the reaction mixture filtered. The filtrate is washed with methanol. The combined liquid phases are evaporated and redissolved in methanol twice. After removal of the methanol in vacuo, the residue is redissolved in water and the pH brought to 12 with 1N KOH. The solvent is removed in vacuo and the residue coevaporated twice with toluene. The residue is purified by flash chromatography (silica, CH₂Cl₂/methanol 8:2). ES+ MS *m/e* 337 (MH⁺).

Example 13

5-[2-(5,6-Dimethoxy-indan-2-ylamino)-1-hydroxy-ethyl]-8-hydroxy-1H-quinolin-2-one

This compound is prepared from Intermediate 11 by a procedure analogous to that of Example 12. ES+MS *m/e* 397 (MH⁺)

Example 14

5-[2-(5,6-Diethyl-indan-2-ylamino)-1-hydroxy-ethyl]-8-hydroxy-3-methyl-1H-quinolin-2-one

This is prepared from Intermediate 13 (21mg) by the hydrogenation procedure for removal of the benzyl group used in Example 1.

¹H-NMR (d₄-CH₃OH) ppm 1.11 (t, 6H), 2.11 (s, 3H), 2.58 (q, 4H), 3.01-3.37 (m, 6H), 4.10-4.16 (m, 1H), 5.31-5.38 (m, 1H), 6.91 (d, 1H), 7.00 (s, 2H), 7.21 (d, 1H), 8.13 (s, 1H).

Example 15

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

2020
Bogotá, D.C.,

Abogado
CARLOS R. OLARTE
Apoderado

ASUNTO	Radicación	06-113683
	Trámite	002
	Evento	001
	Actuación	430
	Oficio	002
	Folios	088 171

Como resultado del examen de búsqueda de anterioridades y con fundamento en el artículo 46 de la Decisión 486 de la Comisión de la Comunidad Andina, se le comunica:

1. SOLICITUD DE SUMINISTRO DE INFORMACIÓN

El artículo 46 de la Decisión 486 de la Comisión de la Comunidad Andina establece que: "La Oficina Nacional competente podrá requerir el informe de expertos o de organismos científicos o tecnológicos que se consideren idóneos, para que emitan opinión sobre la patentabilidad de la invención. Asimismo, cuando lo estime conveniente, podrá requerir informes de otras oficinas de propiedad industrial. De ser necesario, a efectos del examen de patentabilidad y a requerimiento de la oficina nacional competente, el solicitante proporcionará, en un plazo que no excederán de 3 meses, uno o más de los siguientes documentos relativos a una o más de las solicitudes extranjeras referidas total o parcialmente a la misma invención que se examina: ... b) copia de los resultados de exámenes de novedad o de patentabilidad efectuados respecto a esa solicitud extranjera; ... Si el solicitante no presentara los documentos requeridos dentro del plazo señalado en el presente artículo la oficina nacional competente denegará la patente".

Como consecuencia de la búsqueda de anterioridades de materia relacionada con la de la presente invención, se determinó que existen en el estado de la técnica los siguientes documentos, que eventualmente afectarían los requisitos de patentabilidad de esta solicitud:

CYDULKA R K ET AL: "EFFECTS OF COMBINED TREATMENT WITH GLYCOPYRROLATE AND ALBUTEROL IN ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE" ANNALS OF EMERGENCY MEDICINE, LANSING, MI, US, VOL. 25, April 1995, pages 470-473, XP000979833, ISSN: 0196-0644. Abstract

TZELEPIS G ET AL: "COMPARISON OF NEBULIZED GLYCOPYRROLATE AND METAPROTERENOL IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE" EUROPEAN RESPIRATORY JOURNAL, MUNKSGAARD INTERNATIONAL

PUBLISHERS, COPENHAGEN, DK, Vol. 9, no. 8, 1996, pages 100-103, XP000979863, abstract.

Siendo que las publicaciones referenciadas hacen parte del resultado del examen de búsqueda realizado esta solicitud colombiana, y no siendo viable la consecución de dichos artículos por este despacho, se requiere que el solicitante, en virtud de lo establecido en el artículo 46 de la Decisión 486 de la Comisión de la Comunidad Andina, proporcione las publicaciones completas, con lo que podrá realizarse un análisis absoluto de la patentabilidad de la invención correspondiente a la presente solicitud.

Notifíquese el presente oficio conforme a lo dispuesto en el numeral 5.2, literal e), del capítulo quinto (5), del título primero de la circular única N° 10 de 2001.

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

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

09 JUL. 2010

CONCEPTO TÉCNICO Nº: 1133	EXAMINADOR TÉCNICO Código N°: 202087	EXAMINADOR JURÍDICO Código N°:
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161 158

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

2020
Bogotá, D.C.,

Abogado
CARLOS R. OLARTE
Apoderado

ASUNTO

Radicación 06-113683
Trámite 011
Evento 379
Actuación 430
Oficio **08816**
Folios 164

Patente de Invención ☒ Patente de Modelo de Utilidad ☐
Vía Nacional ☐
Vía PCT (fase nacional) ☒ Cap. I ☒ Cap. II ☐
No. Sol. Internacional PCT/EP2005/005354
Fecha de Presentación Internal. 2005/05/17

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

Descripción: Folios: 50 a 98

Reivindicaciones: Folios 130 a 143

Prioridad: Fecha: 2004/05/18, país: GB y número: 0411056.5

2. Objeto de la invención

- Título de la solicitud: Combinaciones de glicopirrolato y agonistas del adrenoceptor-beta2 y número de folio: 1

El problema planteado en esta solicitud es la necesidad de combinaciones útiles para la enfermedad pulmonar obstructiva crónica.

Para solucionar este problema técnico la solicitud en estudio proporciona combinaciones de glicopirrolato antagonista del receptor muscarínico M3 y agonistas adrenoceptores beta 2 de rápida acción y larga duración que minimice o evite dosis diarias a repetición, preferiblemente una vez por día.

3. De la solicitud de Patente

Título (*artículo 28 D. 486*)

- El título no es específico en cuanto a lo que realmente se pretende proteger. Se requiere al solicitante realizar los ajustes necesarios.

Reivindicaciones (*artículo 30 D 486*)

Una vez revisado el capítulo reivindicatorio esta dependencia encuentra:

- Reivindicación 1: no puede aceptarse tal como está ya que al hacer referencia de que el medicamento puede comprender por separado dos compuestos está sugiriendo que no es una composición como tal sino un método de administración o tratamiento.
- Reivindicación 1: Se puede deducir que se obtienen millones de combinaciones que dan como resultado compuestos agonistas adrenoreceptores beta2 de fórmula (I). Se requiere restricción del alcance de la invención que se desea proteger dada la amplitud de la materia que se pretende reivindicar y señalar inequívocamente que compuestos prueban su superioridad contra las anterioridades.
- Reivindicación 2: Contiene la misma materia de la reivindicación 1, no aporta nada adicional.
- Reivindicación 8: Se reivindica una "sustancia fármaco" con propiedades antiinflamatorias, broncodilatadoras, antihistamínicas, descongestionantes o antitusivos, dicho termino no se acepta tal como está por ser demasiado ambiguo y general.
- Reivindicación 11: No es clara ni concisa ya que se reivindica un medicamento, sin aportar ninguna característica definida. Un medicamento no se caracteriza mediante el tamaño de partícula de sus componentes sino mediante los componentes como tal, por lo tanto no es tenida en cuenta.
- Reivindicación 19: Se reivindican medicamentos por su posterior uso en administración simultánea, en secuencia o separada y tratamiento de una enfermedad inflamatoria u obstructiva por lo cual no puede aceptarse ya que un medicamento se caracteriza únicamente por sus componentes fórmula.

El objeto de la solicitud no es claro e incumple así mismo con el requisito de concisión, dadas las observaciones esbozadas en los numerales precedentes. En este sentido se requiere al interesado para que realice las modificaciones correspondientes a fin de subsanar las no conformidades encontradas por este Despacho.

4. Unidad de invención (*artículo 25 D 486*)

Reivindicación 18: Se refiere a un estuche farmacéutico. Los componentes del estuche (frasco, composición, empaque, instrucciones, dispositivos de inhalación, formas de dosificación unitarias, etc) pertenecen a diferentes campos técnicos de manera que no dan cabida al principio de unidad de invención.

5. Reivindicaciones relativas a un uso o a un segundo uso (artículos 14 y 21 D 486)

Reivindicación 14-17: Se refieren a usos para la fabricación de medicamentos por lo tanto están exceptuadas de patentabilidad según la legislación vigente

6. Determinación del Estado de la Técnica

La fecha que se ha tenido en cuenta para determinar el Estado de la Técnica es:

Fecha de presentación de la solicitud prioritaria 2004/05/18

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

Nº	Documento	Título	Fecha de publicación*
D ₁	WO 00/75114	BETA2-ADRENOCEPTOR AGONISTS	2000/12/14

7. Análisis de patentabilidad (artículo 14 D486)

Novedad (artículo 16 D486)

Reivindicaciones 1: medicamento que comprende (A) glicopirrolato y (B) compuesto de fórmula (I) o (II)

D1 enseña (ver folio 148 y siguientes) compuestos agonistas adrenoceptores beta2 de fórmula (I) y (II) (folio 149 pag 14, folio 153, pág 49) para el tratamiento de EPOC y otras enfermedades obstructivas de vías aéreas, los cuales son de acción rápida y prolongada estimulación y son dosificados una vez al día. Pueden ser mezclados (folio 152 página 17) en forma de composición con antiinflamatorios o broncodilatadores que incluyen anticolinérgicos o agentes antimuscarínicos (folio 152 página 17).

- ♦ Los elementos característicos medicamento de la reivindicación 1, es decir: compuestos **agonistas adrenoceptores beta2 de fórmula (I) o (II) y un agente antimuscarínico** habían sido divulgados previamente en el Estado de la Técnica.

De manera que el objeto de esta solicitud, tal como aparece en las reivindicaciones 1 - 13, no es nuevo.

6. Conclusión:

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

N°	Documento N°	Reivindicaciones afectadas	Requisito que afecta
D ₁	WO 00/75114	1-13	NOVEDAD

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

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


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

El anterior requerimiento fue notificado por fijación en lista, de fecha
_____ **09 JUL 2010**

CONCEPTO TÉCNICO No. 1133	EXAMINADOR TÉCNICO Código No. 202087
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