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Señores

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

DIVISION DE NUEVAS CREACIONES

E. S.

Radicacion : 00024431 03686082 Folios: 2
Fecha (AMD): 2002-07-17 17:18:33
Tramite : 002 PATENTES D 1 REGISTRO/ 538 PETICION
Dependencia: 2020 DIVISION DE NUEVAS CREACIONES

Ref.: Expediente No. **00.024.431.**

Solicitud de Patente de Invención Titulada:
"COMPUESTOS INHIBIDORES DE NPY PARA TRATAR LA OBESIDAD Y COMPOSICIONES QUE LOS COMPRENDEN".

Solicitante: **PFIZER PRODUCTS INC.**

SOLICITUD DE EXAMEN DE FONDO SEGÚN EL ARTICULO 44 DE LA DECISION 486, GACETA No. 517

CARLOS R. OLARTE, mayor de edad y vecino de Bogotá, D.C., identificado según aparece al pie de mi firma, en mi condición de apoderado del solicitante, 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 $ 318.000 pesos para cubrir la tasa correspondiente, según la Resolución 44691 del año 2001.

Atentamente,

CARLOS R. OLARTE
C.C. No. 79'782.747 de Bogotá
T.P. 74.295

Anexos: Recibo por $ 318.000 pesos

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NIT : 800176089-2

Radicacion : C0324431 C0330802
Fecha (AMD): 2002-07-17 17:18:33 Folios: 2
Tramite : 002 PATENTES D 1 REGISTRO/ 538 PETICION
Dependencia: 2020 DIVISION DE NUEVAS CREACIONES

RECIBO OFICIAL DE CAJA : 02 - 37,055
FECHA : JUNIO 7 DE 2002

C O N S I G N A C I O N

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PGO	Vr. PAGO
JORGE LUIS GOMEZ	CONSIGNACION	BANCO POPULAR	050-00110-6	9226066	07/06/2002	28,841,000.00

C O N C E P T O

CANT.	RENTISTICO	CONCEPTO		TOTAL CONCEPTO
1	50005-01-01 SOLICITUDES	85	EXAMEN DE PATENTABILIDAD DE INVEN	318,000.00
			TOTAL : $	318,000.00

CION: TRESCIENTOS DIEZ Y OCHO MIL PESOS

RESPONSABLE : _____

RECIBO DE CAJA APLICADO AL EXPEDIENTE No._____

600

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2005-03-03

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIVISIÓN DE NUEVAS CREACIONES

2020

Bogotá, DC, 17 de febrero de 2005

Apoderado: Carlos Reinaldo Olarte Oficio: 12260
ASUNTO Radicación: 0-24431
Trámite 002
Evento 001
Actuación 430
Folios

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:

Documentos estudiados:

- capitulo descriptivo, folios 122 a 417;
- capitulo reivindicatorio, folios 493 a 478;
- 1° examen de forma, folios a 473 y 474 ;
- respuesta técnica al 1° examen de forma, folios 476 y 478;
- solicitud de la cual se reivindica prioridad, junto con la traducción requerida, folios 15 a 119 y 542 a 556;
- 2° examen de forma, folio 597;
- Solicitud del examen de patentabilidad, folios 598 y 599.

Objeto de la invención:

El titulo de la invención es"COMPUESTOS INHIBIDORES DE NPY PARA TRATAR LA OBESIDAD Y COMPOSICIONES QUE LO COMPRENDEN".
El objeto de la presente solicitud se refiere a derivados 1H-imidazol sustituidos en las posiciones 2, 4 del anillo.

Claridad de la solicitud:

En el artículo 30 de la Decisión 486 de la Comisión de la Comunidad Andina se establece: "*Las reivindicaciones definirán la materia que se desea proteger*

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mediante la patente. Deben ser claras y concisas y estar enteramente sustentadas por la descripción".

La reivindicación 40 no es clara, puesto que el encabezado no es congruente con el resto del texto de la reivindicación, se encabeza como una composición y luego se pretende caracterizar por los efectos farmacológicos a obtener.
-Además todas las reivindicaciones que hacen referencia al profármaco, que tal como se le había indicado en el 1° examen de forma, y que debió corregir, pero lo hizo de una manera ambigua e inapropiada, para crear confusión, ahora debe hacerlo de la manera apropiada y correcta.

Excepciones de Patentabilidad:

El artículo 20 de la Decisión 486 de la Comisión de la Comunidad Andina establece en su inciso *d) que no serán patentables: "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*".

La reivindicación 38 pretende proteger un método para tratamiento del cuerpo animal, el cual incluye la administración de una composición farmacéutica que contiene unos de los derivados de la solicitud, por lo tanto está inmersa bajo el alcance del artículo 20 de la Decisión 486.

Determinación del estado de la técnica:

El artículo 16 de la Decisión 486 de la Comisión establece: "*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.*
Sólo 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 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."

Item	Documento	Fecha de publicación	Titulo
D1	WO9901128	14-enero-1999	Certain diarylimidazole derivatives; a new class of NPY specific ligands

Evaluación de los requisitos de patentabilidad:

El artículo 14 de la Decisión 486 de la Comisión de la Comunidad Andina establece: "*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.*"

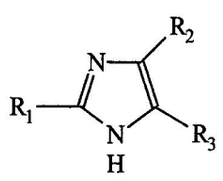
En cumplimiento con este artículo, se procedió a evaluar los requisitos de novedad, nivel inventivo y aplicación industrial con el fin de establecer la patentabilidad de la invención reivindicada en la solicitud en estudio.

Evaluación de la Novedad:

El art.16 de la Decisión 486 de la Comisión de la Comunidad Andina establece: "*Una invención se considerará nueva cuando no está comprendida en el estado de la técnica. 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*".

La solicitud en estudio reclama derivados 1H-imidazol sustituidos en las posiciones 2,4 y las composiciones que los contienen.

La anterioridad D1 enseña compuestos 1H-Imidazol sustituidos de formula:



-Cuando R2 o R_3 uno de los dos es hidrogeno. Por los tantos los compuestos son biarilo sustuidos, tal como los que se reclaman como nuevos en solicitud en estudio. Esta anterioridad que enseña compuestos específicos como por ejemplo el 4-(4-clorofenil)-2-(2-piridil)-imidazol. Tal como lo muestra la anterioridad en las páginas adjuntas de la anterioridad, que indican con antelación a la fecha de

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presentación de la solicitud de la cual se reivindica prioridad, que los compuestos reclamados en la solicitud en estudio, eran conocidos.

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 No. 10 de 2001.

ALIX CARMENZA CESPEDES DE VERGEL
Jefe de División de Nuevas Creaciones

El anterior requerimiento fue notificado por fijación en lista, de fecha 03 MAR. 2005

CONCEPTO TÉCNICO No 263	EXAMINADOR TÉCNICO Código No.202012

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PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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A1

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60/051,711 3 July 1997 (03.07.97) US

(71) Applicants: NEUROGEN CORPORATION [US/US]; 35 Northeast Industrial Road, Branford, CT 06405 (US). PFIZER INC. [US/US]; East 42nd Street, New York, NY 10017 (US).

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(74) Agents: RICHARDS, John; Ladas & Parry, 26 West 61st Street, New York, NY 10023 (US) et al.

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, 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, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, 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: CERTAIN DIARYLIMIDAZOLE DERIVATIVES; A NEW CLASS OF NPY SPECIFIC LIGANDS

(57) Abstract

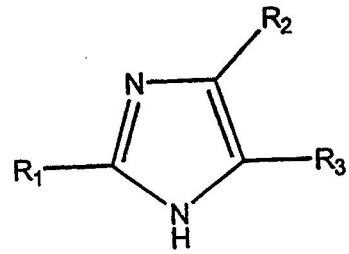
Certain diarylimidazoles act as partial agonists or antagonists for NPY receptors, in particular NPY 5 receptors. They are of use, for example in treating loss of appetite. Such compounds bear aryl groups in the 2 position. Many of the compounds are novel.

D1

135437-68-2; 135437-66-0; 135437-65-9; 135437-64-8; 135437-63-7; 135437-62-6; 135437-61-5; 135437-60-4 and 135437-59-1); analogous 2(1H)-3,4-dihydroquinolones (C.A. Registry Nos 135437-70-6 and 135437-67-1), 2,4-bis-(2-aminophenyl)-imidazole (C.A. Registry No 131623-81-9); 4-(4-hydroxyphenyl)-2-phenylimidazole (C.A. Registry No 111273-30-4); 2,4-bis(4-phenoxyphenyl)imidazole (C.A. Registry 107783-02-8); 2,4-bis(bi-phenyl-4-yl)imidazole (C.A. Registry 106304-01-2); 4-(2-phenyl-1H-imidazol-4-yl)benzeneamine (C.A. Registry No.96139-68-3); various 2-(2-hydroxyphenyl) 4-(possibly substituted) phenylimidazoles having methyl, ethyl, butyl or phenyl substituents in the 5-position; and a number of more complicated structures.

SUMMARY OF THE INVENTION

This invention provides pharmaceutical compositions comprising compounds of Formula I which interact with Neuropeptide Y receptors and in particular with NPY5 receptors and methods of treatment of conditions susceptible to such interactions. It further relates to the use of such compounds in treating feeding disorders such as obesity and bulima as well as certain cardiovascular diseases such as essential hypertension. Suitable compounds are those of Formula I:



where R_1 is an unsubstituted or mono, di or trisubstituted aryl group wherein said aryl group is mono or bicyclic, in which case only the ring bound to the imidazole group ring need be aromatic, and said aryl group may be carbocyclic or contain up to 2 hetero atoms which may be nitrogen, oxygen or sulfur, and said substituents are selected from the group consisting of halogen, trihalomethyl, cyano, hydroxy, straight or branched chain lower alkyl having 1-6 carbon atoms, straight or branched chain lower alkoxy having 1-6 carbon atoms (which alkyl or alkoxy groups themselves may be substituted by an amino or mono- or di- alkyl amino group or an acyl group), straight or branched chain lower thioalkoxy having 1-6 carbon atoms, acyloxy groups, amino, amino mono or disubstituted with straight or branched chain lower alkyl having

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1-6 carbon atoms, said alkyl groups being optionally substituted with a hydroxy or amino group, mono or disubstituted carbamyl where the CO group is bound to the aryl group and wherein the substituents are lower alkyl or aryl lower alkyl, mono or di-alkyl carbamates having up to 6 carbon atoms in each alkyl group or mono or diaryl carbamates or any 2 adjacent substituents on the aryl ring may be represented as $X(CH_2)_nY(CH_2)_mZ$ where X, Y and Z are either a direct bond, oxygen, sulfur, or NR where R is hydrogen or lower alkyl and n and m are 1, 2 or 3.

One of R_2 and R_3 is selected from the group consisting of hydrogen, hydroxymethyl, alkoxymethyl having up to 6 carbon atoms in each alkoxy group, straight or branched chain lower alkyl having 1-6 carbon atoms, cyano, or a carboxylic or carboxylate ester group wherein the esterifying group typically contains up to six carbon atoms.

The other of R_2 and R_3 is an aryl group which is either unsubstituted or mono, di or trisubstituted wherein said aryl groups are mono or bicyclic (in which case only the ring bound to the imidazole grouping need be aromatic) and may be carbocyclic or contain up to 2 hetero atoms and said substituents are selected from the group consisting of halogen, trihalomethyl, cyano, hydroxy, straight or branched chain lower alkyl having 1-6 carbon atoms, straight or branched chain lower alkoxy having 1-6 carbon atoms (which alkyl or alkoxy groups themselves may be substituted by amino or a mono- or di- alkyl amino groupor an acyl group), straight or branched chain lower thioalkoxy having 1-6 carbon atoms, acyloxy groups, amino, amino mono or disubstituted with straight or branched chain lower alkyl having 1-6 carbon atoms (said alkyl groups being optionally substituted with a hydroxy or amino group), mono- or disubstituted carbamyl where the CO group is bound to the atyl group and the substituents are lower alkyl or aryl lower alkyl, mono- or di-alkyl carbamates having up to 6 carbon atoms in each alkyl group or mono or diaryl carbamates additionally any two adjacent substituents on the aryl ring may be represented as $-X-(CH_2)_n-Y(CH_2)_mZ$ where X, Y and Z are either a direct bond, oxygen, sulfur, or NR where R is hydrogen or lower alkyl and n and m are 1, 2 or 3.

These compounds are selective partial agonists or antagonists at human NPY5 receptors and are useful in the diagnosis and treatment in mammals of feeding disorders such as obesity and bulimia as well as certain cardiovascular diseases such as

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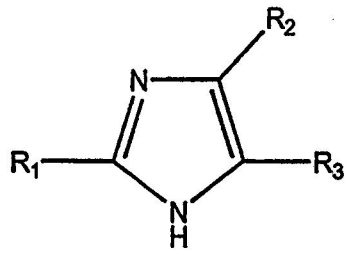
essential hypertension and congestive heart failure.

DETAILED DESCRIPTION OF THE INVENTION

The compounds of use in the present invention can be described by general Formula:



where R_1 is an aryl group, which may be unsubstituted or mono, di or trisubstituted. The aryl groups from which R_1 may be selected are typically mono or bicyclic groups, in which case only the ring bound to the imidazole group need be aromatic, and may be carbocyclic or heterocyclic containing up to 4 hetero atoms but no more than 2 hetero atoms in each ring. Typically each ring of the aryl group is a five or six membered ring. Suitable aryl groups include phenyl, naphthyl, indanyl, pyrrolyl, furanyl, thienyl, pyridyl, pyrimidinyl, indolyl, benzofuranyl, thianaphthyl, isoindolyl, isobenzofuranyl, quinolinyl, isoquinolinyl, quinazolinyl, indazolyl, quinoxalinyl, cinnolinyl 1,2,3,4-tetrahydroquinolinyl, 2,3-dihydroindolyl, phenomorpholinyl, benzodioxazinyl, phenothiomorpholinyl and methylenedioxyphenyl groups. Suitable substituents include: halogen, trihalomethyl, cyano, hydroxy, straight or branched chain lower alkyl having 1-6 carbon atoms, straight or branched chain lower alkoxy having 1-6 carbon atoms, which alkyl and alkoxy groups themselves may be substituted by an amino or a mono- or di-alkylamino group or a mono- or di-alkaryl group such as benzyl or by an acyl group, straight or branched chain lower thioalkoxy having 1-6 carbon atoms, acyloxy groups such as alkanoyloxy groups of from 2 to 7 carbon atoms, such as acetoxy, and aroyloxy groups such as benzoyloxy, amino, amino mono or disubstituted with straight or branched chain lower alkyl having 1-6 carbon atoms, said alkyl groups being optionally substituted with a hydroxy or amino group, mono or disubstituted carbamyl groups wherein the substituent is lower alkyl or aryl lower alkyl, mono or disubstituted carbamyl where the CO group is bound to the aryl ring and the substituents are lower alkyl or aryl lower alkyl, carbamates such as mono- or

6-[(2-(4-fluoropheny)limidazol-4-yl)-2H,3H-benzo[e]1,4dioxin

6-{2-[4-trifluoromethyl)pheny]limidazol-4-yl}-2H,3H-benzo[e]1,4dioxin

6-[(2-(4-fluoropheny)-5-methylimidazol-4-yl)-2H,3H-benzo[e]1,4dioxin

6-(2-2-pyridyl)imidazol-4-yl)-2H,3H-benzo[e]1,4dioxin

6-(2-phenylimidazol-4-yl)benzo[b]morpholine

4-methyl-6-{2-phenylimidazol-4-yl)benzo[b]morpholine

4-propyl-7-{2-phenylimidazol-4-yl)benzo[b]morpholine

6-[2-(4-fluorophenylimidazol-4-yl)benzo[b]morpholine

6-[2-(4-fluorophenylimidazol-4-yl)-4-methylbenzo[b]morpholine

4-ethyl-6-[2-(4-fluorophenyl)imidazol-4-yl)benzo[b]morpholine

6-[2-(4-fluorophenylimidazol-4-yl)-2H,3H,4H-benzo[e]1,4-thiazine

4-methyl-6-[2-(4-fluorophenylimidazol-4-yl)-2H,3H,4H-benzo[e]1,4-thiazine

4-(4-chlorophenyl-2-(2-pyridyl)imidazole

2-[4-(4-chlorophenyl)imidazol-2-yl]pyrazine

4-[2-(4-fluorophenyl)imidazol-4-yl-chlorobenzene

2-indole-3yl-5-methyl-4-phenylimidazole

2-[4-(4-chlorophenyl)imidazol-2-yl]thiophene

4-(6-chloro(2-pyridyl)-2-phenylimidazole

dimethyl[2-(2-phenylimidazol-4-yl)(4-pyridyl)]amine

[3-(2-phenylimidazol-4-yl)phenyl]methylamine

{3-[2-(4-fluorophenyl)imidazol-4-yl]phenyl}methylamine

methyl[3-(2-phenylimidazol-4-yl)phenyl]methyl}amine

dimethyl[3-(2-phenylimidazol-4-yl)phenyl]methyl}amine

methyl[4-(2-phenylimidazol-4-yl)phenyl]methyl}amine

dimethyl[4-(2-phenylimidazol-4-yl)phenyl]methyl}amine

ethyl[3-(2-phenylimidazol-4-yl)phenyl]amine

({3-[2-(4-fluorophenyl)imidazol-5-yl]phenyl}methyl)(2-methylbutyl)amine

(ethylbutyl)({3-[2-(4-fluoropheyl)imidazol-5-yl]phenyl}methyl)amine

(1,2-dimethylpropyl)({3-[2-(4-fluorophenyl)imidazol-5-yl}methyl)amine

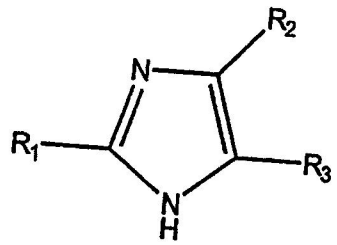
(3-cyclohexyl-1-phenylpropyl)methyl{[3-(2-phenylimidazol-5-yl)phenyl]methyl}amine

({3-[2-(4-fluorophenyl)imidazol-5-yl]phenyl}methyl)methylbutyl)amine

(2-methylbutyl){[3-(2-phenylimidazol-5-yl)phenyl]methyl}amine

CLAIMS

1. A pharmaceutical composition for interacting with an NPY5 receptor comprising an amount of a compound of the formula:



or a pharmaceutically acceptable salt

where R_1 is an unsubstituted or mono, di or trisubstituted aryl group wherein said aryl group is mono or bicyclic, in which case only the ring bound to the imidazole ring need be aromatic, and said aryl group is carbocyclic or contain up to 2 hetero atoms which may be nitrogen, oxygen or sulfur and said substituents are individually selected from the group consisting of halogen, trihalomethyl, cyano, hydroxy, straight or branched chain lower alkyl having 1-6 carbon atoms, straight or branched chain lower alkoxy having 1-6 carbon atoms (which alkyl or alkoxy groups themselves may be substituted by an amino or a mono- or di-alkyl amino group or by a mono- or di-alkarylamino group or by an acyl group), straight or branched chain lower thioalkoxy having 1-6 carbon atoms, acyloxy groups, amino, amino mono or disubstituted with straight or branched chain lower alkyl having 1 - 6 carbon atoms, said alkyl groups being optionally substituted with a hydroxy or amino group, an alkyl, aryl or alkaryl amide group, the nitrogen atom of which is is bound to the aryl group, mono or di substituted carbamyl wherein the CO group is bound to the aryl ring and each substituent is a lower alkyl or aryl lower alkyl group, mono or di-alkyl carbamates having up to 6 carbon atoms in each alkyl group or mono or diaryl carbamates or any 2 adjacent substituents on the aryl ring may be represented as -X-$(CH_2)_n$-Y-$(CH_2)_m$-Z- where X, Y and Z are either a direct bond, oxygen, sulfur, or NR where R is hydrogen or lower alkyl and n and m are 1, 2 or 3;

one of R_2 and R_3 is selected from the group consisting of hydrogen, hydroxymethyl, alkoxymethyl having up to 6 carbon atoms in each alkoxy group, straight or branched chain lower alkyl having 1-6 carbon atoms, cyano, or a carboxylic

or carboxylate ester group wherein the esterifying group typically contains up to six carbon atoms;

the other of R_2 and R_3 is an aryl group which is either unsubstituted or mono, di or trisubstituted wherein said aryl groups are mono or bicyclic (in which case only the ring bound to the imidazole ring need be aromatic) and may be carbocyclic or contain up to 2 hetero atoms and said substituents are individually selected from the group consisting of halogen; trihalomethyl; cyano; hydroxy; straight or branched chain lower alkyl having 1-6 carbon atoms; straight or branched chain lower alkoxy having 1-6 carbon atoms (which alkyl and alkoxy groups themselves may be substituted by an amino group or a mono- or di-alkylamino group , the alkyl groups of which may form a ring together with the nitrogen to which they are bound, or a mono- or di-alkaryl group or by an acyl group or a carbamate); straight or branched chain lower thioalkoxy having 1-6 carbon atoms; acyloxy groups; amino; amino mono or disubstituted with straight or branched chain lower alkyl having 1-6 carbon atoms (said alkyl groups being optionally substituted with a hydroxy or amino group); an alkyl, aryl or alkaryl amide group , the nitrogen atom of which is bound to the aryl group, mono- or di-substituted carbamyl wherin the CO group is bound to the aryl group and the substituents are lower alkyl or aryl lower alkyl; mono- or di-alkyl carbamates having up to 6 carbon atoms in each alkyl group; or mono or diaryl carbamates; additionally any two adjacent substituents on the aryl ring may be represented as $-X-(CH_2)_n-Y-(CH_2)_m-Z-$ where X, Y and Z are either a direct bond, oxygen, sulfur, or NR where R is hydrogen or lower alkyl and n and m are 1,2 or 3;

and a pharmaceutically acceptable diluent, carrier or solvent.

2. A composition as claimed in claim 1, wherein each aryl group is selected independently from the group consisting of unsubstituted or substituted phenyl, naphthyl, indanyl, pyrrolyl, furanyl, thienyl, pyridyl, pyrimidinyl, indolyl, benzofuranyl, thianaphthyl, isoindolyl, isobenzofuranyl, quinolinyl, isoquinolinyl, quinazolinyl, indazolyl, quinoxalinyl, cinnolinyl 1,2,3,4-tetrahydroquinolinyl, 2,3-dihydroindolyl, phenomorpholinyl, benzodioxazinyl, phenothiomorpholinyl and methylenedioxyphenyl groups

3. A composition as claimed in claim 2, wherein R_1 is a substituted or unsubstituted phenyl or naphthyl group.

4. A composition according to claim 2, wherein R_1 is a phenyl, 4-fluorophenyl, pyridin-2-yl or a 2- or 3-thienyl group.

5. A composition according to claim 1, wherein the non-aryl R_2 or R_3 group is selected from hydrogen and, alkyl.

6. A composition according to claim 1, wherein whichever of R_2 and R_3 is aryl is selected from the group consisting of phenyl, 2- or 3-thienyl, 1,4 benzodioxan-6-yl, benzo[b]morpholinyl, and naphthyl optionally bearing up to three substituents selected from halo, cyano, alkoxy and alkyl groups.

7. A composition according to claim 6, wherein said aryl group bears one or two substituents selected from the group consisting of alkyl of 1-6 carbon atoms, fluoro, chloro, bromo, cyano and alkoxy of 1 to 6 carbon atoms.

8. A composition according to claim 6, wherein said aryl group bears an N-substituted aminomethyl substituent.

9. A composition according to claim 3, wherein whichever of R_2 and R_3 is aryl is selected from the group consisting of phenyl, 2- or 3-thienyl, 1,4 benzodioxan-6-yl, benzo[b]morpholinyl, and naphthyl optionally bearing up to three substituents selected from halo, cyano, alkoxy and alkyl groups.

10. A composition according to claim 9, wherein said aryl group bears one or two substituents selected from the group consisting of alkyl of 1-6 carbon atoms, fluoro, chloro, bromo, cyano and alkoxy of 1 to 6 carbon atoms.

11. A composition according to claim 9, wherein said aryl group bears an N-substituted aminomethyl substituent.

12. A composition according to claim 6, wherein R_2 or R_3 is selected from the group consisting of 4-methylphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 3-bromophenyl, 4-bromophenyl, 4-chlorophenyl, 4-fluorophenyl, 3-cyanophenyl, 4-cyanophenyl, 4-methoxy-2-fluorophenyl, 4-ethoxy-2-fluorophenyl, 3-fluoro-4-methoxyphenyl, 2-fluoro-4-methoxyphenyl, 3-acetylphenyl, naphthyl, 1,4-benzodioxan-6-yl and benzo [b] morpholinyl, 4-alkyl benzo[b]morpholinyl and 4-alkyl-2H,3H,4H-benzo[e]1,4-thiazinyl.

13. A composition according to claim 6, wherein R_2 or R_3 is selected from the group consisting of 3-methylaminophenyl. 4-dimethylaminophenyl, 3-ethylaminophenyl, 3-(2-methylbutylaminomethyl)phenyl, 3-(ethylbutyl-