

Señores

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIVISION DE NUEVAS CREACIONES

E. _____ S. _____

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 07-053834- -00003-0000

Fecha: 2008-11-14 17:12:23 Dep. 2020 NUECREACION
Ita 11 PATENTILYII Lvs 379 FASENACIONALII
Act. 538 PETICION Folios 2

Ref: Expediente No. 07-053.834

Solicitud de Patente de Invención titulada: "PIRAZOLO[3,4-b]PIRIDINAS E
INDAZOLES TERAPEUTICOS".

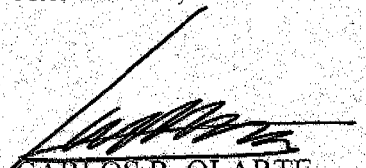
Solicitante: WARNER LAMBERT COMPANY LLC.

Nuestra Ref.: P2007/000094

SOLICITUD DE EXAMEN DE PATENTABILIDAD SEGÚN
EL ARTÍCULO 44 DE LA DECISION 486, GACETA No. 596

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, 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 \$210.000 pesos para cubrir la tasa correspondiente, según la Resolución 44372 del año 2007.

Atentamente,


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

Anexo: Recibo por \$210.000 pesos

249
2

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

MIT : 800176089-2

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
No. 07-053834-00003-0000
Fecha: 2008-11-14 17:12:23 Dep. 2020 NULCREACIONE
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Act 538 PLICION Folios: 2

RECIBO OFICIAL DE CAJA : 08 - 89,267
FECHA : NOVIEMBRE 13 DE 2008

***** CONSIGNACION *****

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PAGO	Vr. PAGO
OLARTE RAISBEK	CONSIGNACION	BANCO DE BOGOTA	062754387	81235490	12/11/2008	4,818,000.00

***** CONCEPTO *****

CANT.	RENTISTICO	CONCEPTO	TOTAL CONCEPTO
1	50005-01-01	SOLICITUDES	
		114 PTC CAP-II EXAMEN DE PATENTABILIDAD	210,000.00
		TOTAL :	\$ 210,000.00

SON: DOSCIENTOS DIEZ MIL PESOS

[Handwritten signature]

RESPONSABLE :

DIVISIÓN DE NUEVAS CREACIONES

RADICACIÓN EXPEDIENTE No. 07-53834

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

FUE PUBLICADO EN LA GACETA DE PROPIEDAD INDUSTRIAL No 596 DE

FECHA **30 DE SEPTIEMBRE DE 2008** EL TÉRMINO HÁBIL SEÑALADO POR

LA LEY EXPIRA EL 30 DE DICIEMBRE 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.

SI _____

NO X

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(19) World Intellectual Property Organization
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PCT

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(81) Designated States (national): **CA, JP, MX.**

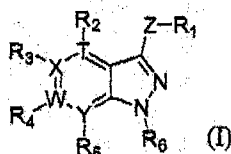
(84) Designated States (regional): European patent (AT, BE,
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Published:

— *without international search report and to be republished
upon receipt of that report*

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: **INDAZOLE DERIVATIVES THAT ARE ACTIVATORS OF SOLUBLE GUANYLATE CYCLASE**



(57) Abstract: Compounds of formula (I) are novel indazoles useful for increasing cGMP levels in a mammal.

WO 03/076408 A2

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Definitions of the Present Invention

As used throughout this specification and the appended claims, the following terms have the following meanings:

The term "alkenyl," as used herein, refers to a straight or branched chain hydrocarbon containing from 2 to 10 carbons and containing at least one carbon-carbon double bond formed by the removal of two hydrogens. Representative examples of alkenyl include, but are not limited to, ethenyl, 2-propenyl, 2-methyl-2-propenyl, 3-butenyl, 4-pentenyl, 5-hexenyl, 2-heptenyl, 2-methyl-1-heptenyl, and 3-decenyl.

The term [REDACTED] as used herein, refers to an alkyl group, as defined herein, appended to the parent molecular moiety through an oxygen atom. Representative examples of [REDACTED] ethoxy, propoxy, 2-propoxy, butoxy, tert-butoxy, pentyloxy, and hexyloxy.

The term "alkoxyalkoxy," as used herein, refers to an alkoxy group, as defined herein, appended to the parent molecular moiety through another alkoxy group, as defined herein. Representative examples of alkoxyalkoxy include, but are not limited to, tert-butoxymethoxy, 2-ethoxyethoxy, 2-methoxyethoxy, and methoxymethoxy.

The term "alkoxyalkyl," as used herein, refers to an alkoxy group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of alkoxyalkyl include, but are not limited to, tert-butoxymethyl, 2-ethoxyethyl, 2-methoxyethyl, and methoxymethyl.

The term "alkoxycarbonyl," as used herein, refers to an alkoxy group, as defined herein, appended to the parent molecular moiety through a carbonyl group, as defined herein. Representative examples of alkoxycarbonyl include, but are not limited to, methoxycarbonyl, ethoxycarbonyl, and tert-butoxycarbonyl.

The term "alkoxycarbonylalkyl," as used herein, refers to an alkoxycarbonyl group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of alkoxycarbonylalkyl include, but are not limited to, 3-methoxycarbonylpropyl, 4-ethoxycarbonylbutyl, and 2-tert-butoxycarbonylethyl.

The term "alkoxysulfonyl," as used herein, refers to an alkoxy group, as defined herein, appended to the parent molecular moiety through a sulfonyl group, as

5 defined herein. Representative examples of alkoxysulfonyl include, but are not limited to, methoxysulfonyl, ethoxysulfonyl and propoxysulfonyl.

The term "alkyl," as used herein, refers to a straight or branched chain hydrocarbon containing from 1 to 10 carbon atoms. Representative examples of alkyl include, but are not limited to, methyl, ethyl, n-propyl, iso-propyl, n-butyl, sec-butyl, iso-butyl, tert-butyl, n-
10 pentyl, isopentyl, neopentyl, n-hexyl, 3-methylhexyl, 2,2-dimethylpentyl, 2,3-dimethylpentyl, n-heptyl, n-octyl, n-nonyl, and n-decyl.

The term "alkylcarbonyl," as used herein, refers to an alkyl group, as defined herein, appended to the parent molecular moiety through a carbonyl group, as defined herein. Representative examples of alkylcarbonyl include, but are not limited to, acetyl, 1-
15 oxopropyl, 2,2-dimethyl-1-oxopropyl, 1-oxobutyl, and 1-oxopentyl.

The term "alkylcarbonylalkyl," as used herein, refers to an alkylcarbonyl group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of alkylcarbonylalkyl include, but are not limited to, 2-oxopropyl, 3,3-dimethyl-2-oxopropyl, 3-oxobutyl, and 3-oxopentyl.

20 The term "alkylcarbonyloxy," as used herein, refers to an alkylcarbonyl group, as defined herein, appended to the parent molecular moiety through an oxygen atom. Representative examples of alkylcarbonyloxy include, but are not limited to, acetyloxy, ethylcarbonyloxy, and tert-butylcarbonyloxy.

The term "alkylene," denotes a divalent group derived from a straight or branched
25 chain hydrocarbon of from 1 to 10 carbon atoms. Representative examples of alkylene include, but are not limited to, $-\text{CH}_2-$, $-\text{CH}_2\text{CH}_2-$, $-\text{CH}_2\text{CH}_2\text{CH}_2-$, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2-$, and $-\text{CH}_2\text{CH}(\text{CH}_3)\text{CH}_2-$.

The term "alkylsulfinyl," as used herein, refers to an alkyl group, as defined herein, appended to the parent molecular moiety through a sulfinyl group, as defined herein.
30 Representative examples of alkylsulfinyl include, but are not limited to, methylsulfinyl and ethylsulfinyl.

The term "alkylsulfonyl," as used herein, refers to an alkyl group, as defined herein, appended to the parent molecular moiety through a sulfonyl group, as defined herein. Representative examples of alkylsulfonyl include, but are not limited to, methylsulfonyl and
35 ethylsulfonyl.

The term "alkylthio," as used herein, refers to an alkyl group, as defined herein, appended to the parent molecular moiety through a sulfur atom. Representative examples

5 of alkylthio include, but are not limited, methylsulfanyl, ethylsulfanyl, tert-butylsulfanyl, and hexylsulfanyl.

The term "alkylthioalkyl," as used herein, refers to an alkylthio group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of alkylthioalkyl include, but are not limited,
10 methylsulfanylmethyl and 2-(ethylsulfanyl)ethyl.

The term "alkynyl," as used herein, refers to a straight or branched chain hydrocarbon group containing from 2 to 10 carbon atoms and containing at least one carbon-carbon triple bond. Representative examples of alkynyl include, but are not limited, to acetylenyl, 1-propynyl, 2-propynyl, 3-butynyl, 2-pentynyl, and 1-butynyl.

15 The term "aryl" as used herein, refers to a phenyl group, or a bicyclic or a tricyclic fused ring system wherein one or more of the fused rings is a phenyl group. Bicyclic fused ring systems are exemplified by a phenyl group fused to a cycloalkyl group, as defined herein, or another phenyl group. Tricyclic fused ring systems are exemplified by a bicyclic fused ring system, as defined herein, fused to a cycloalkyl group, as defined herein, or
20 another phenyl group. Representative examples of aryl include, but are not limited to, anthracenyl, azulenyl, fluorenyl, 2,3-dihydroindenyl, indenyl, naphthyl, ~~phenyl~~ and tetrahydronaphthyl.

The aryl groups of this invention are substituted with 0, 1, 2, 3, 4 or 5 substituents independently selected from alkenyl, ~~alkoxy~~, alkoxyalkoxy, alkoxyalkyl, alkoxycarbonyl,
25 alkoxycarbonylalkyl, alkoxysulfonyl, ~~alkyl~~alkylcarbonyl, alkylcarbonylalkyl, alkylcarbonyloxy, alkylsulfinyl, alkylsulfonyl, alkylthio, alkylthioalkyl, alkynyl, arylalkyl, arylcarbonyl, carboxy, carboxyalkyl, cycloalkyl, cycloalkylalkyl, cyano, cyanoalkyl, ethylenedioxy, formyl, haloalkoxy, haloalkyl, ~~halogen~~, heterocyclealkyl, heterocyclecarbonyl, hydroxy, hydroxyalkyl, mercapto, methylenedioxy, nitro,
30 (NZ₁Z₂)alkyl, -NR_AR_B, (NR_AR_B)carbonyl and (NR_AR_B)sulfonyl. The aryl groups of this invention may also be substituted with 1 additional aryl group or 1 additional heterocycle wherein the additional aryl group and the additional heterocycle are substituted with 0, 1, 2, 3, 4 or 5 substituents independently selected from alkenyl, alkoxy, alkoxyalkoxy, alkoxyalkyl, alkoxycarbonyl, alkoxycarbonylalkyl, alkoxysulfonyl, alkyl, alkylcarbonyl,
35 alkylcarbonylalkyl, alkylcarbonyloxy, alkylsulfinyl, alkylsulfonyl, alkylthio, alkylthioalkyl, alkynyl, carboxy, carboxyalkyl, cyano, cyanoalkyl, ethylenedioxy, formyl, haloalkoxy, haloalkyl, halogen, hydroxy, hydroxyalkyl, mercapto, methylenedioxy, nitro, (NZ₁Z₂)alkyl,

- 5 -NR_AR_B, (NR_AR_B)carbonyl and (NR_AR_B)sulfonyl. Representative examples of aryl substituted with 0, 1, 2, 3, 4 or 5 substituents include, but are not limited to, 2-carboxyphenyl, 3-carboxyphenyl, 4-carboxyphenyl, 2-({4-[3-(dimethylamino)propyl]-1-piperazinyl}carbonyl)phenyl, 2-({4-[3-(dimethylamino)propyl]-1-piperazinyl}carbonyl)phenyl, 2-({4-[2-(dimethylamino)ethyl]-1-piperazinyl}carbonyl)phenyl, 2-({[(4-hydroxycyclohexyl)amino]carbonyl}phenyl, 2-({[(1R,2S)-1-hydroxy-2,3-dihydro-1H-inden-2-yl]amino}carbonyl)phenyl, 2-({[1-(hydroxymethyl)butyl]amino}carbonyl)phenyl, 2-({[(2-hydroxy-2-phenylethyl)amino]carbonyl}phenyl, ({[2-(1-methyl-2-pyrrolidinyl)ethyl]amino}carbonyl)phenyl, 2-({[3-(1H-imidazol-1-yl)propyl]amino}carbonyl)phenyl, 2-({[4-morpholinylamino]carbonyl}phenyl, 2-({[[(1S,2R)-2-hydroxycyclohexyl]methyl]amino}carbonyl)phenyl, and (1S)-1-hydroxy-2,3-dihydro-1H-inden-2-yl.

The term "arylalkenyl" as used herein, means an aryl group, as defined herein, appended to the parent molecular moiety through an alkenyl group, as defined herein.

- 20 Representative examples of arylalkenyl include, but are not limited to, 3-phenyl-2-propenyl, 2-phenylvinyl, and 4-phenyl-3-butenyl.

The term "arylalkyl" as used herein, means an aryl group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of arylalkyl include, but are not limited to, 2-phenylethyl,

- 25 3-phenylpropyl, and 2-naphth-2-ylethyl.

The term "arylcarbonyl" as used herein, means an aryl group, as defined herein, appended to the parent molecular moiety through a carbonyl group, as defined herein. Representative examples of arylcarbonyl include, but are not limited to, benzoyl, 2-chlorobenzoyl, 3-methylbenzoyl, 3,4-dichlorobenzoyl, and 2,4 difluorobenzoyl.

- 30 The term "arylhydroxyalkyl" as used herein, means an aryl group, as defined herein, appended to the parent molecular moiety through an hydroxyalkyl group, as defined herein. Representative examples of arylhydroxyalkyl include, but are not limited to, 2-hydroxy-2-phenylethyl, 2-hydroxy-3-phenylpropyl, and 3-hydroxy-3-phenylpropyl.

The term "carbonyl," as used herein, refers to a -C(O)- group.

- 35 The term "carboxy," as used herein, refers to a -CO₂H group.

The term "carboxyalkyl," as used herein, refers to a carboxy group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein.

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5 Representative examples of carboxyalkyl include, but are not limited to, carboxymethyl, 2-carboxyethyl, and 3-carboxypropyl.

The term "cyano," as used herein, refers to a -CN group.

The term "cyanoalkyl," as used herein, refers to a cyano group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein.

10 Representative examples of cyanoalkyl include, but are not limited to, cyanomethyl, 2-cyanoethyl, and 3-cyanopropyl.

The term "cycloalkyl" as used herein, means a saturated cyclic hydrocarbon group containing from 3 to 8 carbons. Examples of cycloalkyl include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl.

15 The cycloalkyl groups of this invention are substituted with 0, 1, 2 or 3 substituents independently selected from alkenyl, alkoxy, alkoxyalkoxy, alkoxyalkyl, alkoxycarbonyl, alkoxycarbonylalkyl, alkoxysulfonyl, alkyl, alkylcarbonyl, alkylcarbonylalkyl, alkylcarbonyloxy, alkylsulfinyl, alkylsulfonyl, alkylthio, alkylthioalkyl, alkynyl, carboxy, carboxyalkyl, cyano, cyanoalkyl, formyl, haloalkoxy, haloalkyl, halogen, hydroxy, hydroxyalkyl, mercapto, oxo, (NZ₁Z₂)alkyl, -NR_AR_B, (NR_AR_B)carbonyl and
20 (NR_AR_B)sulfonyl. Representative examples of cycloalkyl substituted with 0, 1, 2 or 3 substituents include, but are not limited to, 4-hydroxycyclohexyl and 2-hydroxycyclohexyl.

The term "ethylenedioxy," as used herein, refers to a -O(CH₂)₂O- group wherein the oxygen atoms of the ethylenedioxy group are attached to the parent molecular moiety
25 through one carbon atom forming a 5 membered ring or the oxygen atoms of the ethylenedioxy group are attached to the parent molecular moiety through two adjacent carbon atoms forming a six membered ring.

The term "formyl," as used herein, refers to a -C(O)H group.

The term "~~haloalkoxy~~ halogen," as used herein, refers to -Cl, -Br, -I or -F.

30 The term "haloalkoxy," as used herein, refers to at least one halogen, as defined herein, appended to the parent molecular moiety through an alkoxy group, as defined herein. Representative examples of haloalkoxy include, but are not limited to, chloromethoxy, 2-fluoroethoxy, trifluoromethoxy, and pentafluoroethoxy.

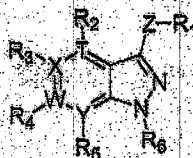
The term "haloalkyl," as used herein, refers to at least one halogen, as defined
35 herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of haloalkyl include, but are not limited to, chloromethyl, 2-fluoroethyl, trifluoromethyl, pentafluoroethyl, and 2-chloro-3-fluoropentyl.

5 The term "heterocycle" or "heterocyclic," as used herein, refers to a monocyclic, bicyclic, or tricyclic ring system. Monocyclic ring systems are exemplified by any 3- or 4-membered ring containing a heteroatom independently selected from oxygen, nitrogen and sulfur; or a 5-, 6- or 7-membered ring containing one, two or three heteroatoms wherein the heteroatoms are independently selected from nitrogen, oxygen and sulfur. The 5-membered
10 ring has from 0-2 double bonds and the 6- and 7-membered ring have from 0-3 double bonds. Representative examples of monocyclic ring systems include, but are not limited to, azetidiny, azepanyl, aziridinyl, diazepinyl, 1,3-dioxolanyl, dioxanyl, dithianyl, furyl, imidazolyl, imidazoliny, imidazolidinyl, isothiazolyl, isothiazolinyl, isothiazolidinyl, isoxazolyl, isoxazoliny, isoxazolidinyl, oxadiazolyl, oxadiazolinyl,
15 oxadiazolidinyl, oxazolyl, oxazolinyl, oxazolidinyl, piperazinyl, pyranyl, pyrazinyl, pyrazolyl, pyrazolinyl, pyrazolidinyl, pyrimidinyl, pyridazinyl, pyrrolinyl, pyrrolidinyl, tetrahydrofuranyl, tetrahydrothienyl, tetrazinyl, tetrazolyl, thiadiazolyl, thiadiazolinyl, thiadiazolidinyl, thiazolyl, thiazolinyl, thiazolidinyl, thienyl, thiomorpholinyl, 1,1-dioxidothiomorpholinyl (thiomorpholine sulfone), thiopyranyl,
20 triazinyl, triazolyl, and trithianyl. Bicyclic ring systems are exemplified by any of the above monocyclic ring systems fused to an aryl group as defined herein, a cycloalkyl group as defined herein, or another monocyclic ring system. Representative examples of bicyclic ring systems include but are not limited to, for example, benzimidazolyl, benzodioxinyl, benzothiazolyl, benzothienyl, benzotriazolyl, benzoxazolyl, benzofuranyl, benzopyranyl,
25 benzothiopyranyl, cinnolinyl, indazolyl, indolyl, 2,3-dihydroindolyl, indoliziny, naphthyridinyl, isobenzofuranyl, isobenzothienyl, isoindolyl, isoquinolinyl, phthalazinyl, pyranopyridinyl, quinolinyl, quinoliziny, quinoxaliny, quinazoliny, tetrahydroisoquinolinyl, tetrahydroquinolinyl, and thiopyranopyridinyl. Tricyclic rings systems are exemplified by any of the above bicyclic ring systems fused to an aryl group as
30 defined herein, a cycloalkyl group as defined herein, or a monocyclic ring system. Representative examples of tricyclic ring systems include, but are not limited to, acridinyl, carbazolyl, carbolinyl, dibenzo[b,d]furanyl, dibenzo[b,d]thienyl, naphtho[2,3-b]furan, naphtho[2,3-b]thienyl, phenazinyl, phenothiazinyl, phenoxazinyl, thianthrenyl, thioxanthenyl and xanthenyl.

35 The heterocycles of this invention are substituted with 0, 1, 2, or 3 substituents independently selected from alkenyl, alkoxy, alkoxyalkoxy, alkoxyalkyl, alkoxycarbonyl, alkoxycarbonylalkyl, alkoxysulfonyl, alkyl, alkylcarbonyl, alkylcarbonylalkyl,

5 What is claimed is:

1. A compound of formula (I)



(I),

or a pharmaceutically acceptable salt, ester, amide or prodrug thereof, wherein

10 T, X, W, and Y are independently selected from the group consisting of C and N provided that at most, only two of T, X, W, and Y can be nitrogen at the same time;

Z is selected from the group consisting of O, S and N(R₇);

R₁ is selected from the group consisting of aryl, arylalkenyl, arylalkyl, heterocycle, heterocyclealkenyl and heterocyclealkyl;

15 R₂ and R₄ are independently selected from the group consisting of hydrogen, alkenyl, alkoxy, alkoxycarbonyl, alkyl, alkylcarbonyl, alkylcarbonyloxy, alkylthio, alkynyl, carboxy, cyano, formyl, halogen, haloalkoxy, haloalkyl, hydroxy, hydroxyalkyl, mercapto, nitro, -NZ₁Z₂, (NZ₁Z₂)carbonyl and (NZ₁Z₂)sulfonyl wherein Z₁ and Z₂ are independently selected from the group consisting of hydrogen, alkyl, alkylcarbonyl and formyl;

20 R₃ and R₅ are independently absent or selected from the group consisting of hydrogen, alkenyl, alkoxy, alkoxycarbonyl, alkyl, alkylcarbonyl, alkylcarbonyloxy, alkylthio, alkynyl, carboxy, cyano, formyl, halogen, haloalkoxy, haloalkyl, hydroxy, hydroxyalkyl, mercapto, nitro, -NZ₁Z₂, (NZ₁Z₂)carbonyl and (NZ₁Z₂)sulfonyl wherein Z₁ and Z₂ are independently selected from the group consisting of hydrogen, alkyl,

25 alkylcarbonyl and formyl;

R₇ is selected from the group consisting of aryl, arylalkenyl, arylalkyl, heterocycle, heterocyclealkenyl and heterocyclealkyl; and

R₇ is selected from the group consisting of hydrogen and alkyl.

30 2. A compound according to claim 1 wherein

T, X, W, and Y are C;

Z is O;

R₁ is selected from the group consisting of aryl, arylalkyl and heterocycle; and

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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIRECCIÓN DE NUEVAS CREACIONES

2020
Bogotá, D.C.,

Abogado
CARLOS R. OLARTE
Apoderado

ASUNTO

Radicación 07-053834
Trámite 002
Evento 001
Actuación 430
Oficio **14792**
Folios 09

Patente de Invención ☒

Patente de Modelo de Utilidad ☐

Vía Nacional ☐

Vía PCT (fase nacional) ☒

Cap. I ☐

Cap. II ☒

No. Sol. Internacional

PCT/IB2005/003549

Fecha de Presentación Interna

17 de noviembre de 2005

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: 103 a 179 y 185 como se radicó inicialmente

Reivindicaciones:

Folios 180 a 184 como se radicó inicialmente

Prioridad:

Folios: 1

29/11/2004, US, 60/631,386

2. Análisis de la Prioridad

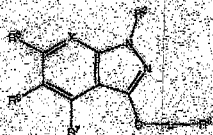
La fecha de prioridad del 29 de noviembre de 2004 y su correspondiente documento, corresponden con la materia solicitada de protección.

3. Objeto de la invención

Título de la solicitud: Pirazolo[3,4-b]piridinas e indazoles terapéuticos

El problema planteado en esta solicitud es la necesidad de obtener compuestos derivados pirazolo[3,4-b]piridinas e indazoles como inhibidores de serotonina y/o inhibidores de norepinefrina, útiles en el tratamiento de enfermedades que incluyen fibromialgia, ADHD, dolor neuropático, incontinencia urinaria, ansiedad, depresión, y esquizofrenia entre otros.

Para solucionar este problema técnico la solicitud en estudio, el solicitante proporciona el compuesto de fórmula I



IPC: A61K 31/4162, C07D 471/04

4. Excepción a la patentabilidad (artículo 20 D486 literal a)-d))

Las reivindicaciones 26 a 29, se refieren a métodos de tratamiento, los cuales no son patentables de acuerdo a los artículos mencionados de la normatividad vigente.

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

Las reivindicaciones 33 a 36, se refieren al uso de los compuestos, los cuales no son patentables de acuerdo a los artículos mencionados de la normatividad 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 la publicación en fase internacional: 29 de noviembre de 2004

Considerando que la fecha de presentación de la primera solicitud de patente de la cual se reivindica prioridad es: 29/11/2004 se encontraron los siguientes documentos del estado de la técnica relacionados, que pueden afectar la patentabilidad del objeto de la presente solicitud:

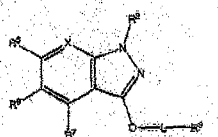
Nº	Documento	Título	Fecha de publicación
D1	WO 03/076408	Indazole derivatives that are activators of soluble guanylate cyclase	18/09/2003

7. Análisis de patentabilidad (artículo 14 D486)

Nivel inventivo (artículo 18 D486)

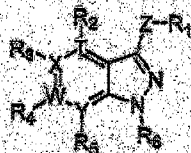
La reivindicación 1 consiste en:

Un compuesto de la fórmula I



O una de sus sales farmacéuticamente aceptables

El Estado de la Técnica más cercano es D1, que da a conocer compuestos derivados del indazol que son activadores de la ciclasa guanilato ciclasa. Las diferentes sustituciones que enseña D1, pueden ser que Z es oxígeno (Ver página 53, línea 12), R¹ es heterociclo, T, X, W y Y pueden ser seleccionados del grupo que consiste de C y N, donde a lo sumo, sólo dos de T, X, W y pueden ser nitrógeno al mismo tiempo (Ver página 53, líneas 10-11), R², R³, R⁴, R⁵ pueden ser hidrógeno, alcoxi y halógeno (Ver página 53, líneas 15-22), y R⁶ es seleccionado de arilo o heterociclo (Ver página 53, línea 26)



(D1)

D1

D1 además enseña que entre los ejemplos del término alcoxi se encuentra metoxi (Ver página 8, líneas 14-16); entre los de alquilo se encuentra metilo, etilo, n-propilo entre otros (Ver página 8, líneas 7-12), entre los de arilo se encuentra fenilo y el arilo puede estar sustituido con 0,1,2,3,4 o sustituyentes seleccionados ente alcoxi, alquilo y halógeno (Ver página 9, líneas 15,24-28); entre los de halógeno se encuentran -Cl, -Br, -I o -F (Ver página 11, línea 29); entre los heterociclos se encuentran morfolinil, piperidinil, piridinil y pirrolidil entre otros (Ver página 12, líneas 5,14-17)

Los compuestos objeto de esta solicitud se diferencian de los compuestos de D1, en que los sustituyentes como arilo o heteroarilo se encuentran explícitamente como fenilo, piridinilo, morfonilo, pirrolidino y piperidino y que se encuentra adicionalmente, el sustituyente L. D1, sin embargo ya sugería los sustituyentes tanto para arilo como para heteroarilo, como se mencionó anteriormente.

El hecho de incluir estas diferentes sustituciones en los compuestos que se daban a conocer en D1, causa que se obtengan compuestos útiles en enfermedades que incluyen fibromialgia, ADHD, dolor neuropático, incontinencia urinaria, ansiedad, depresión, y esquizofrenia entre otros.

Sin embargo, esta diferencia no parece conceder un efecto técnico superior ni inesperado a los compuestos de la solicitud presentada, puesto que los compuestos de D1, también son útiles en los desórdenes del SNC, los cuales incluyen ansiedad, depresión, y dolor entre otros, al igual que los compuestos de la solicitud presentada (Ver página 1). Además, no se evidencia en los resultados de actividad para los compuestos objeto de invención, los cuales se encuentran sugeridos en D1, que no actúan como activadores de guanilato ciclasa.

El Problema Técnico Objetivo era obtener compuestos derivados de indazol útiles para el tratamiento de enfermedades que incluyen fibromialgia, ADHD, dolor neuropático, incontinencia urinaria, ansiedad, depresión y esquizofrenia entre otros.

La reivindicación es obvia, porque el Experto en la Materia enfrentado al problema de obtener "compuestos derivados de indazol útiles para el tratamiento de enfermedades que incluyen fibromialgia, ADHD, dolor neuropático, incontinencia urinaria, ansiedad, depresión y esquizofrenia entre otros", realizaría los reemplazos que se revelan en D1, logrando de esta forma los compuestos objeto de esta solicitud. Por tanto, la reivindicación 1 no tiene Nivel Inventivo. Las reivindicaciones dependientes 2-25 y 30-32, no menciona alguna característica que haga inventivos a los compuestos de la reivindicación 1, por lo cual se considera que no tienen nivel inventivo.

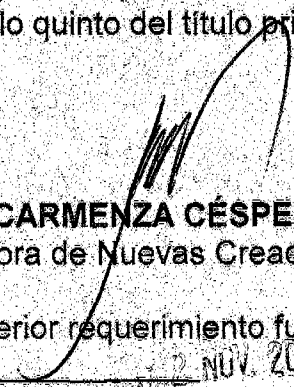
8. Conclusión:

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

N°	Documento N°	Reivindicaciones afectadas	Requisito que afecta
D1.	WO 03/076408	1-25, 30-32	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 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

2 NOV. 2010

CONCEPTO TÉCNICO No. 03344	EXAMINADOR TÉCNICO Código No. 202070
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