

PARRA, RODRIGUEZ & CAVELIER

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Bogotá, D.C., 27 de Julio de 2005

SUPERINDUSTRIA Y COMERCIO

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Dependencia: 2020 DIVISION DE NUEVAS CREACIONES

Señora Jefe
División de Nuevas Creaciones
Superintendencia de Industria y Comercio
E. S. D.

Patente: INHIBIDORES HETEROCICLICOS DE ERK2 Y USO DE
LOS MISMOS

Solicitante: VERTEX PHARMACEUTICALS INCORPORATED

Expediente: 03.067.869

De conformidad con lo dispuesto por el Artículo 44 de la Decisión 486, me permito solicitar a usted que se examine si la invención de la referencia es patentable.

Para tal efecto, acompaño el comprobante de pago de la tasa correspondiente a la realización del examen. \$ 56 455 L 201.28/05 \$186.0002

De la Señora Jefe,

Ernesto Cavelier

Ernesto Cavelier Franco
C.C. 19.081.620
T.P. 11519

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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

NIT : 800176089-2

SUPERINDUSTRIA Y COMERCIO

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Fecha (HH): 2005-07-28 16:23:22
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Dependencia: 3820 DIVISION DE NUEVAS CREACIONES

RECIBO OFICIAL DE CAJA : 05 - 56,435
FECHA : JULIO 28 DE 2005

***** CONSIGNACION *****

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PGO	Vr. PAGO
PARRA RODRIGUEZ & CAVELIE	CONSIGNACION	BANCO POPULAR	050-00110-6	41522121	28/07/2005	607,000.00

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

CANT.	RENTISTICO	CONCEPTO	TOTAL CONCEPTO
1	50005-01-01	SOLICITUDES	114 PTC CAP-II EXAMEN DE PATENTIBILIDAD
			TOTAL : \$ 186,000.00

SON: CIENTO OCHENTA Y SEIS MIL PESOS

RESPONSABLE : 

RECIBO DE CAJA APLICADO AL EXPEDIENTE No. _____

DIVISION DE NUEVAS CREACIONES

RADICACIÓN EXPEDIENTE No. 03- 67889

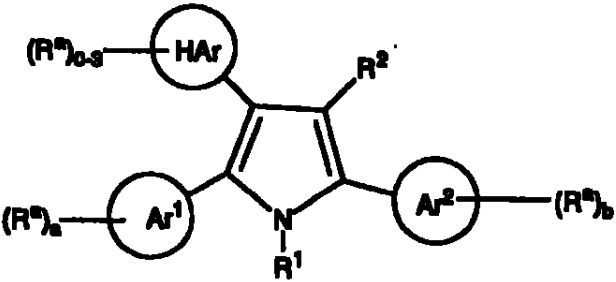
**EL EXTRACTO DE LA PRESENTE SOLICITUD DE PATENTE DE INVENCION –
PCT, FUE PUBLICADO EN LA GACETA DE PROPIEDAD INDUSTRIAL No 548,
DE FECHA 28 DE ENERO DE 2005, EL TERMINO HABIL SEÑALADO POR LA
LEY EXPIRA EL 27 DE ABRIL DE 2005.**

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**

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

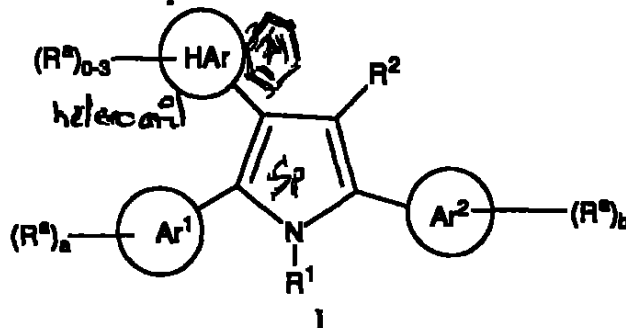
(51) International Patent Classification ⁶ : A61K 31/44, 31/50, 31/445, 31/495, 31/505, 31/535, C07D 211/68, 211/80, 213/02, 239/02, 401/00, 401/04, 471/02, 473/00	A1	(11) International Publication Number: WO 97/05878 (43) International Publication Date: 20 February 1997 (20.02.97)
(21) International Application Number: PCT/US96/12922 (22) International Filing Date: 6 August 1996 (06.08.96) (30) Priority Data: 60002094 10 August 1995 (10.08.95) US 60014182 26 March 1996 (26.03.96) US 96072533 4 April 1996 (04.04.96) GB 96084728 25 April 1996 (25.04.96) GB (71) Applicant (for all designated States except US): MERCK & CO., INC. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). (72) Inventors; and (73) Inventors/Applicants (for US only): DE LASZLO, Stephen, E. [GB/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). MANTLO, Nathan, B. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). PONTICELLO, Gerald, S. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). SELNICK, Harold, G. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). LIVERTON, Nigel, J. [GB/US]; 126 East Lincoln Avenue, Rahway, NJ 07065 (US).	(74) Common Representative: MERCK & CO., INC.; 126 East Lincoln Avenue, Rahway, NJ 07065 (US). (81) Designated States: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CU, CZ, DE, EE, HU, IL, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published With international search report.	
(54) Title: 2,5-SUBSTITUTED ARYL PYRROLES, COMPOSITIONS CONTAINING SUCH COMPOUNDS AND METHODS OF USE  (I) (57) Abstract The present invention addresses 2,5-substituted aryl pyrroles of formula (I); or pharmaceutically acceptable salts thereof, as well as compositions containing such compounds and methods of treatment. The compounds are useful for treating Cytokine mediated diseases, which refers to diseases or conditions in which excessive or unregulated production or activity of one or more cytokines occurs. Interleukin-1 (IL-1), Interleukin-6 (IL-6), Interleukin-8 (IL-8) and Tumor Necrosis Factor (TNF) are cytokines which are involved in immunoregulation and other physiological conditions, such as inflammation. The compounds also have glucagon antagonist activity.		

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WHAT IS CLAIMED IS:

1. A compound of the formula:



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or a pharmaceutically acceptable salt thereof, wherein:



and each independently represent a 5-10 membered aryl or heteroaryl group substituted with R^a groups;

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wherein a and b represents integers, 0, 1, 2 or 3, such that the sum of a plus b is 1, 2, 3 or 4;



- represents a heteroaryl group containing from 5 to 10 atoms, 1-4 of which are heteroatoms, 0-4 of which heteroatoms are N and 0-1 of which are O or S, said heteroaryl group being unsubstituted or substituted with 0-3 R^a groups; each R^a independently represents a member selected from the group consisting of: halo; CN, NO_2 , R^{21} ; OR^{23} ; SR^{23} ; $S(O)R^{21}$; SO_2R^{21} ; $NR^{20}R^{23}$; $NR^{20}COR^{21}$; $NR^{20}CO_2R^{21}$; $NR^{20}CONR^{20}R^{23}$; $NR^{20}SO_2R^{21}$; $NR^{20}C(NR^{20})NHR^{20}$; CO_2R^{23} ; $CONR^{20}R^{23}$; $SO_2NR^{20}R^{23}$; $SO_2NR^{20}COR^{21}$; $SO_2NR^{20}CONR^{20}R^{23}$; $SO_2NR^{20}CO_2R^{21}$; $OCONR^{20}R^{23}$; $OCONR^{20}SO_2R^{20}$; $C(O)OCH_2OC(O)R^{20}$; $C(NR^{20})NR^{20}R^{23}$ and $CONR^{20}SO_2R^{21}$;

25

R^1 is selected from the group consisting of: H, aryl, C_{1-15} alkyl, C_{3-15} alkenyl, C_{3-15} alkynyl and heterocyclyl, said alkyl, aryl, alkenyl, alkynyl and heterocyclyl being optionally substituted with from one

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- to three members selected from the group consisting of: aryl, heteroaryl, heterocyclyl, OR²⁰, SR²⁰, N(R²⁰)₂, S(O)R²¹, SO₂R²¹, SO₂NR²⁰R²³, SO₂NR²⁰COR²¹, SO₂NR²⁰CONR²⁰R²³, NR²⁰COR²¹, NR²⁰CO₂R²¹, NR²⁰CONR²⁰R²³, N(R²⁰)C(NR²⁰)NHR²⁰, CO₂R²⁰, CONR²⁰R²³,
 5 CONR²⁰SO₂R²¹, NR²⁰SO₂R²¹, SO₂NR²⁰CO₂R²¹, OCONR²⁰R²³, OCONR²⁰SO₂R²¹; OCONR²⁰R²³ and C(O)OCH₂OC(O)R²⁰;

- R² is selected from the group consisting of: H, C₁₋₁₅ alkyl, C₂₋₁₅ alkenyl, C₂₋₁₅ alkynyl, halo, NO₂, heterocyclyl, CN, S(O)R²¹,
 10 SO₂R²¹, SO₂N(R²⁰)₂, SO₂NR²⁰COR²¹, SO₂NR²⁰CON(R²⁰)₂, COR²⁰, CO₂R²⁰, CONR²⁰R²³, CONR²⁰SO₂R²¹ and SO₂NR²⁰CO₂R²¹, said alkyl, alkenyl, alkynyl and heterocyclyl being optionally substituted with from one to three members selected from the group consisting of: halo, heterocyclyl, CN, aryl, heteroaryl, R²⁰, OR²⁰, SR²⁰, NR²⁰R²³, S(O)R²¹, SO₂R²¹,
 15 SO₂NR²⁰R²³, SO₂NR²⁰COR²¹, SO₂NR²⁰CONR²⁰R²³, NR²⁰COR²¹, NR²⁰CO₂R²¹, NR²⁰CONR²⁰R²³, NR²⁰C(NR²⁰)NHR²⁰, CO₂R²⁰, CONR²⁰R²³, CONR²⁰SO₂R²², NR²⁰SO₂R²¹, SO₂NR²⁰CO₂R²², OCONR²⁰SO₂R²¹ and OCONR²⁰R²³;

- 20 R²⁰ represents a member selected from the group consisting of: H, C₁₋₁₅ alkyl, C₂₋₁₅ alkenyl, C₂₋₁₅ alkynyl, heterocyclyl, aryl and heteroaryl, said alkyl, alkenyl, alkynyl, heterocyclyl, aryl and heteroaryl being optionally substituted with 1-3 groups selected from halo, aryl and heteroaryl;

- 25 R²¹ represents a member selected from the group consisting of: C₁₋₁₅ alkyl, C₂₋₁₅ alkenyl, C₂₋₁₅ alkynyl, heterocyclyl, aryl and heteroaryl, such alkyl, alkenyl and alkynyl being optionally interrupted with oxo and/or 1-2 heteroatoms selected from O, S, S(O), SO₂ and NR²⁰, said alkyl, alkenyl, alkynyl, aryl and heteroaryl being optionally substituted with from 1-3 of halo, heterocyclyl, aryl, heteroaryl, CN, OR²⁰, O((CH₂)_nO)_mR²⁰, NR²⁰((CH₂)_nO)_mR²⁰ wherein n represents an integer of from 2 to 4, and m represents an integer of from 1 to 3; SR²⁰, N(R²⁰)₂, S(O)R²², SO₂R²², SO₂N(R²⁰)₂, SO₂NR²⁰COR²², SO₂NR²⁰CON(R²⁰)₂, NR²⁰COR²²,
 30 NR²⁰CO₂R²², NR²⁰CON(R²⁰)₂, NR²²C(NR²²)NHR²², CO₂R²⁰,

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CON(R²⁰)₂, CONR²⁰SO₂R²², NR²⁰SO₂R²², SO₂NR²⁰CO₂R²²,
OCONR²⁰SO₂R²²OC(O)R²⁰, C(O)OCH₂OC(O)R²⁰ and OCON(R²⁰)₂;

5 R²² is selected from the group consisting of: C₁₋₁₅ alkyl, C₂₋₁₅ alkenyl, C₂₋₁₅ alkynyl, heterocyclyl, aryl and heteroaryl, said alkyl, alkenyl, and alkynyl being optionally substituted with 1-3 halo, aryl or heteroaryl groups;

10 R²³ is R²¹ or H;

R²⁴ is selected from COR²², CO₂R²², CON(R²⁰)₂, SO₂R²² and R²³;

15 and when two R²⁰ groups are present, when R²⁰ and R²¹ are present, or when R²¹ and R²³ are present, said two R²⁰ groups, R²⁰ and R²¹ or said R²⁰ and R²³ may be taken in combination with the atoms to which they are attached and any intervening atoms and represent heterocyclyl containing from 5-10 atoms, at least one atom of which is a heteroatom selected from O, S or N, said heterocyclyl optionally containing 1-3 additional N atoms and 0-1 additional O or S atom.

20

2. A compound in accordance with claim 1 wherein:
Ar¹ and Ar² are independently and selected from the group consisting of:

- 25 a) phenyl,
b) pyridyl,
c) pyrimidinyl,
d) thiophenyl,
e) furanyl,
f) imidazolyl,
g) thiazolyl,
30 h) isothiazolyl,
i) oxazolyl,
j) isoxazolyl, and
k) naphthyl.

35 3. A compound in accordance with claim 1 wherein
HAr is selected from the group of consisting of:

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- 5
- a) pyridyl,
 - b) quinolyl,
 - c) purinyl,
 - d) imidazolyl,
 - e) imidazopyridyl,
 - f) pyrimidinyl and
 - g) pyridazinyl.
- 10 4. A compound in accordance with claim 1 wherein R¹ is hydrogen.
- 5 A compound in accordance with claim 1 wherein R¹ is substituted or unsubstituted C₁₋₁₅ alkyl.
- 15 6. A compound in accordance with claim 1 wherein R² represents a member selected from the group consisting of:
- a) H;
 - b) C₁₋₆ alkyl;
 - c) halo;
 - 20 d) CN;
 - e) C(O)C₁₋₆ alkyl;
 - f) C(O)C₁₋₆ alkylphenyl;
 - g) CO₂H;
 - h) CO₂C₁₋₆ alkyl
 - 25 i) CO₂C₁₋₆ alkylphenyl;
 - j) CONH₂;
 - k) CONHC₁₋₆ alkyl;
 - l) C(O)N(C₁₋₆ alkyl)₂;
 - m) SO₂NH₂;
 - 30 n) SO₂NHC₁₋₆ alkyl and
 - o) SO₂N(C₁₋₆ alkyl)₂.
7. A compound in accordance with claim 1 wherein: Ar¹ and Ar² are independently selected from:
- 35 a) phenyl,
 - b) pyridyl,

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- 5 c) pyrimidinyl,
 d) thiophenyl,
 e) furanyl,
 f) imidazolyl,
 g) thiazolyl,
 h) isothiazolyl,
 i) oxazolyl,
 j) isoxazolyl and
 k) naphthyl;
- 10 one, two or three R^a groups are present and attached to Ar¹
and Ar², and each R^a is independently selected from the group consisting
of: halo, R²¹, OR²³, NR²⁰R²³, CO₂R²³, CONR²⁰R²³, SO₂R²¹ and
S(O)R²¹, R²⁰, R²¹ and R²³ are as originally defined;
- 15 HAr is selected from:
- a) pyridyl,
 b) quinolyl,
 c) purinyl,
 d) imidazolyl,
20 e) imidazopyridyl,
 f) pyrimidinyl and
 g) pyridazinyl;
- R¹ is: a) H or
25 b) substituted or unsubstituted alkyl; and
- R² is selected from the group consisting of:
- a) H,
 b) alkyl,
30 c) halo,
 d) CN,
 e) C(O)C₁₋₆ alkyl,
 f) C(O)C₁₋₆ alkylphenyl,
 g) CO₂H,
35 h) CO₂C₁₋₆ alkyl,
 i) CO₂C₁₋₆ alkylphenyl,

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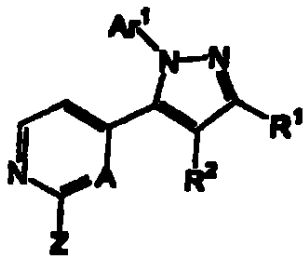
H	Ph	4-(CONH(CH ₂) ₂ - (2-pyridyl))-Ph	4-pyr	H
H	Ph	4-(CONHCH ₂ - (3-pyridyl))-Ph	4-pyr	H
H	Ph	3-(NHCO(CH ₂) 3NMe ₂)-Ph	4-pyr	H
H	Ph	4-(NHCO(CH ₂) ₂ - (1-piperidyl))-Ph	4-pyr	H
H	2-Cl-Ph	Ph	4-pyr	H
H	3-Cl-Ph	4-SMe-Ph	4-pyr	H
H	4-F-Ph	Ph	4-pyrimidinyl	F
H	4-F-Ph	4-SMe-Ph	4-(2-methyl)-pyr	H
H	3-Cl-Ph	4-S(O)Me-Ph	4-pyr	H
H	4-F-Ph	4-S(O)Me-Ph	4-(2-methyl)-pyr	H
H	3,4-di-F-Ph	4-SMe-Ph	4-pyr	H
H	3,4-di-F-Ph	4-S(O)Me-Ph	4-Pyr	H
H	4-F-Ph	4-SO ₂ Me-Ph	4-pyr	H
H	3,4-di-F-Ph	Ph	4-pyr	CO ₂ Et
H	3,4-di-F-Ph	Ph	4-pyr	CN
H	3-CF ₃ -Ph	Ph	4-pyr	CO ₂ Et
H	3-CF ₃ -Ph	Ph	4-pyr	CN
H	3-Cl-Ph	4-SO ₂ Me-Ph	4-pyr	H

21. A method of treating a cytokine mediated disease in a mammal in need of such treatment, which comprises administering to said mammal an effective cytokine interfering amount of a compound of claim 1.
22. The method according to claim 21 wherein the cytokine inhibited is IL-1.
23. The method according to claim 21 wherein the cytokine inhibited is IL-6.
24. The method according to claim 21 wherein the cytokine inhibited is TNF.

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WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C07D 401/04, 401/14, 403/04, A61K 31/44, 31/505		A1	(11) International Publication Number: WO 99/58523 (43) International Publication Date: 18 November 1999 (18.11.99)
(21) International Application Number: PCT/US99/07036 (22) International Filing Date: 12 May 1999 (12.05.99) (30) Priority Data: 60/085,494 14 May 1998 (14.05.98) US (71) Applicant (for all designated States except US): G.D. SEARLE & CO. [US/US]; Corporate Patent Dept., P.O. Box 5110, Chicago, IL 60680-5110 (US). (72) Inventors; and (73) Inventors/Applicants (for US only): WHEER, Richard, M. [US/US]; 240 Hickory Court, Lake Bluff, IL 60044 (US). COLLINS, Paul, W. [US/US]; 1357 Hawthorne Place, Deerfield, IL 60015 (US). XU, Xiangdong [CN/US]; Apartment 715, 855 Hinman Avenue, Evanston, IL 60202 (US). CRECH, Joyce, Z. [US/US]; 1301 Topp Lane, Glenview, IL 60025 (US). RAO, Shashidhar, N. [IN/US]; 736 Balkovic Manor Drive, St. Louis, MO 63141 (US). (74) Agents: SCRIVNER, Alan, L. et al.; G.D. Searle & Co., Corporate Patent Dept., P.O. Box 5110, Chicago, IL 60680-5110 (US).		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GR, GM, HR, HU, ID, IL, IN, JP, KR, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, EE, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.	
(54) Title: 1,5-DIARYL SUBSTITUTED PYRAZOLES AS p38 KINASE INHIBITORS			
(57) Abstract The present invention contemplates 1,5-diaryl-substituted pyrazole compounds which correspond in structure to Formula (I), or a pharmaceutically-acceptable salt thereof; wherein A is -N- or -CH-; and which inter alia, inhibit the activity of p38 MAP kinase. Also contemplated by the invention are processes for the preparation of the contemplated compounds and for the use of a contemplated compound in treating a mammalian host having a p38 kinase- or TNF-mediated disease.			
 (I)			

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1,5-DIARYL SUBSTITUTED PYRAZOLES
AS p38 KINASE INHIBITORS

Description

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Technical Field

This invention is directed to kinases inhibitors, and more particularly to 1,5-diaryl substituted pyrazole compounds that, *inter alia*,
10 inhibit the activity of mitogen-activated protein kinases, compositions of those inhibitors, intermediates for the syntheses of those compounds, and processes for treating pathological mitogen-activated protein kinase activity.

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Background of the Invention

Mitogen-activated protein (MAP) kinases are a family of proline-directed serine/threonine kinases that activate their substrates by dual
20 phosphorylation. The kinases are activated by a variety of signals including nutritional and osmotic stress, UV light, growth factors, endotoxin and inflammatory cytokines.

The p38 MAP kinase group is a MAP family of
25 various isoforms, including p38 α , p38 β and p38 γ , and is responsible for phosphorylating and activating transcription factors (e.g. ATF2, CHOP and MEF2C) as well as other kinases (e.g. MAPKAP-2 and MAPKAP-3). The p38 isoforms are activated by
30 bacterial lipopolysaccharide, physical and chemical stress and by pro-inflammatory cytokines, including tumor necrosis factor alpha (TNF- α) and interleukin-1 (IL-1). The products of the p38 phosphorylation mediate the production of
35 inflammatory cytokines, including TNF and IL-1, and cyclooxygenase-2.

TNF- α is a cytokine produced primarily by activated monocytes and macrophages. Excessive or unregulated TNF production has been implicated in mediating a number of diseases. Recent studies
5 indicate that TNF has a causative role in the pathogenesis of rheumatoid arthritis. Additional studies demonstrate that inhibition of TNF has broad application in the treatment of inflammation,^{f34}
inflammatory bowel disease, multiple sclerosis and
10 asthma.^{f34} ^{f43} ^{f37}

TNF has also been implicated in viral infections, such as HIV, influenza virus, and herpes virus including herpes simplex virus type-1 (HSV-1), herpes simplex virus type-2 (HSV-2),
15 cytomegalovirus (CMV), varicella-zoster virus (VZV), Epstein-Barr virus, human herpesvirus-6 (HHV-6), human herpesvirus-7 (HHV-7), human herpesvirus-8 (HHV-8), pseudorabies and rhinotracheitis, among others.

20 IL-8 is another pro-inflammatory cytokine, which is produced by mononuclear cells, fibroblasts, endothelial cells, and keratinocytes, and is associated with conditions including inflammation.

25 IL-1 is produced by activated monocytes and macrophages and is also involved in the inflammatory response. IL-1 plays a role in many pathophysiological responses including rheumatoid arthritis, fever and reduction of bone resorption.

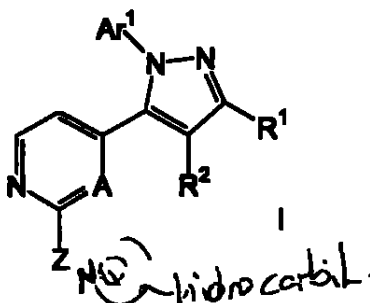
30 TNF, IL-1 and IL-8 affect a wide variety of cells and tissues and are important inflammatory mediators of a wide variety of disease states and conditions. The inhibition of these cytokines by inhibition of the p38 kinase is of benefit in
35 controlling, reducing and alleviating many of these disease states.

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What is claimed:

1. A compound that corresponds in structure to Formula I, or a pharmaceutically-acceptable salt thereof:



wherein A is =N- or =CH-;

- 10 Ar¹ is an aryl group that is optionally substituted by one or more substituents selected from the group consisting of a halogen, hydrocarbyl, hydrocarbyloxy, nitro, cyano, perfluorohydrocarbyl, trifluoromethylhydrocarbyl, perfluorohydrocarbyloxy, 15 hydroxy, mercapto, hydroxycarbonyl, aryloxy, arylthio, sulfonyl or sulfoxido, wherein the substituent on the sulfur atom is hydrocarbyl, sulfonamide,

- wherein the substituents on the sulfonamido 20 nitrogen atom are hydrido or hydrocarbyl, arylamino, arylhydrocarbyl, aryl, heteroaryloxy, heteroarylthio, heteroarylamino, heteroarylhydrocarbyl, hydrocarbyloxycarbonylhydrocarbyl, heterocycloxy, hydroxycarbonylhydrocarbyl, heterocyclothio, 25 heterocycloamino, cyclohydrocarbyloxy, cyclohydrocarbylthio, heteroarylhydrocarbyloxy, heteroarylhydrocarbylthio, heteroarylhydrocarbylamino, arylhydrocarbyloxy, arylhydrocarbylthio, arylhydrocarbylamino, 30 heterocyclic, heteroaryl, hydroxycarbonylhydrocarbyloxy, hydrocarbyloxycarbonylhydrocarbyloxy,

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- hydrocarbyloyl, arylcarbonyl, arylhydrocarbyloyl,
hydrocarboyloxy, arylhydrocarboyloxy,
hydroxyhydrocarbyl, hydroxyhydrocarbyloxy,
hydrocarbylthio, hydrocarbyloxyhydrocarbylthio,
5 hydrocarbyloxycarbonyl, hydroxycarbonyl-
hydrocarbyloxy, hydrocarbyloxycarbonylhydrocarbyl,
hydrocarbylhydroxycarbonylhydrocarbylthio,
hydrocarbyloxycarbonylhydrocarbyloxy,
hydrocarbyloxycarbonylhydrocarbylthio,
10 hydrocarbylcarbonylamino, arylcarbonylamino,
cyclohydrocarbylcarbonylamino, heterocyclo-
hydrocarbylcarbonylamino, arylhydrocarbyl-
carbonylamino, heteroarylcarbonylamino,
heteroarylhydrocarbylcarbonylamino,
15 heterocyclohydrocarbyloxy, hydrocarbylsulfonylamino,
arylsulfonylamino, arylhydrocarbylsulfonylamino,
heteroarylsulfonylamino, heteroarylhydrocarbyl-
sulfonylamino, cyclohydrocarbylsulfonylamino,
heterocyclohydrocarbylsulfonylamino, N-
20 monosubstituted or N,N-disubstituted aminohydrocarbyl
group,
wherein the substituent(s) on the amino-
hydrocarbyl nitrogen atom are selected from the
group consisting of hydrocarbyl, aryl;
25 arylhydrocarbyl, cyclohydrocarbyl,
arylhydrocarbyloxycarbonyl,
hydrocarbyloxycarbonyl, and hydrocarboyl, or
wherein the aminohydrocarbyl nitrogen and two
substituents attached thereto form a 5- to 8-
30 membered heterocyclic or heteroaryl ring group,
amino, and a N-monosubstituted or N,N-disubstituted
amino group,
wherein the substituent(s) on the amino
nitrogen are selected from the group consisting of
35 hydrido, hydrocarbyl, aryl, arylhydrocarbyl,
cyclohydrocarbyl, arylhydrocarbyloxycarbonyl,
hydrocarbyloxycarbonyl, hydrocarboyl,

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arylsulfonyl, and hydrocarbylsulfonyl or wherein the amino nitrogen and two substituents attached thereto form a 5- to 8-membered heterocyclic or heteroaryl ring group;

5 Z is independently selected from the group consisting of hydrido, hydrocarbyl, halogen, carboxy, cyano, azido, hydrocarbylsulfonyl, carbonyloxyhydrocarbyl, carbonylamido, and -X-Y wherein

10 -X is -O, -S or -NQ,
 -Y is hydrido, hydrocarbyl or hydrocarbylaryl,
 Q is hydrido, hydrocarbyl,
 hydroxylhydrocarbyl,
15 2-, 3-, or 4-pyridylhydrocarbyl, or arylhydrocarbyl;

 R¹ is independently selected from the group consisting of an azido, hydrido, hydrocarbyl, amido, hydrocarbylamino, halohydrocarbyl, perhalohydrocarbyl
20 and an aryl substituent that is optionally substituted by one or more substituents selected from the group consisting of a halogen, hydrocarbyl, hydrocarbyloxy, nitro, cyano, perfluorohydrocarbyl, trifluoromethylhydrocarbyl, hydroxy, mercapto,
25 hydroxycarbonyl, aryloxy, arylthio, arylamino, arylhydrocarbyl, aryl, heteroaryloxy, heteroarylthio, heteroarylamino, heteroarylhydrocarbyl, hydrocarbyloxycarbonylhydrocarbyl, heterocyclooxy, hydroxycarbonylhydrocarbyl, heterocyclothio,
30 heterocycloamino, cyclohydrocarbyloxy, cyclohydrocarbylthio, cyclohydrocarbylamino, heteroarylhydrocarbyloxy, heteroarylhydrocarbylthio, heteroarylhydrocarbylamino, arylhydrocarbyloxy, arylhydrocarbylthio, arylhydrocarbylamino,
35 heterocyclic, heteroaryl, hydroxycarbonylhydrocarbyloxy, alkoxycarbonylalkoxy, hydrocarbyloyl, arylcarbonyl, arylhydrocarbyloyl, hydrocarbyloxy,

- arylhydrocarbyloxy, hydroxyhydrocarbyl,
hydroxyhydrocarbyloxy, hydrocarbylthio,
hydrocarbyloxyhydrocarbylthio,
hydrocarbyloxycarbonyl, hydroxycarbonyl-
5 hydrocarbyloxy, hydrocarbyloxycarbonylhydrocarbyl,
hydrocarbylhydroxycarbonylhydrocarbylthio,
hydrocarbyloxycarbonylhydrocarbyloxy,
hydrocarbyloxycarbonylhydrocarbylthio, amino,
hydrocarbylcarbonylamino, arylcarbonylamino,
10 cyclohydrocarbylcarbonylamino,
heterocyclohydrocarbylcarbonylamino,
arylhydrocarbylcarbonylamino, heteroaryl-
carbonylamino, heteroarylhydrocarbylcarbonylamino,
heterocyclohydrocarbyloxy, hydrocarbylsulfonylamino,
15 arylsulfonylamino, arylhydrocarbylsulfonylamino,
heteroarylsulfonylamino, heteroarylhydrocarbyl-
sulfonylamino, cyclohydrocarbylsulfonylamino,
heterocyclohydrocarbylsulfonylamino and N-
monosubstituted or N,N-disubstituted aminohydrocarbyl
20 group,
wherein the substituent(s) on the amino-
hydrocarbyl nitrogen atom are selected from the group
consisting of hydrocarbyl, aryl, arylhydrocarbyl,
cyclohydrocarbyl, arylhydrocarbyloxycarbonyl,
25 hydrocarbyloxycarbonyl, and hydrocarboyl, or wherein
the aminohydrocarbyl nitrogen and two substituents
attached thereto form a 5- to 8-membered heterocyclic
or heteroaryl ring group; and
R² is independently selected from the group
30 consisting of an azido, hydrido, hydrocarbyl, amido,
halohydrocarbyl, perhalohydrocarbyl,
hydrocarbyloxycarbonyl, N-piperazinylcarbonyl,
aminocarbonyl, piperazinyl and an aryl group that is
substituted by one or more substituents, said one or
35 more substituents being selected from the group
consisting of a halogen, hydrocarbyl, hydrocarbyloxy,
nitro, cyano, perfluorohydrocarbyl,

- trifluoromethylhydrocarbyl, hydroxy, mercapto, hydroxycarbonyl, aryloxy, arylthio, arylamino, arylhydrocarbyl, aryl, heteroaryloxy, heteroarylthio, heteroarylamino, heteroarylhydrocarbyl,
- 5 hydrocarbyloxycarbonyl-hydrocarbyl, heterocyclooxy, hydroxycarbonyl-hydrocarbyl, heterocyclothio, heterocycloamino, cyclohydrocarbyloxy, cyclohydrocarbylthio, cyclohydrocarbylamino, heteroarylhydrocarbyloxy, heteroarylhydrocarbylthio,
- 10 heteroarylhydrocarby-amino, arylhydrocarbyloxy, arylhydrocarbylthio, arylhydrocarbylamino, heterocyclic, heteroaryl, hydroxycarbonyl-hydrocarbyloxy, alkoxycarbonylalkoxy, hydrocarbyloyl, arylcarbonyl, arylhydrocarbyloyl, hydrocarboxyloxy,
- 15 arylhydrocarboxyloxy, hydroxyhydrocarbyl, hydroxyhydrocarbyloxy, hydrocarbylthio, hydrocarbyloxyhydrocarbylthio, hydrocarbyloxycarbonyl, hydroxycarbonylhydrocarbyloxy, hydrocarbyloxycarbonylhydrocarbyl,
- 20 hydrocarbylhydroxycarbonylhydrocarbylthio, hydrocarbyloxycarbonylhydrocarbyloxy, hydrocarbyloxycarbonylhydrocarbylthio, amino, hydrocarbylcarbonylamino, arylcarbonylamino, cyclohydrocarbylcarbonylamino, heterocyclo-
- 25 hydrocarbylcarbonylamino, arylhydrocarbylcarbonyl-amino, heteroarylcarbonylamino, heteroarylhydrocarbylcarbonylamino, heterocyclohydrocarbyloxy, hydrocarbylsulfonylamino, arylsulfonylamino, arylhydrocarbylsulfonylamino, heteroaryl-
- 30 sulfonylamino, heteroarylhydrocarbylsulfonylamino, cyclohydrocarbylsulfonylamino, heterocyclohydrocarbylsulfonylamino and N-monosubstituted or N,N-disubstituted aminohydrocarbyl group,
- wherein the substituent(s) on the
- 35 aminohydrocarbyl nitrogen are selected from the group consisting of hydrocarbyl, aryl, arylhydrocarbyl, cyclohydrocarbyl, arylhydrocarbyloxycarbonyl,

hydrocarbyloxycarbonyl, and hydrocarboyl, or wherein the aminohydrocarbyl nitrogen and two substituents attached thereto form a 5- to 8-membered heterocyclic or heteroaryl ring group; and

5 provided that when A is =CH- and Z is hydrido, hydrocarbyl, halogen, or hydrocarboyl:

1) Ar¹ is other than an aryl group that is substituted by one or more substituents selected from the group consisting of a hydrido, halogen,
10 hydrocarbyl, perfluorohydrocarbyloxy, nitro, perfluorohydrocarbyl, amino, aminosulfonyl, halohydrocarbyloxyhydrocarbyl, hydroxy, hydrocarbylsulfonylamino, hydrocarbylsulfonyl, acetylamino, carbonylhydrocarbylamino,
15 perfluorohydrocarbylsulfonyl, hydrocarbylamino, carbonyl monosubstituted amino, carbonyl, hydrocarbylthio, hydroxyhydrocarbyl, arylhydrocarbyl, hydrocarbyloxyhydrocarbyl, hydrocarbyloxycarbonyl, hydrocarbyloxyarylhydrocarbyl, halohydrocarbyloxy,
20 hydrocarbyloxyhydrocarbyl; or

2) R¹ is other than hydrido, hydrocarbyl, aryl, haloaryl, cyanoaryl, hydroxyaryl, hydrocarbylaryl, cyano, perfluorohydrocarbyl, hydroxyhydrocarbyl, arylhydrocarbyl, carboxy, hydrocarbyloxycarbonyl,
25 hydrocarboylhydrocarbyl, aminocarbonyl, arylhydrocarbyl-hydrocarboyl-hydrocarbyl monosubstituted amino carbonyl, hydrocarbyl-hydrocarboyl-hydrocarbyl monosubstituted amino carbonyl, hydrocarbyl-hydrocarbylhydrocarboyl-hydrocarbyl monosubstituted amino carbonyl,
30 hydrocarbyl monosubstituted amino carbonyl, hydrocarbyl-hydroxy-disubstituted amino carbonylhydrocarbyl, or a six membered heteroaryl group substituted by a nitrogen atom; or

3) R² is other than hydrido, carboxy,
35 hydrocarbyloxycarbonyl, halogen, or aryl.

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2. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein:

Ar¹ is an aryl group that is substituted by a group selected from fluorine, or lower hydrocarbyl;

5 R¹ is hydrido, or lower hydrocarbyl;

R² is independently selected from the group consisting of hydrido, lower hydrocarbyl and aminocarbonyl;

Z is hydrido, or -X-Y;

10 -X is -O or -NQ;

Q is aryl lower hydrocarbyl; and

-Y is hydrido or lower hydrocarbyl.

3. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein:

15 Ar¹ is an aryl group that is substituted by one or more substituents that are lower hydrocarbyl, or halogen;

R¹ is hydrido, or lower hydrocarbyl;

20 R² is hydrido or lower hydrocarbyl;

Z is hydrido or -X-Y;

-X is -NQ;

Q is lower hydrocarbyl or hydroxyl lower hydrocarbyl; and

25 -Y is hydrido or lower hydrocarbyl.

4. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein:

30 Ar¹ is an aryl group that is substituted by one or more substituents that are lower hydrocarbyl or halogen;

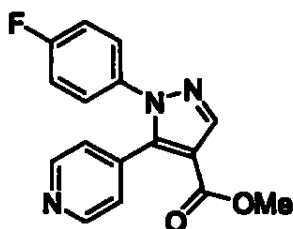
R¹ is hydrido, or lower hydrocarbyl;

R² is hydrido;

Z is cyano or -X-Y;

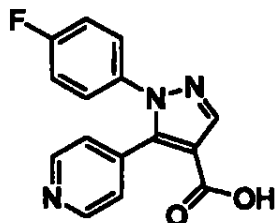
35 wherein -X is -O, or -NQ;

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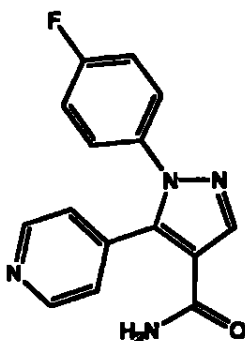


49. A compound corresponding in structure to the formula

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50. A compound corresponding in structure to the formula



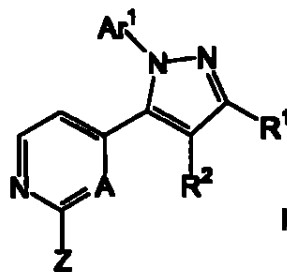
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51. A process for treating a host mammal having a condition associated with pathological p38 MAP kinase activity that comprises administering a compound corresponding in structure to Formula I, or a pharmaceutically-acceptable salt thereof, in a p38 MAP kinase enzyme-inhibiting effective amount to a mammalian host having such a condition:

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wherein A is =N- or =CH-;

Ar¹ is an aryl group that is optionally
 5 substituted by one or more substituents selected from
 the group consisting of a halogen, hydrocarbyl,
 hydrocarbyloxy, nitro, cyano, perfluorohydrocarbyl,
 trifluoromethylhydrocarbyl, perfluorohydrocarbyloxy,
 hydroxy, mercapto, hydroxycarbonyl, aryloxy,
 10 arylthio, sulfonyl or sulfoxido, wherein the
 substituent on the sulfur atom is hydrocarbyl,
 sulfonylamide,

wherein the substituents on the sulfonamido
 nitrogen atom are hydrido or hydrocarbyl,
 15 arylamino, arylhydrocarbyl, aryl, heteroaryloxy,
 heteroarylthio, heteroarylamino, heteroaryl-
 hydrocarbyl, hydrocarbyloxycarbonylhydrocarbyl,
 heterocycloxy, hydroxycarbonylhydrocarbyl,
 heterocyclothio, heterocycloamino,
 20 cyclohydrocarbyloxy, cyclohydrocarbylthio,
 heteroarylhydrocarbyloxy, heteroarylhydrocarbylthio,
 heteroarylhydrocarbylamino, arylhydrocarbyloxy,
 arylhydrocarbylthio, arylhydrocarbylamino,
 heterocyclic, heteroaryl, hydroxycarbonyl-
 25 hydrocarbyloxy, hydrocarbyloxycarbonylhydrocarbyloxy,
 hydrocarbyloyl, arylcarbonyl, arylhydrocarbyloyl,
 hydrocarboyloxy, arylhydrocarboyloxy,
 hydroxyhydrocarbyl, hydroxyhydrocarbyloxy,
 hydrocarbylthio, hydrocarbyloxyhydrocarbylthio,
 30 hydrocarbyloxycarbonyl, hydroxycarbonyl-
 hydrocarbyloxy, hydrocarbyloxycarbonylhydrocarbyl,

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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

DIVISION DE NUEVAS CREACIONES

2020

Bogotá, D.C., Marzo 23 de 2007

Abogado

ERNESTO CAVELIER FRANCO

ASUNTO	Radicación No.	03 067869
	Trámite	002
	Evento	001
	Actuación	430
	Oficio No.	3893
	Folios	0

Solicitante: Vertex Pharmaceuticals Incorporated

Título de la solicitud: "Inhibidores heterocíclicos de ERK2 y uso de los mismos"

Como resultado del examen de fondo, realizado conforme a lo establecido por el artículo 45 de la Decisión 486 de la Comisión de la Comunidad Andina, se notifica el siguiente concepto técnico:

Documentos estudiados

Para el presente estudio se tuvieron en cuenta el capítulo descriptivo comprendido en los folios 13 - 190 y el capítulo reivindicatorio de los folios 191 - 267 de la solicitud en estudio.

Objeto de la Invención

El objeto de la presente solicitud de patente de invención consiste en:

Reivindicaciones 1-9, 19, 43-67: Método de tratamiento que consiste en administrar un compuesto a un paciente

Reivindicaciones 10-18, 68: Método para Inhibir la actividad ERK-2 en una muestra biológica

Reivindicaciones 20-31: Compuestos de fórmulas I', I'', I'''

Reivindicaciones 32-36: Compuestos de fórmula III-a'

Reivindicaciones 37-39: Compuestos de fórmula III-a''

Reivindicación 40: Compuestos

Reivindicaciones 41-42 69-70: Composiciones que los contienen

El problema planteado en esta solicitud es la necesidad de compuestos inhibidores de proteína quinasa, en particular ERK2 para tratar cáncer, inflamación, restenosis, diabetes, enfermedad cardiovascular, enfermedades inflamatorias del intestino, esclerosis múltiple, asma.

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Para resolver este problema técnico la solicitud en estudio proporciona un método de tratamiento, compuestos de fórmulas I', I'', I'', III-a', III-a'' y composiciones que los contienen.

El objeto de la invención definido anteriormente se clasificó de acuerdo con la IPC: A 61 K 31/506. C 07 D 403/04 // 401/14 // 413/14 // 405/14 // 403/14 A 61 P 35/00.

También se reivindica prioridad de las Solicitudes de Patente de los Estados Unidos US 60 267 818 de febrero 9 de 2001 y US 60 328 768 de octubre 12 de 2001, con respecto a la cuales la fecha de presentación de la actual solicitud cumple el plazo máximo permitido.

Excepciones a la Patentabilidad

El artículo 20 de la Decisión 486 establece: *"No serán patentables: d) los métodos terapéuticos o quirúrgicos para el tratamiento humano o animal, así como los métodos de diagnóstico aplicados a los seres humanos o a animales"*

Las Reivindicaciones 1-9, 19, 43-67 que se refieren a un Método de tratamiento que consiste en administrar un compuesto a un paciente y las Reivindicaciones 10-18, 68 a un Método para inhibir la actividad ERK-2 en una muestra biológica no son patentable de acuerdo con la norma citada, que especifica que ni los métodos terapéuticos para el tratamiento humano o animal ni los métodos de diagnóstico son patentables.

Con respecto a los Art. 28 y 30 de la D 486

El artículo 30 de la Decisión 486 establece: *"Las reivindicaciones definirán la materia que se desea proteger mediante la patente. Deben ser claras y concisas y estar enteramente sustentadas por la descripción."*

Las reivindicaciones podrán ser independientes o dependientes. Una reivindicación será independiente cuando defina la materia que se desea proteger sin referencia a otra reivindicación anterior. Una reivindicación será dependiente cuando defina la materia que se desea proteger refiriéndose a una reivindicación anterior. Una reivindicación que se refiera a dos o más reivindicaciones anteriores se considerará una reivindicación dependiente múltiple."

No hay razón por la cual las reivindicaciones 19 y 40 deban ser independientes. Debe hacerse la corrección necesaria.

El artículo 28 de la Decisión 486 establece: *"La descripción deberá divulgar la invención de manera suficientemente clara y completa para su comprensión y para que una persona capacitada en la materia técnica correspondiente pueda ejecutarla."*

La reivindicación 1 no es clara. Contiene una contradicción porque dice que "Sp tiene hasta dos sustituyentes R6" y luego agrega que "con la condición de que dos átomos de carbono sustituibles del anillo en Sp no son substituidos de manera simultánea por R6". Lo cual querría decir que tiene dos sustituyentes y luego que solo tiene uno. Deber hacerse claridad al respecto.

Determinación del Estado de la Técnica

El artículo 16 de la decisión 486 de la comisión de la Comunidad Andina que establece que *"El estado de la técnica comprenderá todo lo que haya sido accesible al público por una descripción escrita u oral, utilización, comercialización o cualquier otro medio antes de la fecha de presentación de la solicitud de patente o, en su caso, de la prioridad reconocida."*

Solo para el efecto de la determinación de la novedad, también se considerará dentro del estado de la técnica, el contenido de una solicitud de patente en trámite ante la oficina nacional

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competente, cuya fecha de presentación o de prioridad fuese anterior a la fecha de presentación o de prioridad de la solicitud de patente que se estuviese examinando, siempre que dicho contenido esté incluido en la solicitud de fecha anterior cuando ella se publique o hubiese transcurrido el plazo previsto en el artículo 40°.

Considerando que la fecha de presentación de la primera solicitud de patente de la cual se reivindica prioridad es febrero 9 de 2001, se consultaron las bases de datos y los archivos con que cuenta la entidad con fecha de publicación anterior y se encontraron los siguientes documentos que anticipan el objeto de esta solicitud:

No.	Documento	Título	Fecha de Publicación
D2	WO 97 05878	2,5-SUBSTITUTED ARYL PYRROLES, COMPOSITIONS CONTAINING SUCH COMPOUNDS AND METHODS OF USE	20-02-1997
D3	WO 99 58523	1,5-DIARYL SUBSTITUTED PYRAZOLES AS p38 KINASE INHIBITORS	18-11-1999

Evaluación de los requisitos de Patentabilidad

El artículo 14 de la Decisión 486 de la Comisión de la Comunidad Andina establece que "Los Países Miembros otorgarán patentes para las invenciones, sean de producto o de procedimiento, en todos los campos de la tecnología, siempre que sean nuevas, tengan nivel inventivo y sean susceptibles de aplicación industrial".

En cumplimiento del artículo 14 de la Decisión 486, se procedió a evaluar el cumplimiento de los requisitos de novedad, nivel inventivo y aplicación industrial, con el fin de establecer la patentabilidad de la invención reivindicada en la solicitud en estudio.

Evaluación del Nivel Inventivo

El artículo 18 de la Decisión 486 de la Comisión de la Comunidad Andina establece que Se considerará que una invención tiene nivel inventivo, si para una persona del oficio normalmente versada en la materia técnica correspondiente, esa invención no hubiese resultado obvia ni se hubiese derivado de manera evidente del estado de la técnica.

El documento del Estado de la Técnica más próximo es D2 que enseña compuestos pirrol sustituidos en los cuales HAr, Ar1, Ar2 son heteroaril 5-10, que son inhibidores de la actividad de citoquinas.

La única diferencia con D2 es que los compuestos de esta solicitud no tienen los grupos Ar1 y Ar2. Pero la ausencia de estos no parece conceder un efecto técnico inesperado porque estos compuestos siguen siendo inhibidores de la actividad de citoquinas.

Además D3 menciona que este tipo de compuestos heterocíclicos inhibidores de la actividad de citoquinas (ver pág 2) es activo para tratar inflamación, enfermedades inflamatorias del intestino, esclerosis múltiple, asma. Por lo cual el hecho de recurrir a tales compuestos para solucionar el problema planteado, es evidente para un experto en la materia. Por lo cual los compuestos de fórmulas I', I'', I°, III-a', III-a° (reivindicaciones 20-31, 32-36, 37-39, 40) no tienen nivel inventivo.

De la misma manera, las composiciones que los contienen (reivindicaciones 41-42, 69-70) no tienen nivel inventivo porque el compuesto que las caracteriza no lo tiene.

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Conclusión

En conclusión, los requisitos de patentabilidad de la presente solicitud están afectados así:

Item	Documento	Reivindicaciones afectadas	Requisito que afecta
D2	WO 97 05878	20 - 31, 32 - 36, 37 - 39, 40, 41-42, 69-70	Nivel inventivo
D3	WO 99 58523	20 - 31, 32 - 36, 37 - 39, 40, 41-42, 69-70	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 la 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 Unica No. 10 de 2001.

ALIX CARMENZA CÉSPEDES DE VERGEL
Jefe de la División de Nuevas Creaciones.

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

30 MAR. 2007

CONCEPTO TÉCNICO No. 505	EXAMINADOR TÉCNICO Código 202007
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EXAMEN TÉCNICO DE FOND			
Nº Radicación	03 067869	Fecha de presentación	08-08-2003
Nº Prioridad	US 60 267 818 US 60 328 768	Fecha de Prioridad	09-02-2001 12-10-2001

Palabras clave	Inhibidores heterocíclicos de Proteína quinasas
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CLASIFICACIONES INTERNACIONALES DE BÚSQUEDA
A 61 K 31/506. C 07 D 403/04 // 401/14 // 413/14 // 405/14 // 403/14 A 61 P 35/00

DOCUMENTOS CORRESPONDIENTES EN OTROS PAÍSES	
Patente Original	WO02064586 (A3)
Otros	WO02064586 (A3) EP1363906 (A3) EP1363906 (A2) MXPA03007049 (A) EP1363906 (A0) CN1494541 (A) CA2437767 (A1)

BASES DE DATOS CONSULTADAS			
OEPM	Epoline	Espacenet	Oficina US

INFORMES DE EXÁMENES EN OTRAS OFICINAS		
Documento	Fecha	Relv. Afectadas
WO02064586 (A3)	2002	20 - 31, 32 - 36, 37 - 39, 40, 41-42, 66-70

ANTERIORIDADES ENCONTRADAS		
Documento de Patentes	Relv. Afectadas	Relevancia
WO 97 05878	20 - 31, 32 - 36, 37 - 39, 40, 41-42, 66-70	Nivel inventivo
WO 99 58523	20 - 31, 32 - 36, 37 - 39, 40, 41-42, 66-70	Nivel inventivo

LITERATURA NO PATENTES		
Documento no Patentes	Relv. Afectadas	Relevancia

Observaciones	
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Fecha del examen	Marzo 23 de 2007
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