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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIVISION DE NUEVAS CREACIONES

SUPERINDUSTRIA Y COMERCIO
Radicación: 00097924 00000004 Fechos: 3
Fecha (AMB): 2003-07-23 12 57 27
Tramite 002 PATENTES D 1 REGISTRO/ 536 PETICION
Dependencia: 2020 DIVISION DE NUEVAS CREACIONES

E S D

Ref Expediente No 00 097 924

Solicitud de Patente de Invención Titulada

"PROCEDIMIENTOS DE TRATAMIENTO DE
CARDIOMIOPATIA UTILIZANDO
INHIBIDORES DE LA GLUCOGENO
FOSFORILASA"

Solicitante PFIZER PRODUCTS INC

**SOLICITUD DE EXAMEN DE FONDO SEGÚN EL ARTICULO 44 DE LA
DECISION 486, GACETA No. 527**

ALVARO CORREA ORDOÑEZ, mayor de edad y vecino de Bogotá, D C ,
identificado segun aparece al pie de mi firma, en mi condición de apoderado sustituto, de la
sociedad Pfizer Products Inc , respetuosamente me permito solicitar, dando cumplimiento a
lo establecido en el artículo 44 de la Decisión 486 de la Comisión de la Comunidad Andina
de Naciones, que se examine si la invención reúne los requisitos de patentabilidad previstos
en la misma Adjunto recibo por el monto de \$ 335 000 pesos para cubrir la tasa
correspondiente, según la Resolución 41687 del año 2002

Atentamente,

ALVARO CORREA ORDOÑEZ
C C No 79 143 366 de Usaquén
T.P 20-281

Anexos Sustitución de Poder
Recibo por \$ 335 000 pesos

**DILIGENCIA DE RECONOCIMIENTO
Y PRESENTACION PERSONAL**

Ante el Notario Once del Circulo de Santafé de Bogotá compareció

Quién exhibió la C.C. No.

expedida en Coopén TP 018

y declaró que la firma y huella que aparecen en el presente memorial son suyas y que el contenido del mismo es cierto

Memorial dirigido a interesado

Santafé de Bogotá, D.C.

25 JUL 2005

Firma del Declarante

HUEDA

Autorizo la anterior Diligencia

NOTARIO ONCE DEL CIRCULO DE SANTAFÉ DE BOGOTÁ, D.C. DE COLOMBIA

MANVARRO DE BAUTISTA
NOTARIA ONCE

RAISBECK LARA, RODRÍGUEZ & RUEDA
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256

Señores

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIVISION DE NUEVAS CREACIONES

E S D

Ref Solicitud colombiana de patente No 00 097.924

Solicitante **PFIZER PRODUCTS INC**

**"PROCEDIMIENTOS DE TRATAMIENTO DE
CARDIOMIOPATIA UTILIZANDO INHIBIDORES
DE LA GLUCOGENO FOSFORILASA"**

SUSTITUCIÓN DE PODER

CARLOS R. OLARTE, mayor y vecino de Bogotá. D C, identificado como aparece al pie de mi firma, actuando en mi caracter de apoderado de la sociedad de la referencia, respetuosamente me permito manifestar que **SUSTITUYO** el poder a mi conferido por la mencionada sociedad en el doctor **ALVARO CORREA ORDONEZ**, identificado con la Cédula de Ciudadanía numero 79 143 366 de Usaquén y con la Tarjeta Profesional numero 20 281, para que sea él quien en adelante, asuma el trámite de la presente solicitud

El apoderado sustituto queda con las mismas facultades del principal

Atentamente,



CARLOS R OLARTE
C C No 79 782 747 de Bogotá
T P No 74 295 del Consejo Superior de la Judicatura

**DILIGENCIA DE RECONOCIMIENTO
Y PRESENTACION PERSONAL**

Ante el Notario Once del Circulo de Santa Fe de Bogotá comparecieron

Quien exhibió la C C No

expedida en

TF

y declaró que la firma y huella que aparecen en el presente memorial son suyas y que el contenido del mismo es cierto X

Memorial dirigido a

interesado

Santafé de Bogotá D C

15 JUL 2003

Firma del Declarante

HUELLA

Autorizó la anterior Diligencia

NOTA: ONCE DEL CIRCULO DE SANTA FE DE BOGOTA, D C

REPUBLICA DE COLOMBIA
BOGOTA 11 DEL CIRCULO DE
SANTAFE DE BOGOTA, D C

MOMICA Z BAPTISTA M
NOTARIA ONCE(É)

SUPERINDUSTRIA Y COMERCIO
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Fecha (AMD) 2003-07-23 12:57:27
Tramite 002 PATENTES B 1 REGISTRO/ 538 PETICION
Dependencia: 2020 DIVISION DE NUEVAS CREACIONES

NIT 800176089-2

RECIBO OFICIAL DE CAJA 03 - 43 897
FECHA JUNIO 24 DE 2003

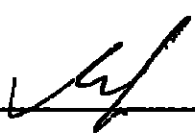
***** CONSIGNACION *****

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No PAGO	FECHA PGO	Vr PAGO
JULIAN ANDRES VARGAS	CONSIGNACION	BANCO POPULAR	050-00110-6	13228244	24/06/2003	18 050 000 00

***** CONCEPTO *****

CANT	RENTISTICO	CONCEPTO	TOTAL CONCEPTO
1	50005-01-01 SOLICITUDES	8 ^o EXAMEN DE PATENTABILIDAD DE INVEN	335 000 00
		TOTAL	\$ 335,000 00

SON TRESCIENTOS TREINTA Y CINCO MIL PESOS

RESPONSABLE 

RECIBO DE CAJA APLICADO AL EXPEDIENTE No _____

DIVISION DE NUEVAS CREACIONES

RADICACIÓN EXPEDIENTE No 00-97924

EL EXTRACTO DE LA PRESENTE SOLICITUD DE PATENTE DE INVENCION

FUE PUBLICADO EN LA GACETA DE PROPIEDAD INDUSTRIAL No 527, DE

FECHA 30 DE ABRIL DE 2003, EL TERMINO HABIL SEÑALADO POR LA LEY

EXPIRA EL 29 DE JULIO DE 2003

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

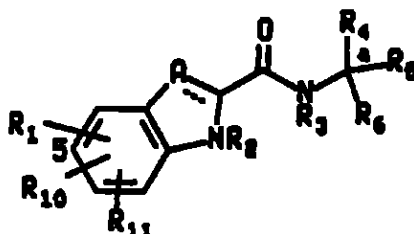
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NO **X** _____

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 C07D 209/42, A61K 31/40, C07D 403/12, 401/12, 417/12, 401/14, 409/12, 413/12		A1	(11) International Publication Number: WO 96/39384 (43) International Publication Date: 12 December 1996 (12.12.96)
(21) International Application Number: PCT/IB95/00442 (22) International Filing Date: 6 June 1995 (06.06.95)			(81) Designated States: CA, FI, JP, MX US, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published With international search report
(71) Applicant (for all designated States except US): PFIZER, INC. [US/US]; 235 East 42nd Street, New York, NY 10017 (US).			
(72) Inventors; and (73) Inventors/Applicants (for US only): HULIN, Bernard [FR/US]; Pfizer Inc., Eastern Point Road, Groton, CT 06340 (US). HOOVER, Dennis, J [US/US]; Pfizer Inc., Eastern Point Road, Groton, CT 06340 (US). TREADWAY, Judith, L. [US/US]; Pfizer Inc., Eastern Point Road, Groton, CT 06340 (US). MARTIN, William, H. [US/US]; Pfizer Inc., Eastern Point Road, Groton, CT 06340 (US). PHILLIPS, Douglas [US/US]; Pfizer Inc., Eastern Point Road, Groton, CT 06340 (US).			
(74) Agents: SPIEGEL, Allen, J et al., Pfizer Inc., Patent Dept., 235 East 42nd Street, New York, NY 10017 (US).			

(54) Title: SUBSTITUTED N-(INDOLE-2-CARBONYL)-GLYCINAMIDES AND DERIVATIVES AS GLYCOGEN PHOSPHORYLASE INHIBITORS



(1)

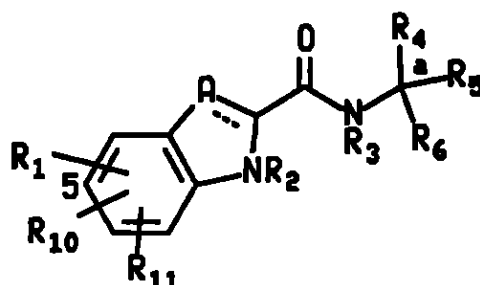
(57) Abstract

Compounds of Formula (1) wherein R₄ is carboxy (C₁-C₆)alkoxycarbonyl, benzyloxycarbonyl, C(O)NR₅R₆ or C(O)R₁₂ as glycogen phosphorylase inhibitors, pharmaceutical compositions containing such inhibitors and the use of such inhibitors to treat diabetes, hyperglycemia, hypercholesterolemia, hypertension, hyperinsulinemia, hyperlipidemia, atherosclerosis and myocardial ischemia in mammals

CLAIMS

1 A compound of Formula I

5



10

Formula I

and the pharmaceutically acceptable salts and prodrugs thereof
wherein

the dotted line (—) is an optional bond,

15 A is $-C(H)=$, $-C((C_1-C_4)alkyl)=$, $-C(halo)=$ or $-N=$, when the dotted line (—) is a bond, or A is methylene or $-CH((C_1-C_4)alkyl)-$, when the dotted line (—) is not a bond,

R_1 , R_{10} or R_{11} are each independently H, halo, cyano, 4-, 6-, or 7-nitro, $(C_1-C_4)alkyl$, $(C_1-C_4)alkoxy$, fluoromethyl, difluoromethyl or trifluoromethyl,

R_2 is H,

20 R_3 is H or $(C_1-C_4)alkyl$,

R_4 is H, methyl, ethyl, n-propyl, hydroxy $(C_1-C_4)alkyl$, $(C_1-C_4)alkoxy(C_1-C_4)alkyl$, phenyl $(C_1-C_4)alkyl$, phenylhydroxy $(C_1-C_4)alkyl$, (phenyl)((C_1-C_4)-alkoxy) $(C_1-C_4)alkyl$, thien-2- or -3-yl $(C_1-C_4)alkyl$ or fur-2- or -3-yl $(C_1-C_4)alkyl$ wherein said R_4 rings are mono-, di- or tri-substituted independently on carbon with H, halo, $(C_1-C_4)alkyl$, $(C_1-C_4)alkoxy$, trifluoromethyl, hydroxy, amino, cyano or 4,5-dihydro-1H-imidazol-2-yl, or

30 R_4 is pyrid-2-, -3- or -4-yl $(C_1-C_4)alkyl$, thiazol-2-, -4- or -5-yl $(C_1-C_4)alkyl$, imidazol-2-, -4- or -5-yl $(C_1-C_4)alkyl$, pyrrol-2- or -3-yl $(C_1-C_4)alkyl$, oxazol-2-, -4- or -5-yl $(C_1-C_4)alkyl$, pyrazol-3-, -4- or -5-yl $(C_1-C_4)alkyl$, isoxazol-3-, -4- or -5-yl $(C_1-C_4)alkyl$, isothiazol-3-, -4- or -5-yl $(C_1-C_4)alkyl$, pyridazin-3- or -4-yl $(C_1-C_4)alkyl$, pyrimidin-2-, -4-, -5- or -6-yl $(C_1-C_4)alkyl$, pyrazin-2- or -3-yl $(C_1-C_4)alkyl$, 1,3,5-triazin-2-yl $(C_1-C_4)alkyl$ or indol-2- $(C_1-C_4)alkyl$, wherein said preceding R_4 heterocycles are optionally mono- or

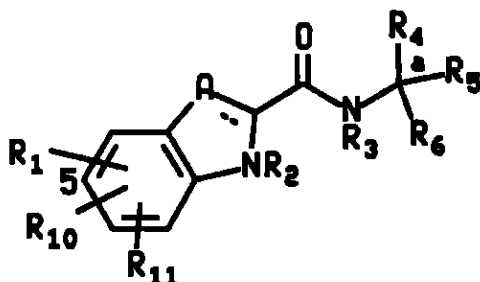
The mechanism(s) responsible for the myocardial injury observed after ischemia and reperfusion is not fully understood. It has been reported (M. F. Allard, et al. Am. J. Physiol. 267, H66-H74, 1994) that "pre ischemic glycogen reduction is associated with improved post ischemic left ventricular functional recovery in hypertrophied rat hearts".

Thus, although there are a variety of hyperglycemia, hypercholesterolemia, hypertension, hyperinsulinemia, hyperlipidemia, atherosclerosis and myocardial ischemia therapies there is a continuing need and a continuing search in this field of art for alternative therapies.

Summary of the Invention

This invention is directed to a glycogen phosphorylase inhibitor compound of Formula I useful for the treatment of diabetes, hyperglycemia, hypercholesterolemia, hyperinsulinemia, hypertension, hyperlipidemia, atherosclerosis and myocardial ischemia.

The compounds of this invention have the Formula I



Formula I

and the pharmaceutically acceptable salts and prodrugs thereof

wherein

the dotted line (—) is an optional bond,

A is $-C(H)=$, $-C((C_1-C_4)alkyl)=$, $-C(halo)=$ or $-N=$, when the dotted line (—) is a bond, or A is methylene or $-CH((C_1-C_4)alkyl)-$, when the dotted line (—) is not a bond,

R_1 , R_{10} or R_{11} are each independently H, halo, cyano, 4-, 6-, or 7-nitro, $(C_1-C_4)alkyl$, $(C_1-C_4)alkoxy$, fluoromethyl, difluoromethyl or trifluoromethyl,

R_2 is H,

R_3 is H or $(C_1-C_6)alkyl$,

According to Reaction Scheme I the Formula I compounds, wherein R_1 , R_{10} , R_{11} , A, R_2 , R_3 , R_4 , R_5 and R_6 are as defined above may be prepared by either of two general processes. In the first process the desired Formula I compound may be prepared by coupling the appropriate Formula II indole-2-carboxylic acid, indoline-2-carboxylic acid or benzimidazole-2-carboxylic acid with the appropriate Formula III amine (i.e., acylating the amine). In the second process the desired Formula I compound may be prepared by coupling the appropriate Formula IV compound (i.e., a Formula I compound wherein R_6 is carboxy) with the appropriate alcohol or formula R_9R_8NH or $R_{12}H$ amine, wherein R_8 , R_9 and R_{12} are as defined above (i.e., acylating the amine or alcohol). The first process (coupling Formula II compounds with Formula III compounds) is typically preferred when R_6 is not H and R_8 is H.

Typically, the Formula II compound is combined with the Formula III compound (or Formula IV compound is combined with the appropriate amine (e.g., $R_{12}H$ or R_9R_8NH)) or alcohol in the presence of a suitable coupling agent. A suitable coupling agent is one which transforms a carboxylic acid into a reactive species which forms an amide or ester linkage on reaction with an amine or alcohol, respectively.

The coupling agent may be a reagent which effects this condensation in a one pot process when mixed together with the carboxylic acid and amine or alcohol. If the acid is to be condensed with an alcohol it is preferable to employ a large excess of the alcohol as the reaction solvent, with or without 1.0 to 1.5 equivalent added dimethylaminopyridine. Exemplary coupling reagents are 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride-hydroxybenzotriazole (DEC/HBT), carbonyldiimidazole, dicyclohexylcarbodiimide/hydroxybenzotriazole (HBT), 2-ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline (EEDQ), carbonyldiimidazole/HBT, propanephosphonic anhydride (propanephosphonic acid anhydride, PPA) and diethylphosphorylcyanide. The coupling is performed in an inert solvent, preferably an aprotic solvent at a temperature of about -20°C to about 50°C for about 1 to about 48 hours, in the optional presence of a tertiary amine base such as triethylamine. Exemplary solvents include acetonitrile, dichloromethane, ethyl acetate, dimethylformamide and chloroform or mixtures thereof. An example of a suitable coupling procedure is Procedure A, contained herein (just prior to the EXAMPLES).

Example 71**5,6-Dichloro-1H-Indole-2-carboxylic acid****((1S)-dimethylcarbamoyl-2-phenyl-ethyl)-amide**

(S)-2-Amino-N,N-dimethyl-3-phenyl-propionamide hydrochloride (0.08 mmol) and
5 5,6-dichloro-1H-indole-2-carboxylic acid (0.05 mmol) were coupled according to
Procedure A (0 - 25 °C reaction temperature, 96 hour reaction time) The crude
product was triturated with 1:1 ether-hexanes and dried Yield 24 mg, 96 %, HPLC
(60/40) 8.05 minutes (97 %), PBMS 405/407 (MH+, 100 %),
Anal Calcd for $C_{20}H_{15}Cl_2N_3O_2 + 0.25 H_2O$ C, 58.76, H, 4.81, N, 10.28
10 Found C, 58.95, H, 4.89, N, 9.90

Example 71a**(S)-2-Amino-N,N-dimethyl-3-phenyl-propionamide hydrochloride**

(1-Dimethylcarbamoyl-2-phenyl-ethyl)-carbamio acid tert-butyl ester (8.6 g, 28
mmol) was dissolved in 4 M HCl - dioxane (110 ml) at 0 °C and the mixture stirred at
15 25°C for 1 hour The mixture was concentrated and the solids triturated with ether
Yield, 6.2 g, 92 %, PBMS 193 (MH+, 100 %)

Example 71b**5,6-Dichloro-1H-Indole-2-carboxylic acid**

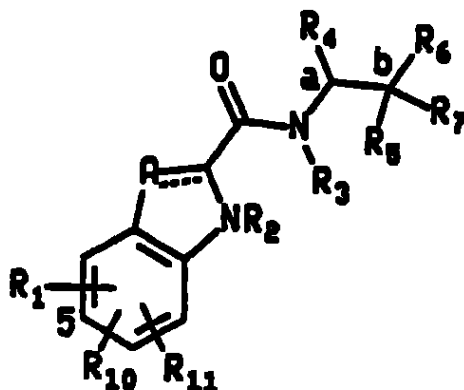
Zinc dust (3.52 g, 54 mmol) was added slowly to a warm solution of 3,4-
20 dichloro-5-nitrophenylpyruvic acid (1.5 g, 5.4 mmol) in acetic acid (15 mL) After a few
minutes, a vigorous reaction occurred (exothermic) The resulting solution was heated
to 80 °C and the reaction appeared complete (TLC) The mixture was filtered, the
filtered solids washed with acetic acid and the filtrate concentrated The residue was
dissolved in 2 N NaOH, the resulting solution washed with ether (3x), dichloromethane
25 (2x) and acidified to pH 1 with 6N HCl and extracted with ethyl acetate The extracts
were dried and concentrated giving a light brown solid (458 mg, 34 %) HPLC (60/40)
5.31 (93 %)

Example 71c**3,4-dichloro-5-nitrophenylpyruvic acid**

30 Absolute ethanol (25 mL) was added at 3 - 15 °C to a stirred mixture of
potassium metal (2.67 g, 68 mmol) in ether (100 mL) The resulting solution was
treated at 3 °C with a solution of diethyl oxalate (10.0 g, 62 mmol) over 5 - 10 minutes,
and the resulting solution stirred 30 minutes at 3 °C and 25 °C for 18 hours The

(51) International Patent Classification ⁶: C07D 209/42, A61K 31/40, C07D 403/12, 413/12, 401/12, 417/12	A1	(11) International Publication Number WO 96/39385 (43) International Publication Date 12 December 1996 (12.12.96)
(21) International Application Number PCT/IB95/00443 (22) International Filing Date 6 June 1995 (06.06.95) (71) Applicant (for all designated States except US): PFIZER INC. [US/US]; 235 East 42nd Street, New York, NY 10017 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): HULIN, Bernard [FR/US]; Pfizer Inc., Eastern Point Road, Groton, CT 06340 (US). HOOVER, Dennis, J. [US/US], Pfizer Inc., Eastern Point Road, Groton, CT 06340 (US). TREADWAY, Judith, L. [US/US], Pfizer Inc., Eastern Point Road, Groton, CT 06340 (US). MARTIN William, H. [US/US], Pfizer Inc., Eastern Point Road, Groton, CT 06340 (US). (74) Agents: SPIEGEL, Allan, J. et al., Pfizer Inc., Patent Dept., 235 East 42nd Street, New York, NY 10017 (US).	(81) Designated States: CA, FI, JP, MX, US, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published <i>With international search report.</i>	

(54) Title: SUBSTITUTED N-(INDOLE-2-CARBONYL-) AMIDES AND DERIVATIVES AS GLYCOGEN PHOSPHORYLASE INHIBITORS



(57) Abstract

This invention relates to certain indole-2-carboxamides of formula (I) and the pharmaceutically acceptable salts and prodrugs thereof, wherein R_5 is carbonyl, (C_1-C_6) alkoxycarbonyl, $C(O)NR_9R_9$ or $C(O)R_{12}$, useful as inhibitors of glycogen phosphorylase, methods of treating glycogen phosphorylase dependent diseases or conditions with such compounds and pharmaceutical compositions comprising such compounds.

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SUBSTITUTED N-(INDOLE-2-CARBONYL-) AMIDES AND DERIVATIVES AS GLYCOGEN PHOSPHORYLASE INHIBITORS**Background of the Invention**

This invention relates to glycogen phosphorylase inhibitors, pharmaceutical compositions containing such inhibitors and the use of such inhibitors to treat diabetes, hyperglycemia, hypercholesterolemia, hypertension, hyperinsulinemias, hyperlipidemia, atherosclerosis and myocardial ischemia in mammals

In spite of the early discovery of insulin and its subsequent widespread use in the treatment of diabetes, and the later discovery of and use of sulfonylureas (e.g. Chlorpropamide™ (Pfizer), Tolbutamide™ (Upjohn), Acetohexamide™ (Eli Lilly), Tolazamide™ (Upjohn)) and biguanides (e.g. Phenformin™ (Ciba Geigy), Metformin™ (G.D. Searle)) as oral hypoglycemic agents, the treatment of diabetes remains less than satisfactory. The use of insulin, necessary in about 10 % of diabetic patients in which synthetic hypoglycemic agents are not effective (Type I diabetes, insulin dependent diabetes mellitus), requires multiple daily doses, usually by self injection. Determination of the proper dosage of insulin requires frequent estimations of the sugar in urine or blood. The administration of an excess dose of insulin causes hypoglycemia, with effects ranging from mild abnormalities in blood glucose to coma, or even death. Treatment of non-insulin dependent diabetes mellitus (Type II diabetes, NIDDM) usually consists of a combination of diet, exercise, oral agents, e.g. sulfonylureas, and in more severe cases, insulin. However, the clinically available hypoglycemics can have other side effects which limit their use. In any event, where one of these agents may fail in an individual case, another may succeed. A continuing need for hypoglycemic agents, which may have fewer side effects or succeed where others fail, is clearly evident.

Atherosclerosis, a disease of the arteries, is recognized to be the leading cause of death in the United States and Western Europe. The pathological sequence leading to atherosclerosis and occlusive heart disease is well known. The earliest stage in this sequence is the formation of "fatty streaks" in the carotid, coronary and cerebral arteries and in the aorta. These lesions are yellow in color due to the presence of lipid deposits found principally within smooth-muscle cells and in macrophages of the intima layer of the arteries and aorta. Further, it is postulated that most of the cholesterol found within the fatty streaks, in turn, give rise to development of the "fibrous plaque", which consists of accumulated intimal smooth muscle cells laden with lipid and surrounded by extra-

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pyrrol-2- or -3-yl(C₁-C₂)alkyl, oxazol-2-, -4- or -5-yl(C₁-C₂)alkyl, pyrazol-3-, -4- or -5-yl(C₁-C₂)alkyl, isoxazol-3-, -4- or -5-yl(C₁-C₂)alkyl wherein said preceding R₄ heterocycles are optionally mono- or di-substituted independently with halo, trifluoromethyl, (C₁-C₄)alkyl, (C₁-C₄)alkoxy, amino or hydroxy and said mono- or di-

6 substituents are bonded to carbon,

R₅ is hydroxy,

R₆ is C(O)NR₇R₈ or C(O)R₁₂, and

R₇ is H

3 A compound as recited in claim 2 wherein

10 the carbon atom a has (S) stereochemistry,

the carbon atom b has (R) stereochemistry;

R₄ is phenyl(C₁-C₂)alkyl, thien-2-yl(C₁-C₂)alkyl, thien-3-yl(C₁-C₂)alkyl, fur-2-yl(C₁-C₂)alkyl or fur-3-yl(C₁-C₂)alkyl wherein said rings are mono- or di- substituted independently with H or fluoro,

15 R₅ is C(O)NR₆R₈,

R₆ is (C₁-C₂)alkyl, hydroxy or (C₁-C₂)alkoxy; and

R₈ is H, (C₁-C₄)alkyl, hydroxy, hydroxy(C₁-C₄)alkyl, (C₁-C₄)alkoxy, pyridyl, morpholinyl, piperazinyl, pyrrolidinyl, piperidinyl, imidazolyl or thiazolyl or (C₁-C₄)alkyl mono-substituted with pyridyl, morpholinyl, piperazinyl, pyrrolidinyl, piperidinyl,

20 imidazolyl or thiazolyl

4 A compound as recited in claim 3 selected from

5-Chloro-1H-Indole-2-carboxylic acid [(1S)-[(R)-hydroxy-dimethylcarbamoyl-methyl]-2-phenyl-ethyl]-amide, }

25 5,6-Dichloro-1H-Indole-2-carboxylic acid {(1S)-[(R)-hydroxy-(methoxy-methyl-carbamoyl)-methyl]-2-phenyl-ethyl}-amide,

5-Chloro-1H-Indole-2-carboxylic acid {(1S)-[(R)-hydroxy-(methoxy-methyl-carbamoyl)-methyl]-2-phenyl-ethyl}-amide,

5-Chloro-1H-Indole-2-carboxylic acid {(1S)-[(R)-hydroxy-[(2-hydroxy-ethyl)-methyl-carbamoyl]-methyl]-2-phenyl-ethyl}-amide,

30 5-Chloro-1H-Indole-2-carboxylic acid {(1S)-[(R)-hydroxy-(methyl-pyridin-2-yl-carbamoyl)-methyl]-2-phenyl-ethyl}-amide or

5-Chloro-1H-Indole-2-carboxylic acid {(1S)-[(R)-hydroxy-[methyl-(2-pyridin-2-yl-ethyl)-carbamoyl]-methyl]-2-phenyl-ethyl}-amide