



Industria y Comercio

S U P E R I N T E N D E N C I A

Delegatura de propiedad Industrial

División de Nuevas Creaciones

PCT
SOLICITUD

PATENTE DE INVENCION

21. EXPEDIENTE No.

06-7747

54. TÍTULO Derivados de 1-sulfonilindol, su preparación y su uso como ligandos de 5-HT-6

51. CLASIFICACIÓN INTERNACIONAL A61K 31/404, C07D 209/40, A61P 3/04, 25/00 C07D.

71. SOLICITANTE Laboratorios del Dr Esteve S.A.

DOMICILIO Barcelona, España

74. APODERADO Delia María Rodríguez D' Alemán

22. BOGOTÁ, D. C., Envío 27, 2006.

FORMULARIO ÚNICO DE SOLICITUD DE PATENTE
PCT

ENTRADA EN FASE NACIONAL 28-01-2006

1) SOLICITUD DE:			
☒ Patente de invención		☐ Patente de Modelo de Utilidad	
☐ Capítulo I..		☒ Capítulo II.	
2) LICITANTE (71)	Nombre: LABORATORIOS DEL DR. ESTÉVE S.A. Dirección: Avenida Mare de Deu de Montserrat 221, E-08041 Barcelona, España Nacionalidad o domicilio: Barcelona, España Lugar de constitución: España		IDENTIFICACIÓN C.C. ☐ NIT: ☐ C.E. ☐ OTRO ☐ NÚMERO Cual _____
	Teléfono: _____ Fax: _____ E. Mail: _____		
3) REPRESENTANTE O APODERADO	Nombre: DILIA MARÍA RODRÍGUEZ D'ALEMAN Dirección: Carrera 11 N°. 86-53 Piso 6 Bogotá D.C. Teléfono: 6181088 Fax: 6350824 E. Mail: info@clarkemodet.com.co		IDENTIFICACIÓN C.C. ☒ NIT: ☐ C.E. ☐ OTRO ☐ NÚMERO: 41.654.882 TP: 20824 CSJ
4) INVENTOR (ES) (72)	Nombre: 1. MERCE VIDAL, Ramon; 2. CODONY SOLER, Xavier; DORDALZUERAS, Alberto Dirección: 1. C/Casanova 284 4º 1a, E-08021 Barcelona, España; 2. C/Lepanto 71-77 2º 1a, E-08016 Barcelona, España; 3. C/Maladeta 26, 3º 3 a, E-08016 Barcelona, España Nacionalidad o Domicilio: Todos lo anteriores, Españoles		
5) PCT (86)			
Solicitud Internacional No. PCT/EP2004/008516 Fecha: Julio 29, 2004			
Publicación Internacional No. WO2005/013974 A1 Fecha: Febrero 17, 2005			
6) Título (54) DERIVADOS DE 1-SULFONILINDOL, SU PREPARACIÓN Y SU US COMO LIGANDOS DE 5-HT-6			
7) Clasificación Internacional: A61K 31/404, C07D 209/40, A61P 3/04, 25/00, C07D 401/04			
8) PRIORIDAD		33) País de Origen	(32) Fecha
SI ☒ NO ☐		ESPAÑA	JULIO 30, 2003
			(31) Número de Solicitud P200301806
9) Comprobante de pag. N°. 06 3290 Fecha: Enero 27, 2006			
Instrucciones para el diligenciamiento del presente formulario. Ver reverso de esta pagina			

212.

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

NIT : 800176089-2

SUPERINDUSTRIA Y COMERCIO
Radicacon : 06007747 00000000
Fecha (RFB): 2006-01-27 17:44:25
Tramite : 011 PCT-PATENT 379 FASE NACI 411 PRESENTA
Dependencia: 2920 DIVISION DE NUEVAS CREACIONES

Folios: 164

RECIBO OFICIAL DE CAJA : 06 - 7,290
FECHA : EMERD 27 DE 2006

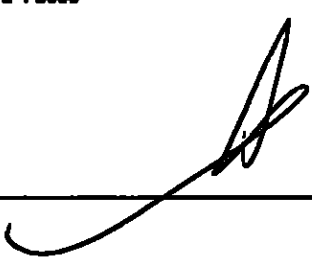
***** CONSIGNACION *****

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PGO	Vr. PAGO
CLARKE NODET Y CD. COLOMB	CONSIGNACION	BANCO POPULAR	050-00110-6	49044331	27/01/2006	3,364,000.00

***** CONCEPTO *****

CANT.	RENTISTICO	CONCEPTO	TOTAL CONCEPTO
1	50005-01-01	SOLICITUDES	
1		TRAMITES DE SOL. DE PATENTE DE IN	463,000.
		TOTAL :	463,000.00

SUN: CUATROCIENTOS SESENTA Y TRES MIL PESOS

RESPONSABLE : 

RECIBO DE CAJA APLICADO AL EXPEDIENTE No. _____

10)

ANEXOS

- ☒ Comprobante de pago de la tasa de presentación de la solicitud
- ☐ Comprobante de pago por reivindicación de prioridad
- ☐ Documento que acredite la existencia y representación legal cuando el solicitante sea persona jurídica
- ☒ Poderes, si fuera el caso
- ☐ Documento de cesión del inventor al solicitante o a su causante
- ☐ Declaraciones
- ☒ Copia de la solicitud internacional. (Resumen, descripción, reivindicación, Dibujos).
- ☒ Traducción de la solicitud internacional al castellano. (Resumen, descripción, reivindicación, Dibujos)
- ☒ Copia del examen preliminar efectuado por la IPEA
- ☐ De ser el caso, copia del contrato de acceso
- ☐ De ser el caso, documento que acredite la licencia o autorización de uso de conocimientos tradicionales de las comunidades indígenas
- ☐ De ser el caso, certificado de depósito del material biológico
- ☐ Arte final 12 x 12 y 6 x 6 cm
- ☐ De ser el caso, información sobre otras solicitudes de patente o títulos obtenidos en el extranjero por el mismo titular o su causante, relacionados parcial o totalmente con la invención de esta solicitud.
- ☒ Otros:
1. Reporte internacional de búsqueda
 2. Solicitud PCT

11) FIGURA CARACTERÍSTICA:

12) Solicitud concesión de la patente,

NOMBRE: DILIA RODRÍGUEZ D'ALEMAN

FIRMA: 

C.C. 41.654.882 de Bogotá TP 20824 CSJ

Instrucciones para el diligenciamiento del presente formulario. Ver reverso de esta página

COLOMBIA

Carrera 11 n° 93-43, Of. 404 Bogotá Colombia Tel: (57 1) 6350813-Fax: (57 1) 6350824-E-mail:clarkemoder@clarkemoder.com.co

PODER

Yo (nosotros), abajo firmante(s)

en mi (nuestro) carácter de representante(s) legales de

una sociedad organizada y existente de acuerdo con las leyes de

y en actual cumplimiento de su objeto social, con domicilio en

por el presente instrumento confiero (conferimos) poder especial a favor de DILIA MARIA RODRIGUEZ D'ALEMAN, con Cédula de Ciudadanía No. 41.654.882 de Bogotá, y tp. 20824 y CLAUDIA LUCIA CARO RAMIREZ, con Cédula de Ciudadanía No. 40.017.374 de Tunja, y tp. 36448, con domicilio en Bogotá, Colombia, para que actuando en su orden en nombre del (de la) otorgante le (la) representen ante cualquier entidad, autoridad y/o persona, especialmente ante las del orden Administrativo, Contencioso Administrativo, Judicial, Tribunales de Arbitramento y/o cualquier otro en lo referente a los siguientes asuntos:

- 1) Solicitar, tramitar, obtener y/o registrar cualquiera de las modalidades de Propiedad Industrial, tales como: patentes de invención, modelos de utilidad; diseños industriales, variedades vegetales; marcas, lemas, nombres y enseñanzas comerciales y denominaciones de origen; así como sus renovaciones, prórrogas, transferencias, cambios de nombre y/o domicilio, contratos y licencias.
- 2) Solicitar, tramitar, obtener y/o registrar derechos de autor, en cualquiera de sus presentaciones así como la protección de secretos industriales y know-how.
- 3) Solicitar, tramitar, obtener y/o registrar registros sanitarios, permisos y/o licencias de funcionamiento; así como sus renovaciones o prórrogas, transferencias, cambios de nombre y/o domicilio, contratos y licencias.
- 4) Ejercer acciones de oposición, observación, reclamos, reconsideración, reposición, apelación, cancelación administrativa o judicial, nulidad, protección al consumidor, concesión de licencias, protección de secretos industriales y demás acciones y recursos relacionados con derechos derivados de los asuntos arriba indicados y en contra de la competencia desleal, acciones derivadas de la obtención o explotación de licencias, acciones de indemnización de perjuicios. También podrá(s) intervenir en juicios civiles, comerciales, penales, contencioso-administrativos, tutelas y de policía; en acciones o juicios promovidos por el (la) mandante o en contra el (ella).
- 5) Registrar nombres de dominio ante la entidad competente.
- 6) En el ejercicio de este mandato los mandatarios arriba mencionados quedan facultados para: conciliar, cancelar, transigir, comprometer en árbitros, desistir, recibir y tomar posesión de la cosa objeto de litigio y renunciar o desistir a derechos concedidos o en curso de concesión, admitir los hechos del proceso.
- 7) Ratificar o no la agencia oficiosa.
- 8) Así mismo faculto (facultamos) a los mencionados apoderados para recibir notificaciones y designar apoderados judiciales o extrajudiciales, sustituir el presente poder y revocar las sustituciones que hicieren.

Dado y firmado en

a los

días de

Granted and signed at Barcelona

on this

day of 31 ENE.

José María RAFOLS FERRER
Attorney

POWER OF ATTORNEY

I (we), Jose Maria RAFOLS FERRER the undersigned legal representative(s) of

Laboratorios del Dr. Ennave S. A:

an organization existing under the laws of

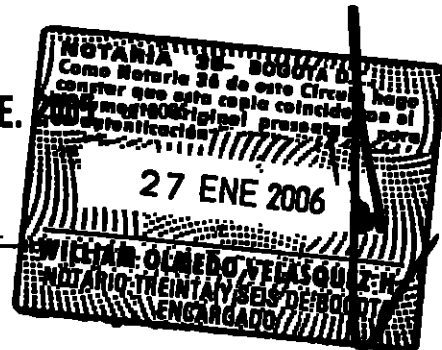
SPAIN

and in present execution of its business activity, domiciled at
Av. Mare de Déu de Montserrat, E-08041, SPAIN

do hereby grant POWER OF ATTORNEY to DILIA MARIA RODRIGUEZ D'ALEMAN, identification card No. 41.654.882 of Bogotá, and tp. 20824 and CLAUDIA LUCIA CARO RAMIREZ, tp. 36448, identification card No. 40.017.374 of Tunja, residing in Bogotá, Colombia, to act in the order of their appointment in behalf of grantor before any entity, authority and/or natural or juridical person, specially before those Administrative, Administrative-Contentious, Judicial, arbitration courts, and/or any other, in all matters concerning the following:

PCT/EP03/03629

- 1) To apply, process, obtain and/or register any of the modalities of Industrial Property, such as: Patents of Invention, Utility Models; Designs, plant varieties; Marks, Slogans, Trade Names and emblems and appellations of Origin; as well as their renewals, assignments, changes of name and/or domicile, agreements and licenses.
- 2) To apply, process, obtain and/or register copyrights of any kind as well as protection of industrial secrets or know-how.
- 3) To apply, process, obtain and/or register sanitary registrations, operating authorizations and/or licenses; as well as their renewals or assignments, changes of name and/or domicile, agreements and licenses.
- 4) To bring actions of opposition, observations, claims, reconsideration, appeal or legal remedies, cancellations, nullity, protection to the consumer, granting of licenses, protection of trade secrets and other actions related with rights derived from the above-mentioned matters and against the unfair competition, actions resulting from the obtaining or exploitation of licenses, recovering damages actions. They can also intervene or participate in Civil, Commercial, Criminal or Contentious-Administrative Trials; the actions for writ mandamus, police actions; in actions, lawsuits or litigations instituted by the grantor or against him.
- 5) To register domain names before the competent entity.
- 6) To the effect of this mandate the above-named proxy are empowered to: conciliate, cancel, settle, submit to arbitration, withdraw and to receive and take possession of the litigation related object and waive or renounce the rights granted or in process of granting, admit the facts of the case.
- 7) To ratify or not the officious agency.
- 8) I (we) hereby appoint the afore mentioned attorneys with powers to receive notifications and to designate judicial and extrajudicial attorneys, substitute this Power of Attorney and to revoke such substitutions.

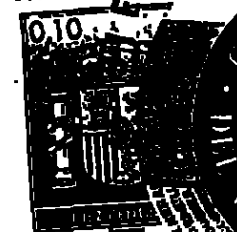


-GENCIA.- La extiendo yo, TOMÁS GIMÉNEZ DUART, Notario del Ilustre Colegio de Notarios de Cataluña, para hacer constar que la firma que antecede de DON JOSÉ MARÍA RAFOLS FERRER, como apoderado de la entidad "LABORATORIOS DEL DR. ESTEVE, S.A.", la considero legítima por haber sido puesta en mi presencia. Hago constar que tiene concedido un poder otorgado a su favor, mediante escritura autorizada ante mí el día 1 de febrero de 2.000, bajo el número 480 de protocolo, que causó la inscripción 90ª en la hoja número B-19079, folio 190 del tomo 21254, en el Registro Mercantil de Barcelona, cuyo poder le faculta para este acto.

Igualmente hago constar que la sociedad LABORATORIOS DEL DR. ESTEVE, S.A., es una compañía mercantil de nacionalidad española, que se rige por las leyes de España, debidamente inscrita en el Registro Mercantil de Barcelona, al tomo 21254, folio 190, hoja número B-19079, inscripción 76ª y con número de identificación fiscal A-08-037236.

Y para que así conste y surta efecto en Colombia, la extiendo en Barcelona, a 31 de enero de 2005.

Asiento número 131, Libro Indicador número 8.





10/2004



5Y0174010

5/

10/2004

APOSTILLE (o legalización única)

(Convención de la Haya du 5 de octubre, 1961-Real Decreto/1978,
de 2 de octubre)

1. País ESPAÑA

El presente documento público

2. ha sido firmado por D. Tomás Giménez Duart-----

3. Actuando en calidad de Notario, en legitimación de firma--

de D. José María Ràfols Ferrer, puesta al pie de un Poder,

en representación de "LABORATORIOS DEL DR. ESTEVE, S.A.", -

libro indicador n°. 131, de fecha 31 de enero de 2005.-----

4. Se halla sellado/timbrado con el de su Notaría.

C E R T I F I C A D O

5. En BARCELONA

6. El 01 de Febrero de 2005.

7. Por DON RAFAEL MARTÍNEZ DIE, Secretario.

8. Con el N° : -6155-

9. Sello/timbre:

10. Firma:



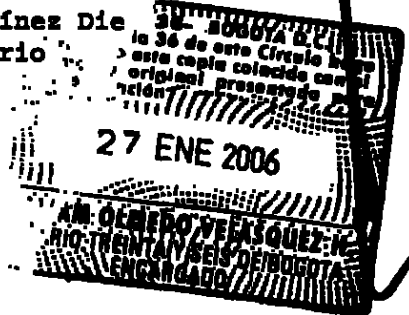
SELO DE
LEGITIMACIONES Y
LEGALIZACIONES



NOTA PUBLICA
FIDE

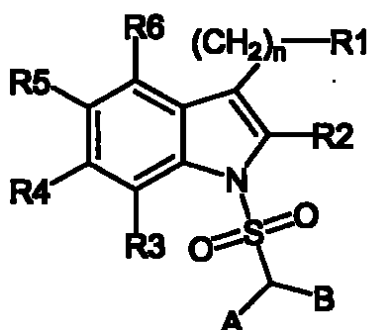


Rafael Martínez Die
Secretario



1-SULFONYLINDOLE DERIVATIVES, THEIR PREPARATION AND THEIR USE AS 5-HT₆ LIGANDS

5 The present invention refers to new sulfonamide derivatives, of general formula (Ia, Ib, Ic),



(Ia, Ib, Ic),

optionally in form of one of their stereoisomers, preferably enantiomers or diastereomers, their racemate, or in form of a mixture of at least two of their stereoisomers, preferably enantiomers or diastereomers, in any mixing ratio, or their salts, preferably their corresponding, physiologically acceptable salts, or corresponding solvates; to the processes for their preparation, to their application as medicaments in human and/or veterinary therapeutics, and to the pharmaceutical compositions containing them.

15

The new compounds of the present invention can be used in the pharmaceutical industry as intermediates and for preparing medicaments.

20 The superfamily of serotonin receptors (5-HT) comprises 7 classes (5-HT₁-5-HT₇), which cover 14 human subclasses [D. Hoyer, et al., *Neuropharmacology*, 1997, 36, 419]. The 5-HT₆ receptor has been the last serotonin receptor identified by molecular cloning in rats [F.J. Monsma, et al., *Mol. Pharmacol.*, 1993, 43, 320; M. Ruat, et al., *Biochem. Biophys. Res. Commun.*, 1993, 193, 268] as well as in humans [R. Kohen, et al., *J.*

Neurochem., 1996, 66, 47]. The compounds with an affinity for the 5-HT₆ receptor are useful in treating different disorders of the Central Nervous System and of the Gastrointestinal system, as well as the irritable bowel syndrome. The compounds with an affinity for the 5-HT₆ receptor are useful for treating anxiety, depression and cognitive memory disorders [M. Yoshioka, et al., *Ann. NY Acad. Sci.*, 1998, 861, 244; A. Bourson, et al., *Br. J. Pharmacol.*, 1998, 125, 1582; D.C. Rogers, et al., *Br. J. Pharmacol. Suppl.*, 1999, 127, 22P; A. Bourson, et al., *J. Pharmacol. Exp. Ther.*, 1995, 274, 173; A.J. Sleight, et al., *Behav. Brain Res.*, 1996, 73, 245; T.A. Branchek, et al., *Annu. Rev. Pharmacol. Toxicol.*, 2000, 40, 319; C. Routledge, et al., *Br. J. Pharmacol.*, 2000, 130, 1606]. It has been shown that the typical and atypical antipsychotics for treating schizophrenia have a high affinity for the 5-HT₆ receptors [B.L. Roth, et al., *J. Pharmacol. Exp. Ther.*, 1994, 268, 1403; C.E. Glatt, et al., *Mol. Med.*, 1995, 1, 398; F.J. Mosma, et al., *Mol. Pharmacol.*, 1993, 43, 320; T. Shinkai, et al., *Am. J. Med. Genet.*, 1999, 88, 120]. The compounds with an affinity for the 5-HT₆ receptor are useful for treating infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder) [W.D. Hirst, et al., *Br. J. Pharmacol.*, 2000, 130, 1597; C. Gérard, et al., *Brain Research*, 1997, 746, 207; M.R. Pranzatelli, *Drugs of Today*, 1997, 33, 379].

Patent application WO 01/32646 discloses sulfonamides derived from bicycles whereby each of the rings is 6-membered, aromatic or heteroaromatic rings with 5-HT₆ receptor antagonist activity.

Patent application EP 0 733 628 discloses sulfonamides derived from indole with 5-HT_{1F} receptor antagonist activity, useful for the treatment of migraines.

25

Furthermore, it has been shown that the 5-HT₆ receptor plays a role in the ingestion of food [Neuropharmacology, 41, 2001, 210-219].

Eating disorders, particularly obesity, are a serious and increasingly frequent threat for the health of humans of all ages, since these diseases increase the risk of developing other serious and even mortal diseases, preferably diabetes and coronary artery diseases.

30

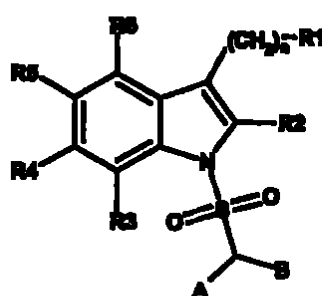
Therefore, an object of the present invention was to provide new compounds, particularly suitable as active substances in medicaments, preferably in medicaments for 5-HT₆ receptor regulation, for the prophylaxis and/or treatment of a disorder or disease related to food intake, preferably for the regulation of appetite, for the maintenance, increase or reduction of body weight, for the prophylaxis and/or treatment of obesity, bulimia, anorexia, cachexia or type II diabetes (non insulin dependent diabetes mellitus), preferably type II diabetes caused by obesity, for the prophylaxis and/or treatment of gastrointestinal tract disorders, preferably irritable bowel syndrome, for cognitive enhancement, for the prophylaxis and/or treatment of disorders of the central nervous system, anxiety, panic disorders, depression, preferably bipolar disorders, cognitive memory disorders, senile dementia processes, neurodegenerative disorders, preferably Alzheimer's disease, Parkinson's disease, Huntington's disease and/or Multiple Sclerosis, schizophrenia, psychosis or infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder), and other disorders mediated by the 5-HT₆ serotonin receptor in humans and/or in animals, preferably in mammals, more preferably in humans.

It has been found that the 1-sulfonylindole derivatives of general formulas (Ia, Ib, Ic) described below show an affinity for the 5-HT₆ receptor.

These compounds are therefore suitable for preparing a medicament for the prophylaxis and/or treatment of a disorder or disease related to food intake, preferably for the regulation of appetite, for the maintenance, increase or reduction of body weight, for the prophylaxis and/or treatment of obesity, bulimia, anorexia, cachexia or type II diabetes (non insulin dependent diabetes mellitus), preferably type II diabetes caused by obesity, for the prophylaxis and/or treatment of gastrointestinal tract disorders, preferably irritable bowel syndrome, for cognitive enhancement, for the prophylaxis and/or treatment of disorders of the central nervous system, anxiety, panic disorders, depression, preferably bipolar disorders, cognitive memory disorders, senile dementia processes, neurodegenerative disorders, preferably Alzheimer's disease,

Parkinson's disease, Huntington's disease and/or Multiple Sclerosis, schizophrenia, psychosis or infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder), and other disorders mediated by the 5-HT₆ serotonin receptor in humans and/or in animals, preferably in mammals, more preferably in humans. These compounds are also suitable for the preparation of a medicament for cognitive enhancement.

Thus, one aspect of the present invention are compounds of general formula (Ia),



(Ia)

wherein

R¹ represents a -NR⁷R⁸ radical or a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing cycloaliphatic radical, which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system,

R², R³, R⁴, R⁵ and R⁶, identical or different, each represent hydrogen, halogen, cyano, nitro, a saturated or unsaturated, linear or branched aliphatic radical, a linear or branched alkoxy radical, a linear or branched alkylthio radical, hydroxy, trifluoromethyl, a saturated or unsaturated cycloaliphatic radical; an alkylcarbonyl radical, a phenylcarbonyl or a -NR⁹R¹⁰ group,

R⁷ and R⁸, identical or different, each represent hydrogen or a saturated or unsaturated, optionally at least mono-substituted linear or branched aliphatic radical,

- 5 with the proviso that R⁸ and R⁹ are not hydrogen at the same time, and if one of them, R⁸ or R⁹, is a saturated or unsaturated, linear or branched, optionally at least mono-substituted C₁-C₄ aliphatic radical, the other one is a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical with at least five carbon atoms,**

10

or

- 15 R⁷ and R⁸, together with the bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted, optionally at least one further heteroatom as a ring member containing heterocyclic ring which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system,**

- 20 R⁹ and R¹⁰, identical or different, each represent hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,**

or

25

- 25 R⁹ and R¹⁰, together with the bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted, optionally at least one further heteroatom as a ring member containing heterocyclic ring which may be condensed with a saturated or unsaturated, optionally at least mono-**
- 30 substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system,**

-6-

A and B, identical or different, each represent a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical

or

5

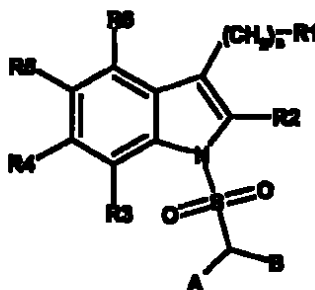
A and B, together with the carbon atom to which they are attached, form a saturated or unsaturated, but not aromatic, optionally at least mono-substituted cycloalkyl ring,

10 and

n is 0, 1, 2, 3, or 4,

optionally in form of one of their stereoisomers, preferably enantiomers or
15 diastereomers, their racemate or in form of a mixture of at least two of their stereoisomers, preferably enantiomers or diastereomers, in any mixing ratio, or a salt thereof, preferably a corresponding physiologically acceptable salt thereof or a corresponding solvate thereof.

20 Another aspect of the present invention are compounds of general formula (Ib)



(Ib)

25 wherein

-7-

R^1 is a $-NR^7R^8$ radical,

R^2 , R^3 , R^4 , R^5 and R^6 , identical or different, each represent hydrogen, halogen, cyano, nitro, a saturated or unsaturated, linear or branched aliphatic radical, a
5 linear or branched alkoxy radical, a linear or branched alkylthio radical, hydroxy, trifluoromethyl, a saturated or unsaturated cycloaliphatic radical, an alkylcarbonyl radical, a phenylcarbonyl or a $-NR^9R^{10}$ group,

R^7 and R^8 , identical or different, each represent hydrogen or a saturated or
10 unsaturated, optionally at least mono-substituted linear or branched C_{1-4} aliphatic radical,

R^9 and R^{10} , identical or different, each represent hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic
15 radical,

or

R^9 and R^{10} , together with the bridging nitrogen atom form a saturated or
20 unsaturated, optionally at least mono-substituted, optionally at least one further heteroatom as a ring member containing heterocyclic ring which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system,

25

A and B, identical or different, each represent a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical

or

30

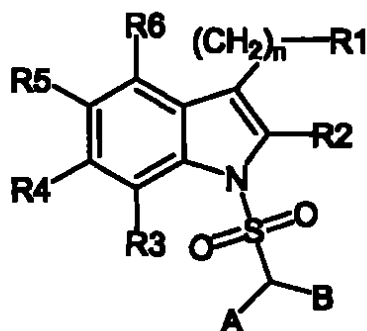
A and B, together with the carbon atom to which they are attached, form a saturated or unsaturated, but not aromatic, optionally at least mono-substituted cycloalkyl ring,

5 and

n is 0, 1, 2, 3 or 4;

optionally in form of one of its stereoisomers, preferably enantiomers or
10 diastereomers, their racemate or in form of a mixture of at least two of their stereoisomers, preferably enantiomers or diastereomers, in any mixing ratio, or a salt thereof, preferably a corresponding physiologically acceptable salt thereof or a corresponding solvate thereof.

15 Yet, another aspect of the present invention are compounds of general formula (Ic)



(Ic),

wherein

20 R^1 represents a $-NR^7R^8$ radical or a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing cycloaliphatic radical, which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system,

-9-

R^2 , R^3 , R^4 , R^5 and R^6 , identical or different, each represent hydrogen, halogen, cyano, nitro, a saturated or unsaturated, linear or branched aliphatic radical, a linear or branched alkoxy radical, a linear or branched alkylthio radical, hydroxy, trifluoromethyl, a saturated or unsaturated cycloaliphatic radical, an
5 alkylcarbonyl radical, a phenylcarbonyl or a $-NR^9R^{10}$ group,

R^7 and R^8 , identical or different, each represent hydrogen or a saturated or unsaturated, optionally at least mono-substituted linear or branched aliphatic radical,

10

or

R^7 and R^8 , together with the bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted, optionally at least one further
15 heteroatom as a ring member containing heterocyclic ring which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system,

20 R^9 and R^{10} , identical or different, each represent hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

or

25

R^9 and R^{10} , together with the bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted, optionally at least one further
heteroatom as a ring member containing heterocyclic ring which may be condensed with a saturated or unsaturated, optionally at least mono-
30 substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system,

A and B, identical or different, each represent a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical

or

5

A and B, together with the carbon atom to which they are bonded, form a saturated or unsaturated, but not aromatic, optionally at least mono-substituted cycloalkyl ring,

10 and

n is 0, 1, 2, 3, or 4,

optionally in form of one of their stereoisomers, preferably enantiomers or
15 diastereomers, their racemate or in form of a mixture of at least two of their stereoisomers, preferably enantiomers or diastereomers, in any mixing ratio, or a salt thereof, preferably a corresponding physiologically acceptable salt thereof or a corresponding solvate thereof.

20 If one or more of the moieties R^2 - R^{10} , A and B, represent an alkyl radical, an alkenyl radical or an alkynyl radical, which is substituted by one or more substituents, each one of these substituents can preferably be chosen from the group consisting of hydroxy, halogen, linear or branched C_1 - C_6 alkyl, linear or branched C_1 - C_6 alkoxy, linear or branched C_1 - C_6 perfluoroalkyl, linear or
25 branched C_1 - C_6 perfluoroalkoxy, or an optionally at least mono-substituted phenyl radical.

If said phenyl radical is substituted by one or more substituents as well, each one of these substituents can preferably be chosen from the group
30 consisting of fluorine, chlorine, bromine, a linear or branched C_1 - C_6 alkyl, a linear or branched C_1 - C_6 alkoxy, a linear or branched C_1 - C_6 alkylthio, a trifluoromethyl radical, a cyano radical and an $NR^{11}R^{12}$ radical, wherein R^{11} and

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R^{12} , identical or different, are defined as R^7 and R^8 .

If R^1 is a saturated or unsaturated, optionally at least one heteroatom as a ring member containing cycloaliphatic radical, which is substituted by one or more substituents and/or if R^1 comprises a saturated or unsaturated, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system, which is substituted by one or more substituents, each one of these substituents can, unless defined otherwise, preferably be chosen from the group consisting of hydroxy, fluorine, chlorine, bromine, linear or branched C_1 - C_6 alkyl, linear or branched C_1 - C_6 alkoxy, linear or branched C_1 - C_6 perfluoroalkyl, linear or branched C_1 - C_6 perfluoroalkoxy and benzyl, more preferably from the group consisting of linear or branched C_1 - C_6 alkyl and benzyl.

The heteroatoms of the cycloaliphatic radical and/or of the mono- or bicyclic cycloaliphatic ring can, independently from one another, preferably be chosen from the group consisting of nitrogen, sulphur and oxygen, more preferably nitrogen is chosen as a heteroatom.

Said cycloaliphatic radical may contain 0, 1, 2 or 3 heteroatoms chosen from the above mentioned group, preferably it contains 0, 1 or 2 heteroatoms chosen from the above mentioned group.

If R^7 and R^8 together with the bridging nitrogen form a saturated or unsaturated, optionally at least one further heteroatom as a ring member containing heterocyclic ring, which is substituted by one or more substituents and/or condensed with a saturated or unsaturated, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system, which is substituted by one or more substituents, each one of these substituents can, unless defined otherwise, preferably be chosen from the group consisting of hydroxy, fluorine, chlorine, bromine, linear or branched C_1 - C_6 alkyl, linear or branched C_1 - C_6 alkoxy, linear or branched C_1 - C_6

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perfluoroalkyl, linear or branched C₁-C₈ perfluoroalkoxy and benzyl, more preferably from the group consisting of linear or branched C₁-C₈ alkyl and benzyl.

5 If the heterocyclic ring contains one or more additional heteroatoms, and/or if one or both mono- or bicyclic rings contain one or more heteroatoms, these heteroatoms can, independently from one another, preferably be chosen from the group consisting of nitrogen, sulphur and oxygen, more preferably nitrogen is chosen as a heteroatom.

10

Said heterocyclic ring may contain 0, 1, 2 or 3 additional heteroatoms chosen from the above mentioned group, preferably it contains 0 or 1 heteroatoms chosen from the above mentioned group.

15 If A is an aliphatic radical, i.e. an alkyl, alkenyl or alkynyl radical, substituted by one or more substituents, each one of these substituents can preferably be chosen from the group consisting of hydroxy, halogen, linear or branched C₁-C₈ alkyl, linear or branched C₁-C₈ alkoxy, linear or branched C₁-C₈ perfluoroalkyl, linear or branched C₁-C₈ perfluoroalkoxy or an optionally at least
20 mono-substituted phenyl radical.

If said phenyl radical is substituted by one or more substituents as well, each one of these substituents can preferably be chosen from the group consisting of fluorine, chlorine, bromine, linear or branched C₁-C₈ alkyl, linear or branched
25 C₁-C₈ alkoxy, linear or branched C₁-C₈ alkylthio, a trifluoromethyl radical, a cyano radical and an NR¹³R¹⁴ radical, wherein R¹³ and R¹⁴, identical or different, are defined as R⁷ and R⁸.

If B is an aliphatic radical, i.e. an alkyl radical, an alkenyl radical or an
30 alkynyl radical, which is substituted by one or more substituents, each one of these substituents can preferably be chosen from the group consisting of hydroxy, halogen, linear or branched C₁-C₈ alkyl, linear or branched C₁-C₈

alkoxy, linear or branched C₁-C₈ perfluoroalkyl, linear or branched C₁-C₈ perfluoroalkoxy, or an optionally at least mono-substituted phenyl radical.

If said phenyl radical is substituted by one or more substituents as well, each
5 one of the substituents can preferably be chosen from the group consisting of
fluorine, chlorine, bromine, linear or branched C₁-C₈ alkyl, linear or branched
C₁-C₈ alkoxy, linear or branched C₁-C₈ alkylthio, a trifluoromethyl radical, a
cyano radical and a NR¹⁵R¹⁶ radical, wherein R¹⁵ and R¹⁶, identical or different,
are defined as R⁷ and R⁸.

10

If A and B together with the carbon atom to which they are bonded form a
saturated or unsaturated, but not aromatic, cycloalkyl ring, which is substituted
by one or more substituents, each one of these substituents can preferably be
chosen from the group consisting of hydroxy, halogen, linear or branched C₁-C₈
15 alkyl, linear or branched C₁-C₈ alkoxy, linear or branched C₁-C₈ perfluoroalkyl,
linear or branched C₁-C₈ perfluoroalkoxy or an optionally at least mono-
substituted phenyl radical.

If said phenyl radical is substituted by one or more substituents as well, each
20 one of these substituents can preferably be chosen from the group consisting of
fluorine, chlorine, bromine, linear or branched C₁-C₈ alkyl, linear or branched C₁-
C₈ alkoxy, linear or branched C₁-C₈ alkylthio, a trifluoromethyl radical, a cyano
radical and a NR¹⁷R¹⁸ radical, wherein R¹⁷ and R¹⁸, identical or different, are
defined as R⁷ and R⁸.

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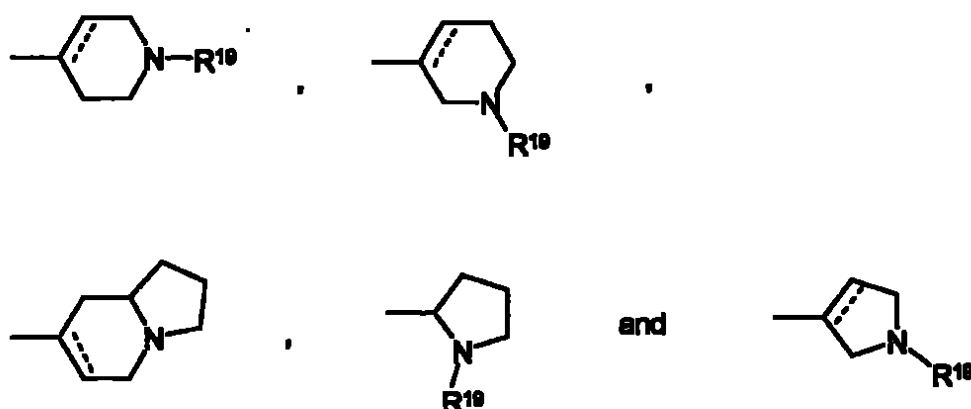
If one of the substituents R², R³, R⁴, R⁵ and R⁶ represents a linear or branched
aliphatic radical, a linear or branched alkoxy radical or a linear or branched
alkylthio radical, the carbon chain may have preferably 1-6, more preferably 1-3
carbon atoms.

30

Those skilled in the art understand that the term "condensed" indicates that the condensed rings share more than one atom. The terms "annulated" or "fused" may also be used for this type of bonding.

5 Sulfonamide derivatives of general formula (Ia) are preferred, wherein R^1 represents a $-NR^7R^8$ radical or a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing 5- or 6-membered cycloaliphatic radical, which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally
 10 at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system, whereby the rings of the ring system are 5- or 6-membered,

more preferably R^1 represents a NR^7R^8 radical or a radical chosen from the
 15 group consisting of



wherein, if present, the dotted line represents an optional chemical bond, and R^{10} represents hydrogen, a linear or branched C_1-C_6 alkyl radical or a benzyl radical, preferably hydrogen or a C_1-C_2 alkyl radical and R^2-R^6 , R^9 , R^{10} , A, B
 20 and n are defined as above.

Sulfonamide derivatives of general formula (Ia) are also preferred, wherein R^2 , R^3 , R^4 , R^5 and R^6 , identical or different, each represent hydrogen, F, Cl, Br, cyano, nitro, a linear or branched C_{1-6} alkyl radical, a linear or branched C_{2-6}
 25 alkenyl radical, a linear or branched C_{2-6} alkynyl radical, a linear or branched C_1 -

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alkoxy, a linear or branched C₁₋₈ alkylthio, hydroxy, trifluoromethyl, a saturated or unsaturated C₃₋₈ cycloaliphatic radical, a linear or branched C₁₋₈ alkylcarbonyl radical, phenylcarbonyl or an -NR⁹R¹⁰ group,

- 5 more preferably R², R³, R⁴, R⁵ and R⁶, identical or different, each represent H, F, Cl, NO₂, NH₂ or a C₁₋₂ alkyl radical and R¹, R⁷-R¹⁰, A, B and n are defined as above.

- Furthermore, sulfonamide derivatives of general formula (Ia) are also preferred,
10 wherein R⁷ and R⁸, identical or different, each represent hydrogen, a linear or branched, optionally at least mono-substituted C₁₋₁₀ alkyl radical, a linear or branched, optionally at least mono-substituted C₂₋₁₀ alkenyl radical, or a linear or branched, optionally at least mono-substituted C₂₋₁₀ alkynyl radical, with the proviso that R⁸ and R⁹ are not hydrogen at the same time, and if one of them,
15 R⁸ and R⁹, is a saturated or unsaturated, linear or branched, optionally at least mono-substituted, C₁-C₄ aliphatic radical, the other one is a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical with at least five carbon atoms,

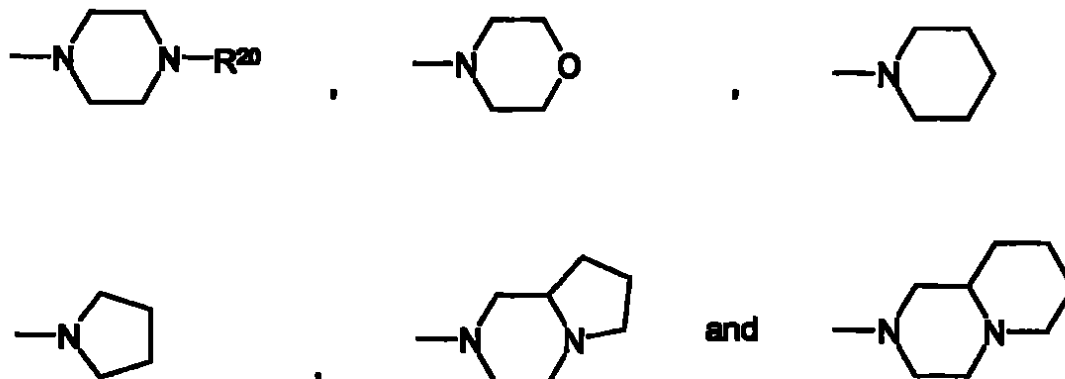
- 20 or R⁷ and R⁸ together with the bridging nitrogen form a saturated or unsaturated, optionally at least mono-substituted, optionally at least one further heteroatom as a ring member containing 5- or 6-membered heterocyclic ring which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member
25 containing mono- or bicyclic cycloaliphatic ring system, whereby the rings of the ring system are 5- 6- or 7-membered and R¹-R⁶, R⁹, R¹⁰, A, B and n are defined as above.

- Particularly preferred are sulfonamide derivatives of general formula (Ia),
30 wherein R⁷ and R⁸, identical or different, represent hydrogen or a linear or branched C₁-C₁₀ alkyl radical, with the proviso that R⁸ and R⁹ are not hydrogen at the same time, and if one of them, R⁸ or R⁹, represents a saturated or

unsaturated, linear or branched, optionally at least mono-substituted C₁-C₄ aliphatic radical, the other one of them represents a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical with at least five carbon atoms, or

5

R⁷ and R⁸ together with the bridging nitrogen atom form a radical chosen from the group consisting of



wherein R²⁰, if present, represents hydrogen, a linear or branched C₁-C₆ alkyl radical or a benzyl radical, preferably hydrogen, or a C₁-C₂ alkyl radical, and R¹, R⁶, R⁹, R¹⁰, A, B and n are defined as above.

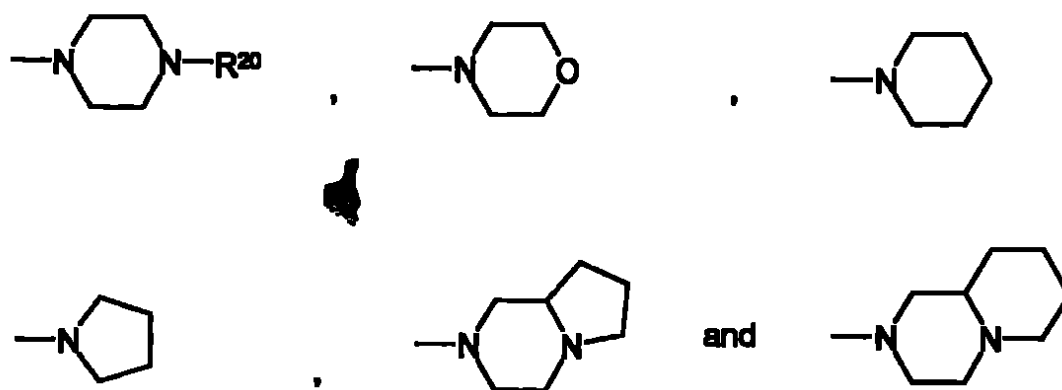
Furthermore, sulfonamide derivatives of general formula (Ia) are also preferred, wherein R⁹ and R¹⁰, identical or different, identical or different, each represent hydrogen, a linear or branched, optionally at least mono-substituted C₁-C₁₀ alkyl radical, a linear or branched, optionally at least mono-substituted C₂-C₁₀ alkenyl radical or a linear or branched, optionally at least mono-substituted C₂-C₁₀ alkynyl radical or

R⁹ and R¹⁰, together with bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted, optionally at least one further heteroatom as a ring member containing 5- or 6-membered heterocyclic ring, which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, , optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system whereby the rings of the

ring system are 5- 6- or 7-membered and R^1 - R^8 , A, B and n are defined as above.

Particularly preferred are sulfonamide derivatives of general formula (Ia),
 5 wherein R^9 and R^{10} , identical or different, each represent hydrogen or a linear or branched C_1 - C_{10} alkyl radical, or

R^9 and R^{10} , together with the bridging nitrogen atom form a radical chosen from the group consisting of



10

wherein R^{20} , if present, represents hydrogen, a linear or branched C_1 - C_8 alkyl radical or a benzyl radical, preferably hydrogen, or a C_1 - C_2 alkyl radical, and R^1 - R^8 , A, B and n are defined as above.

15 Furthermore, sulfonamide derivatives of general formula (Ia) are preferred, wherein A and B, identical or different, each represent a linear or branched C_1 - C_8 alkyl radical, a linear or branched C_2 - C_8 alkenyl radical or a linear or branched C_2 - C_8 alkynyl radical, more preferably A and B, identical or different, each represent a linear or branched C_1 - C_8 alkyl radical, or

20

A and B, together with the carbon atom to which they are bonded, form a saturated or unsaturated, but not aromatic, optionally at least mono-substituted cycloalkyl ring, more preferably A and B together with the carbon atom to which they are bonded form a C_3 - C_8 cycloalkyl ring, even more preferably A and B
 25 together with the carbon atom to which they are bonded form a cyclohexyl ring

and R^1 - R^{10} and n are defined as above.

Furthermore sulfonamide derivatives of general formula (Ia) are preferred, wherein n is 0, 1, 2, 3 or 4; preferably n is 0 or 1; more preferably n is 0 and R^1 to R^{10} and A and B are defined as above.

Those most preferred compounds of general formula (Ia) are selected from the group consisting of

- [1] 1-Cyclohexanesulfonyl-3-(1-methyl-1,2,3,6-tetrahydropyridine-4-yl)-5-nitro-1H-Indole,
- [2] 5-Chloro-1-cyclohexanesulfonyl-3-(1-methyl-1,2,3,6-tetrahydropyridine-4-yl)-1H-Indole,
- [3] 5-Amino-1-cyclohexanesulfonyl-3-(1-methyl-1,2,3,6-tetrahydropyridine-4-yl)-1H-Indole and
- [4] 1-Cyclohexanesulfonyl-5-fluoro-3-(1,2,3,5,8,8a-hexahydro-Indolizine-7-yl)-1H-Indole hydrochloride

and their corresponding salts and solvates.

Sulfonamide derivatives of general formula (Ib) are also preferred, wherein R^2 , R^3 , R^4 , R^5 and R^6 , identical or different, each represent hydrogen, F, Cl, Br, cyano, nitro, a linear or branched C_{1-8} alkyl radical, a linear or branched C_{2-8} alkenyl radical, a linear or branched C_{2-8} alkynyl radical, linear or branched C_{1-8} -alkoxy, a linear or branched C_{1-8} -alkylthio radical, hydroxy, trifluoromethyl, a saturated or unsaturated C_{3-8} cycloaliphatic radical, a linear or branched C_{1-8} -alkylcarbonyl radical, phenylcarbonyl or a $-NR^6R^{10}$ group,

preferably R^2 , R^3 , R^4 , R^5 and R^6 , identical or different, each represent H, F, Cl, NO_2 , NH_2 or a C_{1-2} alkyl radical, and R^1 , R^7 - R^{10} , A, B and n are defined as above.

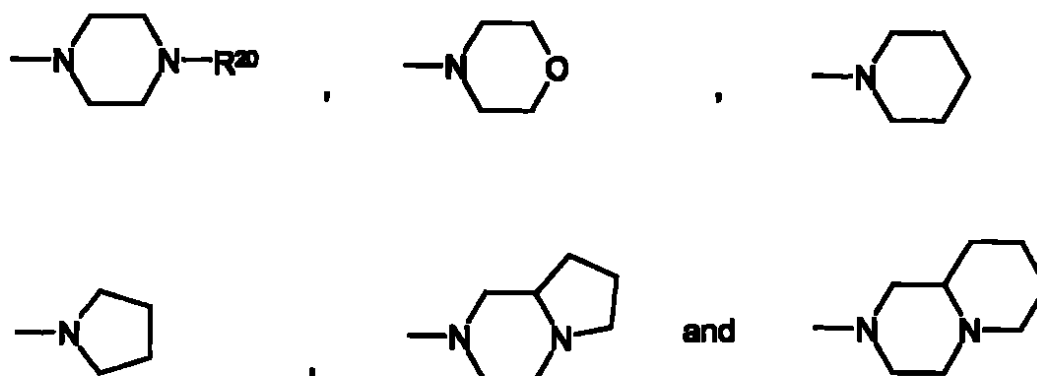
5 Furthermore, sulfonamide derivatives of general formula (Ib) are also preferred, wherein R^7 and R^8 , identical or different, each represent hydrogen, a linear or branched, optionally at least mono-substituted C_1 - C_4 alkyl radical and R^1 - R^6 , R^9 , R^{10} , A, B and n are defined as above.

10 Particularly preferred are sulfonamide derivatives of general formula (Ib), wherein R^7 and R^8 , identical or different, each represent hydrogen or a C_1 - C_2 alkyl radical, with the proviso that R^7 and R^8 are not hydrogen at the same time, and R^1 - R^6 , R^9 , R^{10} , A, B and n are defined as above.

15 Furthermore, sulfonamide derivatives of general formula (Ib) are also preferred, wherein R^9 and R^{10} , identical or different, each represent hydrogen, a linear or branched, optionally at least mono-substituted C_1 - C_{10} alkyl radical, a linear or branched, optionally at least mono-substituted C_2 - C_{10} alkenyl radical or a linear or branched, optionally at least mono-substituted C_2 - C_{10} alkynyl radical
20 or
 R^9 and R^{10} , together with the bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted, optionally at least one further heteroatom as a ring member containing 5- or 6-membered heterocyclic ring, which may be condensed with a saturated or unsaturated, optionally at least
25 mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system whereby the rings of the ring system are 5- 6- or 7-membered and R^1 - R^8 , A, B and n are defined as above.

30 Particularly preferred are sulfonamide derivatives of general formula (Ib), wherein R^9 and R^{10} , identical or different, each represent hydrogen or a linear or branched C_1 - C_{10} alkyl radical, or

R^9 and R^{10} , together with the bridging nitrogen form a radical chosen from the group consisting of



wherein R^{20} , if present, represents hydrogen, a linear or branched C_1 - C_6 alkyl radical or a benzyl radical, preferably hydrogen, or a C_1 - C_2 alkyl radical, and R^1 - R^6 , A, B and n are defined as above.

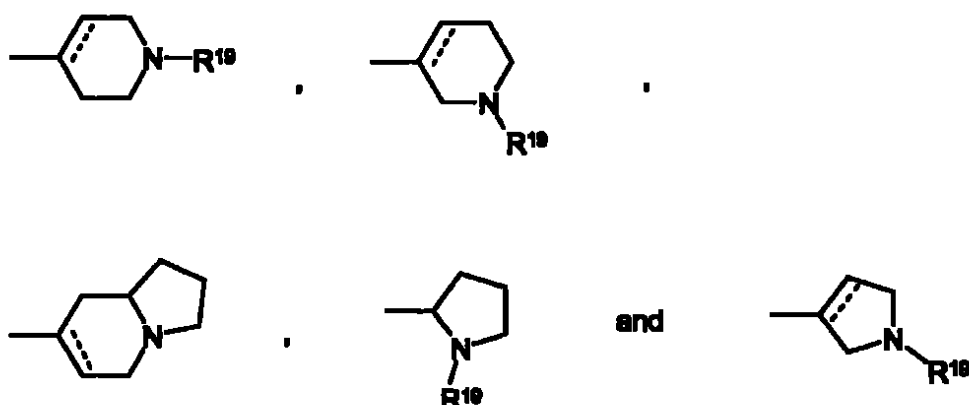
Furthermore, sulfonamide derivatives of general formula (Ib) are preferred, wherein A and B, identical or different, each represent a linear or branched C_1 - C_6 alkyl radical, a linear or branched C_1 - C_6 alkenyl radical, or a linear or branched C_1 - C_6 alkynyl radical, preferably a linear or branched C_1 - C_6 alkyl radical, or

A and B, together with the carbon atom to which they are bonded, form a saturated or unsaturated, but not aromatic, optionally at least mono-substituted cycloalkyl ring, more preferably A and B together with the carbon atom to which they are bonded form a C_3 - C_6 cycloalkyl ring, even more preferably A and B together with the carbon atom to which they are bonded form a cyclohexyl ring and R^1 - R^{10} and n are defined as above.

Furthermore sulfonamide derivatives of general formula (Ib) are preferred, wherein n is 0, 1, 2, 3 or 4; preferably n is 0 or 1; more preferably n is 0 and R^1 to R^{10} and A and B are defined as above.

Sulfonamide derivatives of general formula (Ic) are preferred, wherein R^1 represents a $-NR^7R^8$ radical or a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing 5- or 6-membered cycloaliphatic radical, which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system, whereby the rings of the ring system are 5- or 6-membered,

- more preferably R^1 represents a NR^7R^8 radical or a radical chosen from the group consisting of



wherein, if present, the dotted line represents an optional chemical bond, and R^{10} represents hydrogen, a linear or branched C_1 - C_8 alkyl radical or a benzyl radical, preferably hydrogen or a C_1 - C_2 alkyl radical and R^2 - R^6 , R^9 , R^{10} , A, B and n are defined as above.

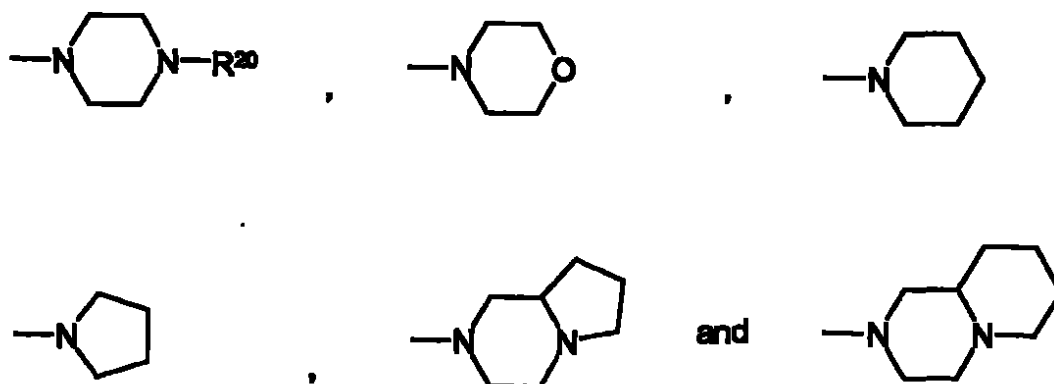
Sulfonamide derivatives of general formula (Ic) are also preferred, wherein R^2 , R^3 , R^4 , R^5 and R^6 , identical or different, each represent hydrogen, F, Cl, Br, cyano, nitro, a linear or branched C_{1-8} alkyl radical, a linear or branched C_{2-8} alkenyl radical, a linear or branched C_{2-8} alkynyl radical, a linear or branched C_{1-8} alkoxy, a linear or branched C_{1-8} alkylthio, hydroxy, trifluoromethyl, a saturated or unsaturated C_{3-8} cycloaliphatic radical, a linear or branched C_{1-8} alkylcarbonyl radical, phenylcarbonyl or an $-NR^9R^{10}$ group,

more preferably R^2 , R^3 , R^4 , R^5 and R^6 , identical or different, each represent H, F, Cl, NO_2 , NH_2 or a C_{1-2} alkyl radical and R^1 , R^7 - R^{10} , A, B and n are defined as above.

- 5 Furthermore, sulfonamide derivatives of general formula (Ic) are also preferred, wherein R^7 and R^8 , identical or different, each represent hydrogen, a linear or branched, optionally at least mono-substituted C_{1-10} alkyl radical, a linear or branched, optionally at least mono-substituted, C_{2-10} alkenyl radical, or a linear or branched, optionally at least mono-substituted, C_{2-10} alkynyl radical,
 10 or R^7 and R^8 together with the bridging nitrogen form a saturated or unsaturated, optionally at least mono-substituted, optionally at least one further heteroatom as a ring member containing 5- or 6-membered heterocyclic ring which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member
 15 containing mono- or bicyclic cycloaliphatic ring system, whereby the rings of the ring system are 5- 6- or 7-membered and R^1 - R^6 , R^9 , R^{10} , A, B and n are defined as above.

- Particularly preferred are sulfonamide derivatives of general formula (Ic),
 20 where R^7 and R^8 , identical or different, represent hydrogen or a linear or branched C_1 - C_{10} alkyl radical, or

R^7 and R^8 together with the bridging nitrogen atom form a radical chosen from the group consisting of



wherein R^{20} , if present, represents hydrogen, a linear or branched C_1 - C_9 alkyl radical or a benzyl radical, preferably hydrogen, or a C_1 - C_2 alkyl radical, and R^1 - R^8 , R^9 , R^{10} , A, B and n are defined as above.

- 5 Furthermore, sulfonamide derivatives of general formula (Ic) are also preferred, wherein R^9 and R^{10} , identical or different, identical or different, each represent hydrogen, a linear or branched, optionally at least mono-substituted C_1 - C_{10} alkyl radical, a linear or branched, optionally at least mono-substituted C_2 - C_{10} alkenyl radical or a linear or branched, optionally at least mono-substituted C_2 - C_{10} alkynyl radical or
- 10

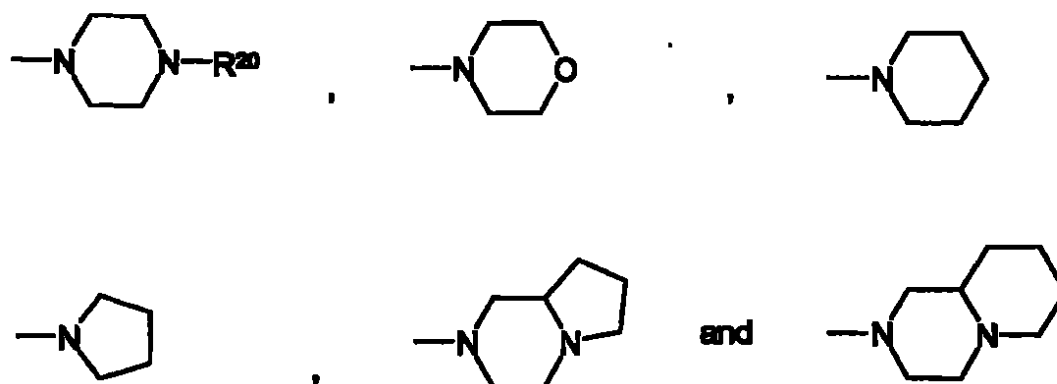
- R^9 and R^{10} , together with bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted, optionally at least one further heteroatom as a ring member containing 5- or 6-membered heterocyclic ring,
- 15 which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system whereby the rings of the ring system are 5- 6- or 7-membered and R^1 - R^8 , A, B and n are defined as above.

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Particularly preferred are sulfonamide derivatives of general formula (Ic), wherein R^9 and R^{10} , identical or different, each represent hydrogen or a linear or branched C_1 - C_{10} alkyl radical, or

- 25 R^9 and R^{10} , together with the bridging nitrogen atom form a radical chosen from the group consisting of

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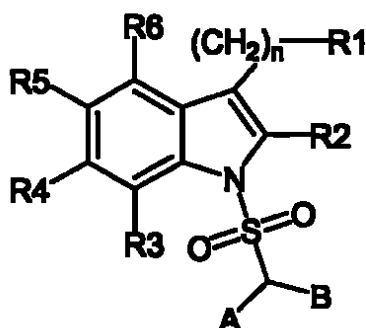
wherein R^{20} , if present, represents hydrogen, a linear or branched C_1 - C_8 alkyl radical or a benzyl radical, preferably hydrogen, or a C_1 - C_2 alkyl radical, and R^1 - R^8 , A, B and n are defined as above.

Furthermore, sulfonamide derivatives of general formula (Ic) are preferred, wherein A and B, identical or different, each represent a linear or branched C_1 - C_8 alkyl radical, a linear or branched C_2 - C_8 alkenyl radical or a linear or branched C_2 - C_8 alkynyl radical, more preferably A and B, identical or different, each represent a linear or branched C_1 - C_8 alkyl radical, or

A and B, together with the carbon atom to which they are bonded, form a saturated or unsaturated, but not aromatic, optionally at least mono-substituted cycloalkyl ring, more preferably A and B together with the carbon atom to which they are bonded form a C_3 - C_8 cycloalkyl ring, even more preferably A and B together with the carbon atom to which they are bonded form a cyclohexyl ring and R^1 - R^{10} and n are defined as above.

Furthermore sulfonamide derivatives of general formula (Ic) are preferred, wherein n is 0, 1, 2, 3 or 4; preferably n is 0 or 1; more preferably n is 0 and R^1 to R^{10} and A and B are defined as above.

Another aspect of the present invention are compounds of general formula (Ic),



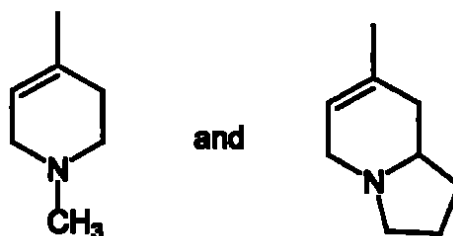
(Ic),

wherein

5

R^1 represents an unsaturated, optionally at least one nitrogen atom as a ring member containing 5- or 6-membered cycloaliphatic radical, which may be substituted by a methyl group and/or which may be condensed with a 5-membered cycloaliphatic ring, more preferably R^1 represents a $-NR^7R^8$ radical or a moiety selected from the group consisting of

10



R^2 , R^3 , R^4 and R^6 each represent hydrogen,

15

R^5 represents H, fluorine, chlorine, nitro or a $-NR^9R^{10}$ group,

R^9 and R^{10} each represent hydrogen,

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A and B together with the carbon atom to which they are bonded form a saturated or unsaturated, but not aromatic, C₃-C₈ cycloalkyl ring, more preferably form a cyclohexyl ring,

5 and

n is 0;

optionally in form of one of their stereoisomers, preferably enantiomers or
10 diastereomers, their racemate or in form of a mixture of at least two of their stereoisomers, preferably enantiomers or diastereomers, in any mixing ratio, or a salt thereof, preferably a corresponding physiologically acceptable salt thereof or a corresponding solvate thereof.

15 Those most preferred compounds of general formula (Ic) are selected from the group consisting of

[1] 1-Cyclohexanesulfonyl-3-(1-methyl-1,2,3,6-tetrahydropyridine-4-yl)-5-nitro-1H-indole,

20

[2] 5-Chloro-1-cyclohexanesulfonyl-3-(1-methyl-1,2,3,6-tetrahydropyridine-4-yl)-1H-indole,

25

[3] 5-Amino-1-cyclohexanesulfonyl-3-(1-methyl-1,2,3,6-tetrahydropyridine-4-yl)-1H-indole and

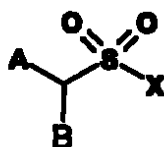
[4] 1-Cyclohexanesulfonyl-5-fluoro-3-(1,2,3,5,8,8a-hexahydro-indolizine-7-yl)-1H-indole hydrochloride

30 and their corresponding salts and solvates.

The present invention likewise refers to the salts, preferably the physiologically acceptable salts of the compounds of general formula (Ia) and/or (Ib) and/or of general formula (Ic), preferably the addition salts of mineral acids, more preferably of hydrochloric acid, hydrobromic acid, phosphoric acid, sulphuric acid, nitric acid, and the salts of organic acids, more preferably of citric acid, maleic acid, fumaric acid, tartaric acid or their derivatives, *p*-toluenesulphonic acid, methanesulphonic acid, camphorsulphonic acid, etc.

Below, the expression sulfonamide derivatives of general formula (I) refers to one or more compounds of general formula (Ia) and/or to one or more compounds of general formula (Ib) and/or to one or more compounds of general formula (Ic), respectively and optionally in form of one of their stereoisomers, preferably enantiomers or diastereomers, their racemate, or in form of a mixture of at least two of their stereoisomers, preferably enantiomers or diastereomers, in any mixing ratio, or a salt thereof, preferably a corresponding physiologically acceptable salt thereof, or a corresponding solvate thereof.

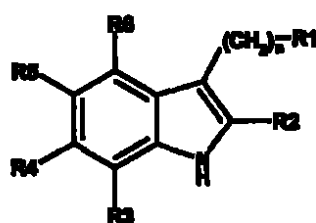
Another aspect of the present invention consists of a process for preparing the new derivatives of general formula (I), wherein R^1 - R^{10} , A, B and n have the previously indicated meaning, according to which at least one compound of general formula (II).



(II)

wherein A and B have the previously mentioned meaning and X is an acceptable leaving group, preferably an halogen atom, more preferably chlorine, is reacted with at least one substituted indole of general formula (III)

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(III)

wherein R^1 - R^6 and n have the previously indicated meaning, or one of their
suitable protected derivatives, and, if necessary, the protective groups are
removed in order to obtain the corresponding sulfonamide derivative of formula
5 (I), which can be purified and/or isolated by means of conventional methods
known in the prior art.

The reaction is preferably carried out in the presence of a suitable strong
base, for example, lithium diisopropylamide, butyllithium, sodium hydride, or
10 sodium bis(trimethylsilyl)amide in an inert solvent, preferably tetrahydrofurane,
hexane or dimethylformamide. The most suitable reaction temperatures range
from -100°C to room temperature, and the reaction time preferably comprises
from 5 minutes to 24 hours. The most preferred conditions are sodium hydride
in dimethylformamide at approximately 0°C .

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The resulting sulfonamide derivative of general formula (I) can be purified
and/or isolated according to conventional methods known in the prior art.

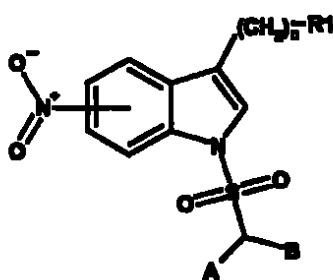
Preferably, the sulfonamide derivatives of general formula (I) can be
20 isolated by evaporating the reaction medium, adding water and, if necessary,
adjusting the pH so that a solid which can be isolated by filtration is obtained; or
the sulfonamide derivatives can be extracted with a water immiscible solvent,
preferably chloroform, and be purified by chromatography or recrystallization of
a suitable solvent.

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The compounds of general formula (II) are commercially available or can be prepared according to standard methods known in the prior art, for example by methods similar to those described in the literature [KHANNA, V.; TAMILSELVAN, P.; KALRA, S.J.S.; IQBAL, J.; Tetrahedron 1994, 35 (32), 5935-5938; L.N. Aristarkhova et al., *J. Org. Chem. USSR*, 1970, 6, 2454-2458; E.E. Gilbert, *Synthesis*, 1969, 1,3]. The compounds of general formula (III) can also be prepared according to standard methods known in the prior art, for example, methods similar to those described in the literature. Substituted aromatic 5-HT_{1f} agonist, WO9846570. Piperidine-Indole compounds having 5-HT₆ affinity, US 6,133,287.

The respective descriptions in the literature are incorporated by reference and form part of the disclosure.

Another aspect of the present invention consists of a process for preparing the new sulfonamide derivatives of general formula (I), wherein one or more of R², R³, R⁴, R⁵ or R⁶ are reduced to an amino group by reduction of the nitro group of derivatives of general formula (IV) by methods known in the prior art, for example BRATTON, L.D.; ROTH, B.D.; TRIVEDI, B.K.; UNANGST, P.C.; *J. Heterocycl Chem*, 2000, 37 (5), 1103-1108. FANGHAENEL, E.; CHTCHEGLOV, D.; *J Prakt Chem/Chem-Ztg*, 1996, 338 (8), 731-737. KUYPER, L.F.; BACCANARI, D.P.; JONES, M.L.; HUNTER, R.N.; TANSIK, R.L.; JOYNER, S.S.; BOYTOS, C.M.; RUDOLPH, S.K.; KNICK, V.; WILSON, H.R.; CADDELL, J.M.; FRIEDMAN, H.S.; ET AL.; *J Med Chem*, 1996, 39 (4), 892-903,



(IV)

and the others R^1 - R^6 , A, B and n have the previously mentioned meaning, or one of their derivatives suitably protected, and, if necessary, the protective groups are removed in order to obtain the corresponding amine of general formula (I), which can be purified and/or isolated by means of conventional methods known in the prior art.

The respective literature descriptions are incorporated by reference and form part of the disclosure.

The salts, preferably pharmaceutically acceptable salts of the compounds of general formula (I), may be prepared by means of conventional methods known in the prior art, preferably by reaction with a mineral acid, more preferably by reaction with hydrochloric acid, hydrobromic acid, phosphoric acid, sulphuric acid or nitric acid, or by reaction with organic acids, more preferably by reaction with citric acid, maleic acid, fumaric acid, tartaric acid, or their derivatives, *p*-toluenesulphonic acid, methanesulphonic acid, camphorsulphonic acid, etc., in a suitable solvent, preferably methanol, ethanol, diethyl ether, ethyl acetate, acetonitrile or acetone, and obtaining the resulting salts by using the usual techniques for the precipitation or crystallization of the corresponding salts.

The preferred physiologically acceptable salts of the sulfonamide derivatives of general formula (I) are the addition salts of mineral acids, more preferably of hydrochloric acid, hydrobromic acid, phosphoric acid, sulphuric acid or nitric acid, and the addition salts of organic acids, more preferably citric acid, maleic acid, fumaric acid, tartaric acid, or their derivatives, *p*-toluenesulphonic acid, methanesulphonic acid, camphorsulphonic acid, etc.

The solvates, preferably the physiologically acceptable solvates, more preferably hydrates, of the sulfonamide derivatives of general formula (I) or of the corresponding physiologically acceptable salts, may be prepared by methods known in the prior art.

During some of the synthetic sequences described or in the preparation of the suitable reagents used, it may be necessary and/or desirable to protect sensitive or reactive groups in some of the molecules used. This can be carried out by means of the use of conventional protective groups preferably those described in the literature [Protective groups in Organic Chemistry, ed. J.F.W. McOmie, Plenum Press, 1973; T.W. Greene & P.G.M. Wuts, Protective Groups in Organic Chemistry, John Wiley & Sons, 1991]. The protective groups can be removed in the suitable subsequent stage by methods known in the prior art. The respective literature descriptions are incorporated by reference and form part of the disclosure.

If the sulfonamide derivatives of general formula (I) are obtained in form of a mixture of stereoisomers, preferably enantiomers or diastereomers, said mixtures can be separated by means of standard processes known in the prior art, for example chromatographic methods or crystallization with chiral agents.

Another aspect of the present invention is a medicament comprising at least one 1-sulfonylindole derivative of general formula (I), optionally in form of one of its stereoisomers, preferably enantiomers or diastereomers, its racemate, or in form of a mixture of at least two of its stereoisomers, preferably enantiomers or diastereomers, in any mixing ratio, or a corresponding physiologically acceptable salt thereof or a corresponding solvate thereof, and optionally one or more pharmaceutically acceptable adjuvants.

This medicament is suitable for 5-HT₆ receptor regulation, for the prophylaxis and/or treatment of a disorder or disease related to food intake, preferably for the regulation of appetite, for the maintenance, increase or reduction of body weight, for the prophylaxis and/or treatment of obesity, bulimia, anorexia, cachexia or type II diabetes (non insulin dependent diabetes mellitus), preferably type II diabetes caused by obesity, for the prophylaxis and/or treatment of gastrointestinal tract disorders, preferably irritable bowel syndrome,

for cognitive enhancement, for the prophylaxis and/or treatment of disorders of the central nervous system, anxiety, panic disorders, depression, preferably bipolar disorders, cognitive memory disorders, senile dementia processes, neurodegenerative disorders, preferably Alzheimer's disease, Parkinson's disease, Huntington's disease and/or Multiple Sclerosis, schizophrenia, psychosis or Infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder) and other disorders mediated by the 5-HT₆ serotonin receptor in humans and/or in animals, preferably in mammals, more preferably in humans.

Another aspect of the present invention is a medicament comprising at least one 1-sulfonylindole derivative of general formula (Ia), optionally in form of one of its stereoisomers, preferably enantiomers or diastereomers, its racemate, or in form of a mixture of at least two of its stereoisomers, preferably enantiomers or diastereomers, in any mixing ratio, or a corresponding physiologically acceptable salt thereof or a corresponding solvate thereof, and optionally one or more pharmaceutically acceptable adjuvants.

This medicament is suitable for 5-HT₆ receptor regulation, for the prophylaxis and/or treatment of a disorder or disease related to food intake, preferably for the regulation of appetite, for the maintenance, increase or reduction of body weight, for the prophylaxis and/or treatment of obesity, bulimia, anorexia, cachexia or type II diabetes (non insulin dependent diabetes mellitus), preferably type II diabetes caused by obesity, for the prophylaxis and/or treatment of gastrointestinal tract disorders, preferably irritable bowel syndrome, for cognitive enhancement, for the prophylaxis and/or treatment of disorders of the central nervous system, anxiety, panic disorders, depression, preferably bipolar disorders, cognitive memory disorders, senile dementia processes, neurodegenerative disorders, preferably Alzheimer's disease, Parkinson's disease, Huntington's disease and/or Multiple Sclerosis, schizophrenia, psychosis or Infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder), and other disorders mediated by the 5-HT₆ serotonin receptor in humans and/or in animals, preferably in mammals, more preferably in humans,

more suitable for 5-HT₆ receptor regulation, for the prophylaxis and/or treatment of a disorder or disease related to food intake, preferably for the regulation of appetite, for the maintenance, increase or reduction of body weight, for the prophylaxis and/or treatment of obesity, bulimia, anorexia, cachexia or type II diabetes (non insulin dependent diabetes mellitus), preferably type II diabetes caused by obesity, for the prophylaxis and/or treatment of gastrointestinal tract disorders, preferably irritable bowel syndrome in humans and/or in animals, preferably in mammals, more preferably in humans.

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Another aspect of the present invention is a medicament comprising at least one 1-sulfonylindole derivative of general formula (Ib), optionally in form of one of its stereoisomers, preferably enantiomers or diastereomers, its racemate, or in form of a mixture of at least two of its stereoisomers, preferably enantiomers or diastereomers, in any mixing ratio, or a corresponding physiologically acceptable salt thereof or a corresponding solvate thereof, and optionally one or more pharmaceutically acceptable adjuvants.

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This medicament is suitable for 5-HT₆ receptor regulation, for the prophylaxis and/or treatment of a disorder or disease related to food intake, preferably for the regulation of appetite, for the maintenance, increase or reduction of body weight, for the prophylaxis and/or treatment of obesity, bulimia, anorexia, cachexia or type II diabetes (non insulin dependent diabetes mellitus), preferably type II diabetes caused by obesity, for the prophylaxis and/or treatment of gastrointestinal tract disorders, preferably irritable bowel syndrome, for cognitive enhancement, for the prophylaxis and/or treatment of disorders of the central nervous system, anxiety, panic disorders, depression, preferably bipolar disorders, cognitive memory disorders, senile dementia processes, neurodegenerative disorders, preferably Alzheimer's disease, Parkinson's disease, Huntington's disease and/or Multiple Sclerosis, schizophrenia, psychosis or infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder), and other disorders mediated by the 5-HT₆ serotonin receptor in

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humans and/or in animals, preferably in mammals, more preferably in humans,

more suitable for cognitive enhancement, for the prophylaxis and/or treatment of disorders of the central nervous system, anxiety, panic disorders, depression, preferably bipolar disorders, cognitive memory disorders, senile dementia processes, neurodegenerative disorders, preferably Alzheimer's disease, Parkinson's disease, Huntington's disease and/or Multiple Sclerosis, schizophrenia, psychosis or Infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder) in humans and/or in animals, preferably in mammals, more preferably in humans.

Another aspect of the present invention is a medicament composed of at least one 1-sulfonylindole derivative of general formula (Ic), optionally in form of one of its stereoisomers, preferably enantiomers or diastereomers, its racemate, or in form of a mixture of at least two of its stereoisomers, preferably enantiomers or diastereomers, in any mixing ratio, or a corresponding physiologically acceptable salt thereof or a corresponding solvate thereof, and optionally one or more pharmaceutically acceptable adjuvants.

This medicament is suitable for 5-HT₂ receptor regulation, for the prophylaxis and/or treatment of a disorder or disease related to food intake, preferably for the regulation of appetite, for the maintenance, increase or reduction of body weight, for the prophylaxis and/or treatment of obesity, bulimia, anorexia, cachexia or type II diabetes (non insulin dependent diabetes mellitus), preferably type II diabetes caused by obesity, for the prophylaxis and/or treatment of gastrointestinal tract disorders, preferably irritable bowel syndrome, for cognitive enhancement, for the prophylaxis and/or treatment of disorders of the central nervous system, anxiety, panic disorders, depression, preferably bipolar disorders, cognitive memory disorders, senile dementia processes, neurodegenerative disorders, preferably Alzheimer's disease, Parkinson's disease, Huntington's disease and/or Multiple Sclerosis, schizophrenia, psychosis or Infantile hyperkinesia (ADHD, attention deficit / hyperactivity

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disorder), and other disorders mediated by the 5-HT₆ serotonin receptor in humans and/or in animals, preferably in mammals, more preferably in humans.

The medicament obtained according to the present invention is particularly
5 suitable for the administration to mammals, including humans. The medicament can preferably be administered to all age groups, namely, children, adolescents and adults.

Another aspect of the present invention is the use of at least one sulfonamide
10 derivative of general formula (I), optionally in form of one of its stereoisomers, preferably enantiomers or diastereomers, its racemate, or in form of a mixture of at least two of its stereoisomers, preferably enantiomers or diastereomers, in any mixing ratio, or a corresponding physiologically acceptable salt thereof or a
15 corresponding solvate thereof, for the manufacture of a medicament for 5-HT₆ receptor regulation, for the prophylaxis and/or treatment of a disorder or disease related to food intake, preferably for the regulation of appetite, for the maintenance, increase or reduction of body weight, for the prophylaxis and/or treatment of obesity, bulimia, anorexia, cachexia or type II diabetes (non insulin
20 dependent diabetes mellitus), preferably type II diabetes caused by obesity, for the prophylaxis and/or treatment of gastrointestinal tract disorders, preferably irritable bowel syndrome, for cognitive enhancement, for the prophylaxis and/or treatment of disorders of the central nervous system, anxiety, panic disorders, depression, preferably bipolar disorders, cognitive memory disorders, senile dementia processes, neurodegenerative disorders, preferably Alzheimer's
25 disease, Parkinson's disease, Huntington's disease and/or Multiple Sclerosis, schizophrenia, psychosis or infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder) and other disorders mediated by the 5-HT₆ serotonin receptor in humans and/or in animals, preferably in mammals, more preferably in humans.

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Another aspect of the present invention is the use of at least one sulfonamide derivative of the previous general formula (Ia), optionally in form of one of its stereoisomers, preferably enantiomers or diastereomers, its racemate, or in form of a mixture of at least two of its stereoisomers, preferably enantiomers or diastereomers, in any mixing ratio, or a corresponding physiologically acceptable salt thereof or a corresponding solvate thereof, for the manufacture of a medicament for 5-HT₆ receptor regulation, for the prophylaxis and/or treatment of a disorder or disease related to food intake, preferably for the regulation of appetite, for the maintenance, increase or reduction of body weight, for the prophylaxis and/or treatment of obesity, bulimia, anorexia, cachexia or type II diabetes (non insulin dependent diabetes mellitus), preferably type II diabetes caused by obesity, for the prophylaxis and/or treatment of gastrointestinal tract disorders, preferably irritable bowel syndrome, for cognitive enhancement, for the prophylaxis and/or treatment of disorders of the central nervous system, anxiety, panic disorders, depression, preferably bipolar disorders, cognitive memory disorders, senile dementia processes, neurodegenerative disorders, preferably Alzheimer's disease, Parkinson's disease, Huntington's disease and/or Multiple Sclerosis, schizophrenia, psychosis or infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder) and other disorders mediated by the 5-HT₆ serotonin receptor in humans and/or in animals, preferably in mammals, more preferably in humans,

preferably for the manufacture of a medicament for 5-HT₆ receptor regulation, for the prophylaxis and/or treatment of a disorder or disease related to food intake, preferably for the regulation of appetite, for the maintenance, increase or reduction of body weight, for the prophylaxis and/or treatment of obesity, bulimia, anorexia, cachexia or type II diabetes (non insulin dependent diabetes mellitus), preferably type II diabetes caused by obesity, for the prophylaxis and/or treatment of gastrointestinal tract disorders, preferably irritable bowel syndrome receptor in humans and/or in animals, preferably in mammals, more preferably in humans.

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Another aspect of the present invention is the use of at least one sulfonamide derivative of the previous general formula (Ib), optionally in form of one of its stereoisomers, preferably enantiomers or diastereomers, its racemate, or in form of a mixture of at least two of its stereoisomers, preferably enantiomers or diastereomers, in any mixing ratio, or a corresponding physiologically acceptable salt thereof or a corresponding solvate thereof, for the manufacture of a medicament for 5-HT₂ receptor regulation, for the prophylaxis and/or treatment of a disorder or disease related to food intake, preferably for the regulation of appetite, for the maintenance, increase or reduction of body weight, for the prophylaxis and/or treatment of obesity, bulimia, anorexia, cachexia or type II diabetes (non insulin dependent diabetes mellitus), preferably type II diabetes caused by obesity, for the prophylaxis and/or treatment of gastrointestinal tract disorders, preferably irritable bowel syndrome, for cognitive enhancement, for the prophylaxis and/or treatment of disorders of the central nervous system, anxiety, panic disorders, depression, preferably bipolar disorders, cognitive memory disorders, senile dementia processes, neurodegenerative disorders, preferably Alzheimer's disease, Parkinson's disease, Huntington's disease and/or Multiple Sclerosis, schizophrenia, psychosis or infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder) and other disorders mediated by the 5-HT₂ serotonin receptor in humans and/or in animals, preferably in mammals, more preferably in humans,

preferably for the manufacture of a medicament for cognitive enhancement, for the prophylaxis and/or treatment of disorders of the central nervous system, anxiety, panic disorders, depression, preferably bipolar disorders, cognitive memory disorders, senile dementia processes, neurodegenerative disorders, preferably Alzheimer's disease, Parkinson's disease, Huntington's disease and/or Multiple Sclerosis, schizophrenia, psychosis or infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder) in animals, preferably in mammals, more preferably in humans.

Another aspect of the present invention is the use of at least one sulfonamide derivative of the previous general formula (Ic), optionally in form of one of its stereoisomers, preferably enantiomers or diastereomers, its racemate, or in form of a mixture of at least two of its stereoisomers, preferably enantiomers or diastereomers, in any mixing ratio, or a corresponding physiologically acceptable salt thereof or a corresponding solvate thereof, for the manufacture of a medicament for 5-HT₆ receptor regulation, for the prophylaxis and/or treatment of a disorder or disease related to food intake, preferably for the regulation of appetite, for the maintenance, increase or reduction of body weight, for the prophylaxis and/or treatment of obesity, bulimia, anorexia, cachexia or type II diabetes (non insulin dependent diabetes mellitus), preferably type II diabetes caused by obesity, for the prophylaxis and/or treatment of gastrointestinal tract disorders, preferably irritable bowel syndrome, for cognitive enhancement, for the prophylaxis and/or treatment of disorders of the central nervous system, anxiety, panic disorders, depression, preferably bipolar disorders, cognitive memory disorders, senile dementia processes, neurodegenerative disorders, preferably Alzheimer's disease, Parkinson's disease, Huntington's disease and/or Multiple Sclerosis, schizophrenia, psychosis or infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder) and other disorders mediated by the 5-HT₆ serotonin receptor in humans and/or in animals, preferably in mammals, more preferably in humans.

The preparation of the corresponding pharmaceutical compositions as well as of the formulated medicaments can be carried out by means of conventional methods known in the prior art, for example, based on the indices of "Pharmaceutics: The Science of Dosage Forms", Second Edition, Aulton, M.E. (Ed. Churchill Livingstone, Edinburgh (2002)); "Encyclopedia of Pharmaceutical Technology", Second Edition, Swarbrick, J. and Boylan, J.C. (Eds.), Marcel Dekker, Inc. New York (2002); "Modern Pharmaceutics", Fourth Edition, Banker G.S. and Rhodes C.T. (Eds.) Marcel Dekker, Inc. New York (2002), and "The Theory and Practice of Industrial Pharmacy", Lachman L.,

Lieberman H. and Kanig J. (Eds.), Lea & Febiger, Philadelphia (1986). The respective literature descriptions are incorporated as a reference and are part of this disclosure.

5 The pharmaceutical compositions, as well as the formulated medicaments prepared according to the present invention, can, in addition to at least one sulfonamide derivative of general formula (I), optionally in form of one of its stereoisomers, preferably enantiomers or diastereomers, its racemate, or in form of a mixture of at least two of its stereoisomers, preferably enantiomers
10 or diastereomers, in any mixing ratio, or a corresponding physiologically acceptable salt thereof or a corresponding solvate thereof, comprise other conventional auxiliary substances known in the prior art, preferably excipients, fillers, solvents, diluents, dyes, coating agents, matrix forming agents and/or binders. As those skilled in the art also know the choice of the auxiliary
15 substances and the amounts thereof depends on the intended administration route, for example, rectal, intravenous, intraperitoneal, intramuscular, intranasal, oral, buccal or topical.

 Medicaments suitable for oral administration are, for example, tablets,
20 coated tablets, capsules or multiparticulates, preferably granules or pellets, optionally subjected to compression in tablets, filled in capsules or suspended in solutions, suspensions or suitable liquids.

 Medicaments suitable for parenteral, topical or inhalatory administration
25 can preferably be chosen from the group consisting of solutions, suspensions, quickly reconstitutable dry preparations and also sprays.

 Medicaments suitable for oral or percutaneous use can release the sulfonamide compounds of general formula (I) in a sustained manner, the
30 preparation of these sustained release medicaments generally being known in the prior art.

The most suitable sustained release forms, as well as the materials and methods for the preparation thereof, are known in the prior art, for example from the indices of "Modified-Release Drug Delivery Technology", Rathbone, M.J., Hadgraft, J. and Roberts, M.S. (Eds.), Marcel Dekker, Inc., New York (2002);
5 "Handbook of Pharmaceutical Controlled Release Technology", Wise, D.L. (Ed.), Marcel Dekker, Inc. New York (2000); "Controlled Drug Delivery", Vol. I, Basic Concepts, Bruck, S.D. (Ed.), CRD Press, Inc., Boca Raton (1983), and by Takada, K. and Yoshikawa, H., "Oral Drug Delivery", Encyclopedia of Controlled Drug Delivery, Mathlowitz, E. (Ed.), John Wiley & Sons, Inc., New York (1999),
10 Vol. 2, 728-742; Fix, J., "Oral drug delivery, small intestine and colon", Encyclopedia of Controlled Drug Delivery, Mathlowitz, E. (Ed.), John Wiley & Sons, Inc., New York (1999), Vol. 2, 698-728. The respective literature references are incorporated by reference and form part of the disclosure.

15 The medicament of the present invention can also have at least one enteric coating, which dissolves according to the pH. As a result of this coating, the medicament can pass through the stomach without dissolving, and the compounds of general formula (I) are only released in the intestinal tract. The enteric coating preferably dissolves at a pH of between 5 and 7.5. The materials
20 and methods suitable for preparing enteric coatings are also known in the prior art.

Typically, the pharmaceutical compositions and the medicaments comprise from 1 to 60% by weight of one or more sulfonamide derivatives of
25 general formula (I), and from 40 to 99% by weight of one or more excipients.

The medicament substance amount to be administered to the patient varies according to the patient's weight, the administration route, the indication and the severity of the disorder. Usually from 1 mg to 2 g of at least one
30 sulfonamide derivative of general formula (I) are administered per patient per day. The total daily dose can be administered to the patient in one or more doses.

Pharmaceutical Methods:**BINDING TO THE 5HT₆ SEROTONIN RECEPTOR**

5 HEK-293 cell membranes expressing the recombinant human 5HT₆ receptor were supplied by Receptor Biology. The receptor concentration in said membranes is 2.18 pmol/mg of protein and the protein concentration is 9.17 mg/ml. The experimental protocol follows the method of B.L. Roth et al. [B.L. Roth, S.C. Cralgo, M.S. Choudhary, A. Uluer, F.J. Monsma, Y. Shen, H.Y. Meltzer, D.R. Sibley: Binding of Typical and Atypical Antipsychotic Agents to 5-Hydroxytryptamine-6 and Hydroxytryptamine-7 Receptors. *The Journal of Pharmacology and Experimental Therapeutics*, 1994, 268, 1403], with slight modifications. The commercial membrane is diluted (1:40 dilution) with the binding buffer: 50 mM Tris-HCl, 10 mM MgCl₂, 0.5 mM EDTA (pH 7.4). The radioligand used is [³H]-LSD at a concentration of 2.7 nM, the final volume being 200 µl. Incubation begins by adding 100 µl of the membrane suspension (≈ 22.9 µg of membrane protein), and is prolonged for 60 minutes at a temperature of 37°C. Incubation ends by quick filtration in a Harvester Brandel Cell through fibreglass filters of the Schleicher & Schuell GF 3362 trademark, pretreated with a 0.5% polyethylenimine solution. The filters are washed three times with three milliliters of 50 mM Tris HCl buffer, pH 7.4. The filters are transferred to vials and 5 ml of Ecoscint H. liquid scintillation cocktail are added to each vial. The vials are left to equilibrate for several hours prior to their counting in a 1414 Wallac Winspectral scintillation counter. The non-specific binding is determined in the presence of 100 µM of serotonin. The assays are carried out in triplicate. The inhibition constants (K_i, nM) are calculated by non-linear regression analysis using the EBDALIGAND program [Munson and Rodbard, *Analytical Biochemistry*, 1980, 107, 220].

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MEASUREMENTS OF FOOD INGESTION (BEHAVIOR MODELS)

Male W rats (200-270 g) from Harlan, S.A. are used. The rats are
5 acclimatized to the housings during at least 5 days prior to being subjected to
any experiment. During this period, the animals are housed (in groups of five) in
translucent cages with water and ad libitum food. The animals are adapted to
individual housing at least 24 hours prior to the tests.

The acute effect of the sulfonamide derivatives of general formula (I)
10 used experimentally on food ingestion in rats in fasting conditions is determined
as follows:

The rats are kept in fasting conditions for 23 hours in their individual
cages of origin. After this period, the rats are orally or intraperitoneally treated
with a composition comprising a sulfonamide derivative of general formula (I) or
15 a corresponding composition (vehicle) without said sulfonamide derivative.
Immediately after this, the rat is left with pre-weighed food; the accumulated
food intake is measured after 1, 2, 4 and 6 hours.

Said food ingestion measuring method is also disclosed in the literature
(Kask et al., *European Journal of Pharmacology* 414 (2001), 215-224, and
20 Turnbull et al., *Diabetes*, Vol. 51, August, 2002). The respective parts of the
descriptions are herein incorporated as a reference, and they form part of the
disclosure.

The preparation of new compounds according to the invention is
indicated in the following examples. The affinity for the 5HT₆ serotonin receptor,
25 as well as the galenic formulas applicable to the compounds of the invention,
are described. The examples indicated below, given as an illustrative example,
should in no way limit the scope of the invention.

Examples:**Example 1.- Preparation of 1-Cyclohexanesulfonyl-3-(1-methyl-1,2,3,6-tetrahydropyridine-4-yl)-5-nitro-1H-indole**

468 mg (9.8 mMol) of 50% sodium hydride in oil were added at 0°C to a solution of 1.0 g (3.9 mMol) of 3-(1-methyl-1,2,3,6-tetrahydropyridine-4-yl)-5-nitro-1H-indole in 50 ml of anhydrous dimethylformamide, and the mixture was left to stir for 30 minutes. Then 2.14 g of cyclohexanesulfonyl chloride were added, and the stirring continued for 3 hours at room temperature. Water was added and evaporated to dryness. The resulting crude was treated with sodium bicarbonate and was extracted with chloroform. The organic phase was dried with anhydrous sodium sulfate and evaporated to dryness; the resulting solid was purified by chromatography, obtaining 900 mg (57%) of 1-cyclohexanesulfonyl-3-(1-methyl-1,2,3,6-tetrahydropyridine-4-yl)-5-nitro-1H-indole as a yellow solid.

Example 2.- 5-Chloro-1-cyclohexanesulfonyl-3-(1-methyl-1,2,3,6-tetrahydropyridine-4-yl)-1H-Indole

900 mg (74%) of the mentioned compound were obtained from 770 mg (3.12 mMol) of 5-chloro-3-(1-methyl-1,2,3,6-tetrahydropyridine-4-yl)-1H-indole, and 1.7 g (9.36 mMol) of cyclohexanesulfonyl chloride by means of the process described in Example 1, as a yellow solid.

Example 3.- 5-Amino-1-cyclohexanesulfonyl-3-(1-methyl-1,2,3,6-tetrahydropyridine-4-yl)-1H-Indole

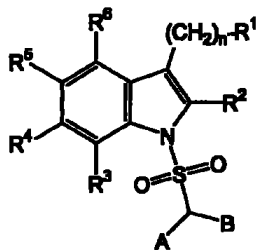
200 mg of 50% Pd/C with a humidity of 5% were added to a solution of
5 403 mg (1 mMol) of 1-cyclohexanesulfonyl-3-(1-methyl-1,2,3,6-tetrahydropyridine-4-yl)-5-nitro-1H-Indole in 200 ml of ethanol. The resulting suspension was hydrogenized at 25 psi of overpressure for 20 hours. Then the catalyst was filtered and evaporated to drying. The resulting crude was purified by chromatography and 150 mg (40%) of the mentioned compound were
10 obtained as a solid cream.

Example 4.- Preparation of 1-Cyclohexanesulfonyl-5-fluoro-3-(1,2,3,5,8,8a-hexahydro-Indolizine-7-yl)-1H-indole

15 1.95 g (78%) of 1-cyclohexanesulfonyl-5-fluoro-3-(1,2,3,5,8,8a-hexahydro-Indolizine-7-yl)-1H-Indole were obtained as an oil from 1.6 g (6.25 mMol) of 5-fluoro-3-(1,2,3,5,8,8a-hexahydro-Indolizine-7-yl)-1H-Indole and 3.42 g (18.76 mMol) of cyclohexanesulfonyl chloride by means of the process described in Example 1. Then 2 ml of a 6N ethanol/HCl solution were added to
20 a solution of 1.95 g (4.85 mMol) of 1-cyclohexanesulfonyl-5-fluoro-3-(1,2,3,5,8,8a-hexahydro-Indolizine-7-yl)-1H-Indole in 20 ml of ethanol, precipitating a solid which was recrystallized from ethanol, obtaining 1.5 g (71%) of the mentioned compound as a white solid.

25 The yields are indicative and no added effort was made to improve them.

The melting point and spectroscopic data for identifying some of the compounds of the present invention are indicated in the following table.



5

Ex	R1	R2	R3	R4	R5	R6	n	A-B	Salt	m p °C	IR cm ⁻¹	¹ H-NMR (300MHz), δ (solvent)
1		H	H	H	NO ₂	H	0		-	155-160	3433, 2938, 2859, 1622, 1371, 1340, 1158, 1126, 988, 612	1.00-1.90 (m, 10H); 2.58 (s, 3H), 2.68 (m, 2H), 2.98 (m, 2H), 3.47 (m, 2H), 3.78 (m, 1H); 6.35 (s, 1H), 7.87 (s, 1H), 8.08 (d, 1H, J=9.2 Hz), 8.28 (dd, 1H, J=9.2 Hz, J'=1.9 Hz), 8.69 (d, 1H, J=1.8 Hz) (DMSO-d ₆)
2		H	H	H	Cl	H	0		-	88-90	3433, 2941, 2858, 2787, 1447, 1364, 1158, 1128, 1116, 614, 557	1.00-1.90 (m, 10H), 2.41 (s, 3H), 2.55 (m, 2H), 2.87 (m, 2H), 3.15 (m, 3H), 6.18 (m, 1H), 7.27 (dd, 1H, J=8.9 Hz, J'=2.0 Hz), 7.32 (s, 1H), 7.79 (d, 1H, J=2.0 Hz), 7.82 (d, 1H, J=1.8 Hz) (CDCl ₃)

8

Ex	R1	R2	R3	R4	R5	R6	n	A B	Salt	m p. °C	IR cm ⁻¹	¹ H-NMR (300MHz), δ (solvent)
3		H	H	H	NH ₂	H	0		-	75 (decomposition)	3376, 2937, 2857, 2784, 1455, 1363, 1342, 1158, 1127, 987, 617, 565	1.00-1.90 (m, 10H), 2.40 (s, 3H), 2.54 (m, 2H), 2.68 (m, 2H); 3.13 (m, 3H), 6.16 (m, 1H); 6.71 (dd, 1H, J=8.8 Hz, J'=2.4 Hz), 7.09 (d, 1H, J=2.2 Hz), 7.23 (s, 1H), 7.67 (d, 1H, J=8.8 Hz) (CDCl ₃)
4		H	H	H	F	H	0		HCl	263 (decomposition)	3424, 2941, 2499, 2451, 1468, 1445, 1371, 1348, 1186, 1157, 1127, 649, 619	1.18 (m, 3H), 1.38 (m, 2H), 1.54 (m, 1H), 1.73 (m, 5H), 2.01 (m, 2H), 2.31 (m, 1H), 2.80 (m, 1H), 3.09 (m, 2H), 3.44 (m, 1H), 3.68 (m, 2H), 3.76 (m, 1H), 4.10 (m, 1H), 6.39 (s, 1H), 7.28 (m, 1H), 7.78 (m, 2H), 7.80 (dd, 1H, J=9.0 Hz, J'=4.6 Hz); (DMSO-d ₆)

46

Pharmaceutical particulars:

Binding of the new compounds of general formula (I) to the 5-HT₆ receptor was determined as previously described.

5

The binding results for some of the compounds of the present invention are indicated in the following table:

Table			
10	Example	% Inhibition 10 ⁻⁶ M	K _i (nM)
	1	59.8 ± 3.0	
	2		98.2
	3		55.1
15	4		191

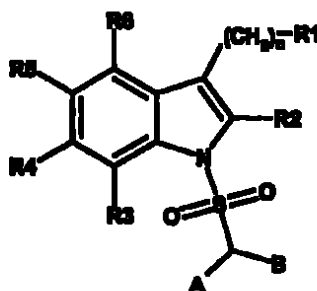
The daily posology in human medicine is comprised between 1 milligram and 2 grams of medicinal product which can be administered in one or several doses. The compositions are prepared under forms that are compatible with the administration route used, preferably tablets, coated tablets, capsules, suppositories, solutions or suspensions. These compositions are prepared by means of known methods and comprise from 1 to 60% by weight of the medicament substance (compound of general formula I), and 40 to 99% by weight of the suitable pharmaceutical vehicle compatible with the medicament substance and the physical form of the composition used. The formula of a tablet containing a product of the invention is provided by way of example:

Example of formula per tablet:

	Example 1	5 mg
5	Lactose	60 mg
	Crystalline cellulose	25 mg
	Povidone K 90	5 mg
	Pregelatinized starch	3 mg
	Colloidal silicon dioxide	1 mg
10	Magnesium stearate	1 mg
	Total weight per tablet	100 mg

CLAIMS

1.- Sulfonamide compounds of general formula (Ia),



(Ia)

5 wherein

10 R^1 represents a $-NR^7R^8$ radical or a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing cycloaliphatic radical, which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system,

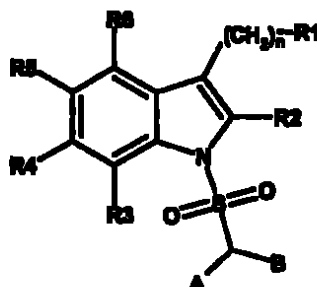
15 R^2 , R^3 , R^4 , R^5 and R^6 , identical or different, each represent hydrogen, halogen, cyano, nitro, a saturated or unsaturated, linear or branched aliphatic radical, a linear or branched alkoxy radical, a linear or branched alkylthio radical, hydroxy, trifluoromethyl, a saturated or unsaturated cycloaliphatic radical, an alkylcarbonyl radical, a phenylcarbonyl or a $-NR^9R^{10}$ group,

20 R^7 and R^8 , identical or different, each represent hydrogen or a saturated or unsaturated, optionally at least mono-substituted linear or branched aliphatic radical,

25

CLAIMS

1.- Sulfonamide compounds of general formula (Ia),



(Ia)

5 wherein

10 R^1 represents a $-NR^7R^8$ radical or a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing cycloaliphatic radical, which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system,

15 R^2 , R^3 , R^4 , R^5 and R^6 , identical or different, each represent hydrogen, halogen, cyano, nitro, a saturated or unsaturated, linear or branched aliphatic radical, a linear or branched alkoxy radical, a linear or branched alkylthio radical, hydroxy, trifluoromethyl, a saturated or unsaturated cycloaliphatic radical, an alkylcarbonyl radical, a phenylcarbonyl or a $-NR^9R^{10}$ group,

20 R^7 and R^8 , identical or different, each represent hydrogen or a saturated or unsaturated, optionally at least mono-substituted linear or branched aliphatic radical,

25

with the proviso that R^8 and R^9 are not hydrogen at the same time, and if one of them, R^8 or R^9 , is a saturated or unsaturated, linear or branched, optionally at least mono-substituted C_1 - C_4 aliphatic radical, the other one is a saturated or unsaturated, linear or branched, optionally at least

5 mono-substituted aliphatic radical with at least five carbon atoms,

or

R^7 and R^8 , together with the bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted, optionally at least one

10 further heteroatom as a ring member containing heterocyclic ring which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system,

15 R^9 and R^{10} , identical or different, each represent hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

20 or

R^9 and R^{10} , together with the bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted, optionally at least one

25 further heteroatom as a ring member containing heterocyclic ring which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system,

A and B, identical or different, each represent a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical

30

or

A and B, together with the carbon atom to which they are bonded, form a saturated or unsaturated, but not aromatic, optionally at least mono-substituted cycloalkyl ring,

5

and

n is 0,

10

optionally in form of one of their stereoisomers, preferably enantiomers or diastereomers, their racemate or in form of a mixture of at least two of their stereoisomers, preferably enantiomers or diastereomers, in any mixing ratio, or a salt thereof, preferably a corresponding physiologically acceptable salt thereof or a corresponding solvate thereof.

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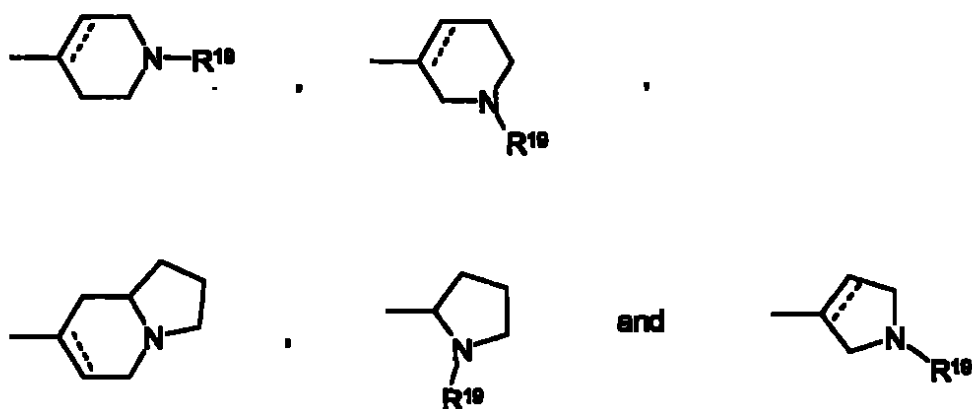
2. The compounds according to claim 1, characterized in that R^1 represents a $-NR^7R^8$ radical or a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing 5- or 6-membered cycloaliphatic radical, which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system, whereby the rings of the ring system are 5- or 6-membered,

20

25

preferably a NR^7R^8 radical or a radical chosen from the group consisting of

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wherein, if present, the dotted line represents an optional chemical bond, and R^{19} represents hydrogen, a linear or branched C_1-C_6 alkyl radical or a benzyl radical, preferably hydrogen or a C_1-C_2 alkyl radical.

5

- 3.- The compounds according to claim 1 or 2, characterized in that R^2 , R^3 , R^4 , R^5 and R^6 , identical or different, each represent hydrogen, F, Cl, Br, cyano, nitro, a linear or branched C_{1-6} alkyl radical, a linear or branched C_{2-6} alkenyl radical, a linear or branched C_{2-6} alkynyl radical, a linear or branched C_{1-6} alkoxy, a linear or branched C_{1-6} alkylthio, hydroxy, trifluoromethyl, a saturated or unsaturated C_{3-6} cycloaliphatic radical, a linear or branched C_{1-6} alkylcarbonyl radical, phenylcarbonyl or an $-NR^9R^{10}$ group,

10

15

preferably H, F, Cl, NO_2 , NH_2 or a C_{1-2} alkyl radical.

- 4.- The compounds according to one or more of claims 1 to 3, characterized in that R^7 and R^8 , identical or different, each represent hydrogen, a linear or branched, optionally at least mono-substituted C_{1-10} alkyl radical, a linear or branched, optionally at least mono-substituted, C_{2-10} alkenyl radical, or a linear or branched, optionally at least mono-substituted, C_{2-10} alkynyl radical or

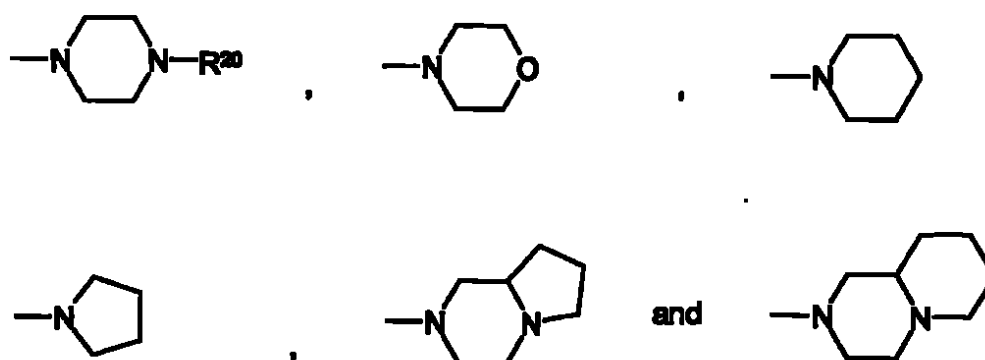
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25

R⁷ and R⁸, together with the bridging nitrogen form a saturated or
 unsaturated, optionally at least mono-substituted, optionally at least one
 further heteroatom as a ring member containing 5- or 6-membered
 heterocyclic ring which may be condensed with a saturated or
 5 unsaturated, optionally at least mono-substituted, optionally at least one
 heteroatom as a ring member containing mono- or bicyclic cycloaliphatic
 ring system, whereby the rings of the ring system are 5- 6- or 7-
 membered.

10 5.- The compounds according to claim 4, characterized in that R⁷ and R⁸,
 identical or different, each represent hydrogen or a linear or branched C₁-
 10 alkyl radical or

15 R⁷ and R⁸, together with the bridging nitrogen atom form a radical chosen
 from the group consisting of



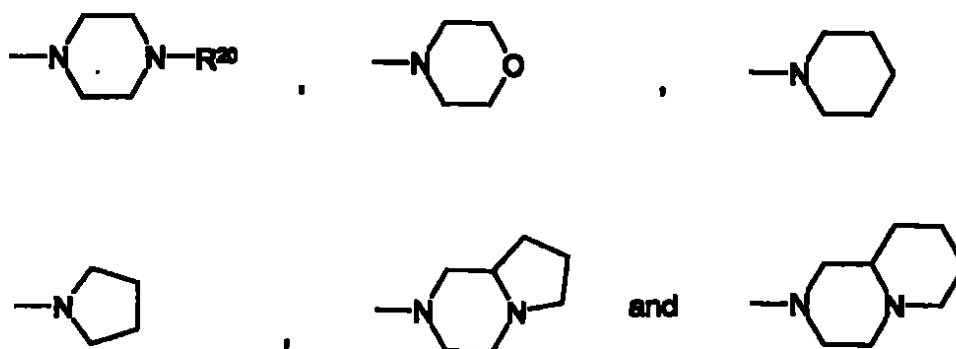
wherein R²⁰, if present, is hydrogen, a linear or branched C₁-C₈ alkyl
 radical or a benzyl radical, preferably hydrogen, or a C₁-C₂ alkyl radical.

- 6.- The compounds according to one or more of claims 1 to 5, characterized in that R^9 and R^{10} , identical or different, each represent hydrogen, a linear or branched, optionally at least mono-substituted C_1 - C_{10} alkyl radical, a linear or branched, optionally at least mono-substituted C_2 - C_{10} alkenyl radical or a linear or branched, optionally at least mono-substituted C_2 - C_{10} alkynyl radical or

R^9 and R^{10} , together with the bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted, optionally at least one further heteroatom as a ring member containing 5- or 6-membered heterocyclic ring, which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system whereby the rings of the ring system are 5- 6- or 7-membered.

- 7.- The compounds according to claim 6, characterized in that R^9 and R^{10} , identical or different, each represent hydrogen or a linear or branched C_1 - C_{10} alkyl radical, or

R^9 and R^{10} , together with the bridging nitrogen atom form a radical chosen from a group consisting of



wherein R^{20} , if present, is hydrogen, a linear or branched C_1 - C_6 alkyl radical or a benzyl radical, preferably hydrogen, or a C_1 - C_2 alkyl radical.

8.- The compounds according to one or more of claims 1-7, characterized in that A and B, identical or different, each represent a linear or branched C₁-C₈ alkyl radical, a linear or branched C₂-C₈ alkenyl radical or a linear or branched C₂-C₈ alkynyl radical,

preferably a linear or branched C₁-C₆ alkyl radical, or

A and B, together with the carbon atom to which they are bonded, form a saturated or unsaturated, but not aromatic, optionally at least mono-substituted cycloalkyl ring,

preferably a C₃-C₈ cycloalkyl ring,

more preferably a cyclohexyl ring.

9.- The compounds according to one or more of claims 1-8, characterized in that the compound is selected from a group consisting of

[1] 1-Cyclohexanesulfonyl-3-(1-methyl-1,2,3,6-tetrahydropyridine-4-yl)-5-nitro-1H-indole,

[2] 5-Chloro-1-cyclohexanesulfonyl-3-(1-methyl-1,2,3,6-tetrahydropyridine-4-yl)-1H-indole,

[3] 5-Amino-1-cyclohexanesulfonyl-3-(1-methyl-1,2,3,6-tetrahydropyridine-4-yl)-1H-Indole and

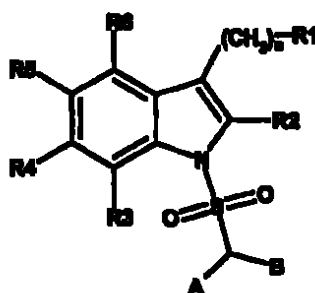
[4] 1-Cyclohexanesulfonyl-5-fluoro-3-(1,2,3,5,8,8a-hexahydro-indolizine-7-yl)-1H-Indole hydrochloride

and their corresponding salts and solvates.

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10.- Sulfonamide compounds of general formula (Ib),



(Ib)

wherein

5

R^1 is a $-NR^7R^8$ radical,

10

R^2 , R^3 , R^4 , R^5 and R^6 , identical or different, each represent hydrogen, halogen, cyano, nitro, a saturated or unsaturated, linear or branched aliphatic radical, a linear or branched alkoxy radical, a linear or branched alkylthio radical, hydroxy, trifluoromethyl, a saturated or unsaturated cycloaliphatic radical, an alkylcarbonyl radical, a phenylcarbonyl or a $-NR^9R^{10}$ group,

15

R^7 and R^8 , identical or different, each represent hydrogen or a saturated or unsaturated, optionally at least mono-substituted linear or branched C_{1-4} aliphatic radical,

20

R^9 and R^{10} , identical or different, each represent hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

or

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R⁹ and R¹⁰, together with the bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted, optionally at least one further heteroatom as a ring member containing heterocyclic ring which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system,

A and B, identical or different, each represent a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical

10

or

A and B, together with the carbon atom to which they are bonded, form a saturated or unsaturated, but not aromatic, optionally at least mono-substituted cycloalkyl ring,

15

and**n is 0;**

20

optionally in form of one of its stereoisomers, preferably enantiomers or diastereomers, their racemate or in form of a mixture of at least two of their stereoisomers, preferably enantiomers or diastereomers, in any mixing ratio, or a salt thereof, preferably a corresponding physiologically acceptable salt thereof or a corresponding solvate thereof.

25

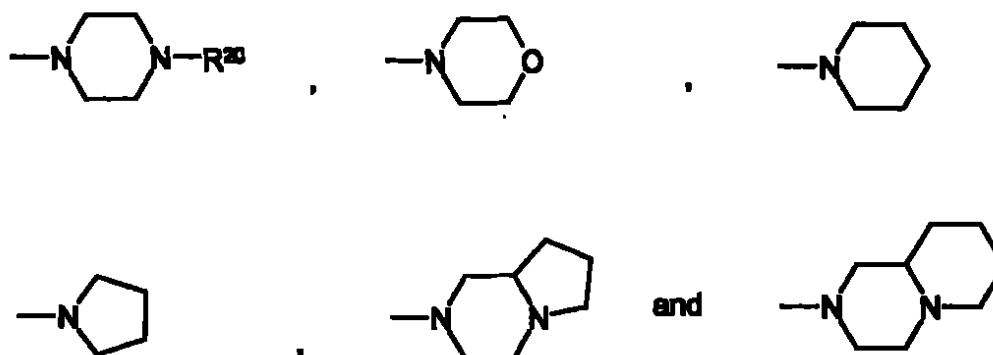
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- 11.- The compounds according to claim 10, characterized in that R^2 , R^3 , R^4 , R^5 and R^6 , identical or different, each represent hydrogen, F, Cl, Br, cyano, nitro, a linear or branched C_1 - C_6 alkyl radical, a linear or branched C_2 - C_6 alkenyl radical, a linear or branched C_2 - C_6 alkynyl radical, a linear or branched C_1 - C_6 -alkoxy, a linear or branched C_1 - C_6 -alkylthio, hydroxy, trifluoromethyl, a saturated or unsaturated C_3 - C_6 cycloaliphatic radical, a linear or branched C_1 - C_6 -alkylcarbonyl radical, phenylcarbonyl or an $-NR^9R^{10}$ group,
- preferably H, F, Cl, NO_2 , NH_2 or a C_1 - C_2 alkyl radical.
- 12.- The compounds according to claim 10 or 11, characterized in that R^7 and R^8 , identical or different, wherein R^7 and R^8 , identical or different, each represent hydrogen, a linear or branched, optionally at least mono-substituted C_1 - C_4 alkyl radical,
- preferably hydrogen or a C_1 - C_2 alkyl radical, with the proviso that R^7 and R^8 are not hydrogen at the same time.
- 13.- The compounds according to one or more of claims 10 to 12, characterized in that R^9 and R^{10} , identical or different, each represent hydrogen, a linear or branched, optionally at least mono-substituted C_1 - C_{10} alkyl radical, a linear or branched, optionally at least mono-substituted C_2 - C_{10} alkenyl radical, or a linear or branched, optionally at least mono-substituted C_2 - C_{10} alkynyl radical or
- R^9 and R^{10} , together with the bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted, optionally at least one further heteroatom as a ring member containing 5- or 6-membered heterocyclic which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom

as a ring member containing mono- or bicyclic cycloaliphatic ring system, whereby the rings of the ring system are 5- 6- or 7-membered.

- 14.- The compounds according to claim 13, characterized in that R^9 and R^{10} ,
 5 identical or different, each represent hydrogen or a linear or branched C_1 - C_{10} alkyl radical, or

R^9 and R^{10} , together with the bridging nitrogen atom form a radical chosen from a group consisting of



10

wherein R^{20} , if present, represents hydrogen, a linear or branched C_1 - C_6 alkyl radical or a benzyl radical, preferably hydrogen, or a C_1 - C_2 alkyl radical.

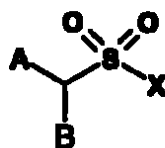
- 15.- The compounds according to one or more of claims 10 to 14,
 characterized in that A and B, together with the carbon atom to which
 they are bonded, form a saturated or unsaturated, but not aromatic,
 optionally at least mono-substituted cycloalkyl ring,

20 preferably a C_3 - C_8 cycloalkyl ring,

more preferably a cyclohexyl ring.

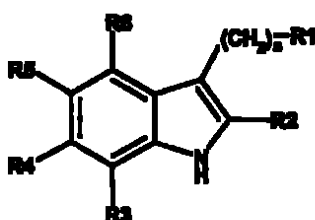
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- 16.- A process for obtaining a sulfonamide derivative of general formula (Ia) and/or (Ib), according to one or more of claims 1 to 15, characterized in that at least one compound of general formula (II), or one of its suitably protected derivatives,



(II)

wherein A and B have the meaning according to one or more of claims 1 to 15 and X is an acceptable leaving group, preferably an halogen atom, more preferably chlorine, is reacted with at least one substituted indole of general formula (III)



(III)

wherein R^1 - R^6 and n have the meaning according to one or more of claims 1 to 15, or one of their suitable protected derivatives, and, if necessary, the protective groups are removed.

- 17.- A process for obtaining a sulfonamide derivative of general formula (Ia) and/or (Ib) according to one or more of claims 1-15, wherein one or more substituents R^2 , R^3 , R^4 , R^5 or R^6 represent a nitro group, characterized in that a sulfonamide derivative of corresponding general formula (Ia) and/or (Ib) is reduced to a sulfonamide derivative of corresponding

general formula (Ia) and/or (Ib), wherein one or more substituents R^2 , R^3 , R^4 , R^5 or R^6 represent an amino group.

- 18.- A process for preparing the salts, preferably the physiologically acceptable salts of the compounds of general formula (Ia) and/or (Ib), according to one or more of claims 1 to 15, consisting of reacting at least one compound of the general formula (Ia) and/or at least one compound of the general formula (Ib) with a mineral acid or organic acid in a suitable solvent.
- 19.- A medicament comprising at least one compound according to one or more of claims 1 to 9 and optionally one or more pharmacologically acceptable excipients.
- 20.- A medicament according to claim 19, for 5-HT₆ receptor regulation, for the prophylaxis and/or treatment of a disorder or disease related to food intake, preferably for the regulation of appetite, for the maintenance, increase or reduction of body weight, for the prophylaxis and/or treatment of obesity, bulimia, anorexia, cachexia or type II diabetes (non insulin dependent diabetes mellitus), preferably type II diabetes caused by obesity, for the prophylaxis and/or treatment of gastrointestinal tract disorders, preferably irritable bowel syndrome, for cognitive enhancement, for the prophylaxis and/or treatment of disorders of the central nervous system, anxiety, panic disorders, depression, preferably bipolar disorders, cognitive memory disorders, senile dementia processes, neurodegenerative disorders, preferably Alzheimer's disease, Parkinson's disease, Huntington's disease and/or multiple sclerosis, schizophrenia, psychosis or infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder),

preferably for 5-HT₆ receptor regulation, for the prophylaxis and/or treatment of a disorder or disease related to food intake, preferably for the regulation of appetite, for the maintenance, increase or reduction of body weight, for the prophylaxis and/or treatment of obesity, bulimia, anorexia, cachexia or type II diabetes (non insulin dependent diabetes mellitus), preferably type II diabetes caused by obesity, for the prophylaxis and/or treatment of gastrointestinal tract disorders, preferably irritable bowel syndrome.

21. - The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for 5-HT₆ receptor regulation.

22.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of a disorder or disease related to food intake.

23.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the regulation of appetite.

24.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the maintenance, increase or reduction of body weight.

25.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of obesity.

26.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of bulimia.

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- 27.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament the prophylaxis and/or treatment of anorexia.
- 5 28.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of cachexia.
- 10 29.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of type II diabetes (non insulin dependent diabetes mellitus), preferably type II diabetes caused by obesity.
- 15 30.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the manufacture of a medicament for the prophylaxis and/or treatment of gastrointestinal tract disorders.
- 20 31.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of irritable bowel syndrome.
- 25 32.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of anxiety.
- 30 33.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of depression.

- 34.- The use of at least one compound according to one more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of bipolar disorders.
- 5 35. - The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of cognitive memory disorders.
- 10 36.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of senile dementia processes.
- 15 37.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of Alzheimer's Disease.
- 20 38.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of Parkinson's Disease.
- 39.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of Huntington's Disease.
- 25 40.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of Multiple Sclerosis.
- 30 41.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of dementias in which a cognitive deficit predominates.

- 42.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of psychosis.
- 5 43.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of Infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder).
- 10 44.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of disorders of the central nervous system.
- 15 45.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of schizophrenia.
- 46.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for cognitive enhancement.
- 20 47. A medicament comprising at least one compound according to one or more of claims 9 to 15 and optionally at least one or more of pharmacologically acceptable excipients.
- 25 48.- A medicament according to claim 47 for 5-HT₆ receptor regulation, for the prophylaxis and/or treatment of a disorder or disease related to food intake, preferably for the regulation of appetite, for the maintenance, increase or reduction of body weight, for the prophylaxis and/or treatment of obesity, bulimia, anorexia, cachexia or type II diabetes (non insulin dependent diabetes mellitus), preferably type II diabetes caused by
- 30 obesity, for the prophylaxis and/or treatment of gastrointestinal tract disorders, preferably irritable bowel syndrome, for cognitive

enhancement, for the prophylaxis and/or treatment of disorders of the central nervous system, anxiety, panic disorders, depression, preferably bipolar disorders, cognitive memory disorders, senile dementia processes, neurodegenerative disorders, preferably Alzheimer's disease, Parkinson's disease, Huntington's disease and/or multiple sclerosis, schizophrenia, psychosis or infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder),

preferably for cognitive enhancement, for the prophylaxis and/or treatment of disorders of the central nervous system, anxiety, panic disorders, depression, preferably bipolar disorders, cognitive memory disorders, senile dementia processes, neurodegenerative disorders, preferably Alzheimer's disease, Parkinson's disease, Huntington's disease and multiple sclerosis, schizophrenia, psychosis or infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder).

49.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for 5-HT₆ receptor regulation.

50.- The use of at least one compound according to one or more of claims 9 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of a disorder or disease related to food intake.

51.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the regulation of appetite.

52.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the maintenance, increase or reduction of body weight.

- 53.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of obesity.
- 5 54.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of bulimia.
- 10 55.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of anorexia.
- 15 56.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of cachexia.
- 20 57.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of type II diabetes (non-Insulin-dependent diabetes mellitus), preferably type II diabetes caused by obesity.
- 25 58.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of gastrointestinal tract disorders.
- 59.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of irritable bowel syndrome.
- 30 60.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of anxiety.

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-68-

- 81.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of depression.
- 5 82.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of bipolar disorders.
- 10 83.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of cognitive memory disorders.
- 15 84.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of senile dementia processes.
- 20 85.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of Alzheimer's Disease.
- 25 86.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of Parkinson's Disease.
- 30 87.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of Huntington's Disease.
- 88.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of Multiple Sclerosis.

- 69.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of dementias in which a cognitive deficit predominates.
- 5
- 70.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of psychosis.
- 10
- 71.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder).
- 15
- 72.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of disorders of the central nervous system.
- 20
- 73.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of schizophrenia.
- 25
74. - The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for cognitive enhancement.

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/404 C07D209/40 A61P3/04 A61P25/00 C07D401/04
C07D471/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BEILSTEIN Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 02/051837 A (WYETH CORP) 4 July 2002 (2002-07-04) claims 1,12,13,20	1-74
Y	WO 01/12629 A (NPS ALLELIX CORP) 22 February 2001 (2001-02-22) claims 1,10,12	1-74
Y	WO 02/060871 A (FLAUGH MICHAEL EDWARD ; GILLIG JAMES RONALD (US); HEINZ LAWRENCE JOSEP) 8 August 2002 (2002-08-08) claims 1,12,14; example 12	1-74

☐ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubt on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"A" document member of the same patent family

Date of the actual completion of the international search

18 November 2004

Date of mailing of the international search report

25/11/2004

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Seymour, L

INTERNATI NAL SEARCH REPORT

Information on patent family members

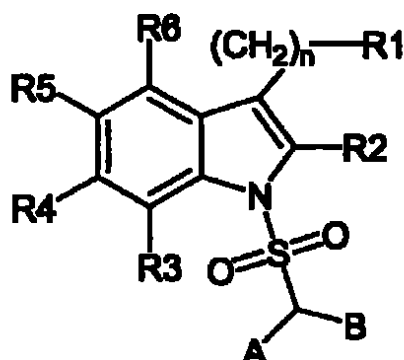
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DERIVADOS DE 1-SULFONILINDOL, SU PREPARACIÓN Y SU USO COMO
LIGANDOS DE 5-HT₆

La presente invención se refiere a nuevos derivados de sulfonamidas, de fórmula general (Ia, Ib, Ic),



(Ia, Ib, Ic),

5

opcionalmente en forma de uno de sus estereoisómeros, preferiblemente enantiómeros o diastereómeros, su racemato o en forma de una mezcla de al menos dos de sus estereoisómeros, preferiblemente enantiómeros o diastereómeros, en cualquier razón de mezcla, o sus sales, preferiblemente sus sales fisiológicamente aceptables, correspondientes o los solvatos correspondientes de los mismos; a los procedimientos para su preparación, a su aplicación como medicamentos en medicina humana y/o veterinaria y a las composiciones farmacéuticas que los contienen.

Los nuevos compuestos de la presente invención pueden utilizarse en la industria farmacéutica como intermedios y para la preparación de medicamentos.

15 La superfamilia de los receptores de serotonina (5-HT) comprende 7 clases (5-HT₁-5-HT₇) que abarcan 14 subclases humanas [D. Hoyer, et al., *Neuropharmacology*, 1997, 36, 419]. El receptor 5-HT₆ ha sido el último receptor de serotonina identificado por clonación molecular en ratas [F.J. Monsma, et al., *Mol. Pharmacol.*, 1993, 43, 320; M. Ruat, et al., *Biochem. Biophys. Res. Commun.*, 1993, 193, 268] así como en
 20 humanos [R. Kohen, et al., *J. Neurochem.*, 1996, 66, 47]. Los compuestos con una afinidad por el receptor 5-HT₆ son útiles en el tratamiento de diversos trastornos del sistema nervioso central y del aparato gastrointestinal así como el síndrome del Intestino irritable. Los compuestos con una afinidad por el receptor 5-HT₆ son útiles para el tratamiento de la ansiedad, depresión y trastornos cognitivos de la memoria [M.
 25 Yoshioka, et al., *Ann. NY Acad. Sci.*, 1998, 861, 244; A. Bourson, et al., *Br. J. Pharmacol.*, 1998, 125, 1562; D.C. Rogers, et al., *Br. J. Pharmacol. Suppl.*, 1999, 127, 22P; A. Bourson, et al., *J. Pharmacol. Exp. Ther.*, 1995, 274, 173; A.J. Sleight, et al.,

Behav. Brain Res., 1996, 73, 245; T.A. Branchek, et al., *Annu. Rev. Pharmacol. Toxicol.*, 2000, 40, 319; C. Routledge, et al., *Br. J Pharmacol.*, 2000, 130, 1606]. Se ha demostrado que los antipsicóticos típicos y atípicos para el tratamiento de la esquizofrenia tienen una elevada afinidad por los receptores 5-HT₂ [B.L. Roth, et al., *J. Pharmacol. Exp. Ther.*, 1994, 268, 1403; C.E. Glatt, et al., *Mol. Med.*, 1995, 1, 398; F.J. Mosma, et al., *Mol. Pharmacol.*, 1993, 43, 320; T. Shinkai, et al., *Am. J. Med. Genet.*, 1999, 88, 120]. Los compuestos con una afinidad por el receptor 5-HT₂ son útiles para el tratamiento de la hiperquinesia infantil (ADHD, déficit de atención/ trastorno de hiperactividad) [W.D. HIRST, et al., *Br. J. Pharmacol.*, 2000, 130, 1597; C. Gérard, et al., *Brain Research*, 1997, 746, 207; M.R. Pranzatelli, *Drugs of Today*, 1997, 33, 379].

La solicitud de patente WO 01/32646 describe sulfonamidas derivadas de biciclos, con 6 miembros en cada uno de los anillos, anillos aromáticos o heteroaromáticos con actividad antagonista del receptor 5-HT₂.

La solicitud de patente EP 0 733 628 describe sulfonamidas derivadas de indol con actividad antagonista del receptor 5-HT_{1F} útiles para el tratamiento de las migrañas.

Además, se ha demostrado que el receptor 5-HT₂ desempeña un papel en la ingestión de alimentos [Neuropharmacology, 41, 2001, 210-219].

Las disfunciones alimentarias, particularmente la obesidad, son una amenaza seria y cada vez más frecuente para la salud de seres humanos de todas las edades, puesto que estas enfermedades incrementan el riesgo de desarrollar otras enfermedades graves e incluso mortales, preferiblemente la diabetes y las enfermedades coronarias.

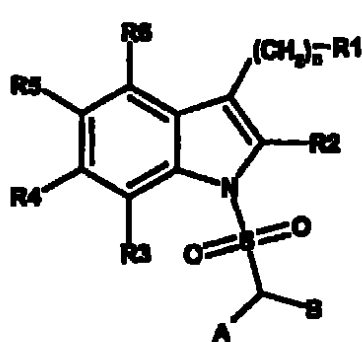
Por consiguiente, un objeto de la presente invención era proporcionar nuevos compuestos, particularmente adecuados como sustancias activas en medicamentos, preferiblemente en medicamentos para la regulación de los receptores 5-HT₂, para la profilaxis y/o el tratamiento de un trastorno o enfermedad relacionada con la ingestión de alimentos, preferiblemente para la regulación del apetito, para el mantenimiento, incremento o reducción del peso corporal, para la profilaxis y/o el tratamiento de la obesidad, bulimia, anorexia, caquexia o diabetes de tipo II (diabetes mellitus insulino independiente), preferiblemente diabetes tipo II que es causada por la obesidad, para la profilaxis y/o el tratamiento de trastornos del tracto gastrointestinal, preferiblemente el síndrome del intestino irritable, para la mejora de la cognición, para la profilaxis y/o el tratamiento de trastornos del sistema nervioso central, ansiedad, pánico, depresión, trastornos bipolares, trastornos cognitivos de la memoria, procesos de demencia senil,

preferiblemente enfermedad de Alzheimer, enfermedad de Parkinson, enfermedad de Huntington, esclerosis múltiple, esquizofrenia, psicosis o hiperquinesia infantil (ADHD, déficit de atención/ trastorno de hiperactividad) y otros trastornos mediados por el receptor 5-HT₆ de la serotonina en humanos y/o en animales, preferiblemente en mamíferos, más preferiblemente en humanos.

Se ha descubierto que los derivados de 1-sulfonilindol de fórmulas generales (Ia, Ib, Ic) descritos a continuación muestran afinidad por el receptor 5-HT₆.

Estos compuestos son por consiguiente adecuados para la fabricación de un medicamento para la profilaxis y/o el tratamiento de los trastornos relacionados con la ingestión de alimentos, preferiblemente para la regulación del apetito, para el mantenimiento, incremento o reducción del peso corporal, para la profilaxis y/o el tratamiento de la obesidad, bulimia, anorexia, caquexia o diabetes de tipo II (diabetes mellitus insulino independiente), preferiblemente diabetes tipo II que sea causada por la obesidad, para la profilaxis y/o el tratamiento de trastornos del tracto gastrointestinal, preferiblemente el síndrome del intestino irritable, para la mejora de la cognición, para la profilaxis y/o el tratamiento de trastornos del sistema nervioso central, ansiedad, pánico, depresión, trastornos bipolares, procesos de demencia senil, trastornos neurodegenerativos, preferiblemente enfermedad de Alzheimer, enfermedad de Parkinson, enfermedad de Huntington y esclerosis múltiple, esquizofrenia, psicosis, hiperquinesia infantil (ADHD, déficit de atención/ trastorno de hiperactividad) y otros trastornos mediados por el receptor 5-HT₆ de la serotonina en humanos y/o en mamíferos, preferiblemente en mamíferos, más preferiblemente en humanos. Estos compuestos son también adecuados para la preparación de un medicamento para la mejora de la cognición.

De este modo, un objeto de la presente invención son compuestos de fórmula general (Ia)



(Ia)

en la que

R^1 representa un radical $-NR^7R^8$ o un radical cicloalifático saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo como miembro del anillo, que puede estar condensado con un sistema cíclico cicloalifático mono- o bicíclico saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo como miembro del anillo,

R^2 , R^3 , R^4 , R^5 y R^6 , idénticos o diferentes, representan cada uno hidrógeno, halógeno, ciano, nitro, un radical alifático lineal o ramificado, saturado o insaturado, un radical alcoxi lineal o ramificado, un radical alquiltio lineal o ramificado, hidroxilo, trifluorometilo, un radical cicloalifático saturado o insaturado, un radical alquilcarbonilo, un fenilcarbonilo o un grupo $-NR^9R^{10}$,

R^7 y R^8 , idénticos o diferentes, representan cada uno hidrógeno o un radical alifático, lineal o ramificado, saturado o insaturado, opcionalmente al menos monosustituido,

con la condición, de que R^8 y R^9 no sean al mismo tiempo hidrógeno, y si uno de ellos R^8 y R^9 , representa un radical alifático C_1-C_4 , lineal o ramificado, saturado o insaturado, opcionalmente al menos monosustituido, el otro de ellos representa un radical alifático lineal o ramificado, saturado o insaturado, opcionalmente al menos monosustituido con al menos cinco átomos de carbono,

o

R^7 y R^8 junto con el átomo puente de nitrógeno forman un anillo heterocíclico saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo más como miembro del anillo, que puede estar condensado con un sistema cíclico cicloalifático mono- o bicíclico saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo como miembro del anillo,

R^9 y R^{10} , idénticos o diferentes, representan cada uno hidrógeno o un radical alifático, lineal o ramificado, saturado o insaturado, opcionalmente al menos monosustituido,

o

R^9 y R^{10} junto con el átomo puente de nitrógeno forman un anillo heterocíclico saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo más como miembro del anillo, que puede estar condensado con un sistema cíclico cicloalifático mono- o bicíclico saturado o

R^7 y R^8 , idénticos o diferentes, representan cada uno hidrógeno o un radical alifático C_1-C_4 , lineal o ramificado, saturado o insaturado, opcionalmente al menos monosustituido,

5 R^9 y R^{10} , idénticos o diferentes, representan cada uno hidrógeno o un radical alifático, lineal o ramificado, saturado o insaturado, opcionalmente al menos monosustituido,

o

10 R^9 y R^{10} junto con el átomo puente de nitrógeno forman un anillo heterocíclico saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo más como miembro del anillo, que puede estar condensado con un sistema cíclico cicloalifático mono- o bicíclico saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo como miembro del anillo,

15 A y B, idénticos o diferentes, representan cada uno un radical alifático, lineal o ramificado, saturado o insaturado, opcionalmente al menos monosustituido,

o

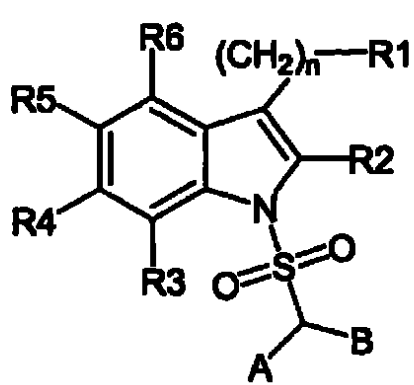
A y B, junto con el átomo de carbono al que están unidos, forman un anillo cicloalquilo saturado o insaturado, pero no aromático, opcionalmente al menos monosustituido,

20 y

n es 0, 1, 2, 3 ó 4;

opcionalmente en forma de uno de sus estereoisómeros, preferiblemente enantiómeros o diasterómeros, su racemato o en forma de una mezcla de al menos dos de sus estereoisómeros, preferiblemente enantiómeros o diasterómeros, en
25 cualquier razón de mezcla, o una sal de los mismos, preferiblemente una sal fisiológicamente aceptable correspondiente de los mismos, o un solvato correspondiente de los mismos.

Todavía otro aspecto de la presente invención son los compuestos de fórmula general (Ic)



(Ic)

en la que

R^1 representa un radical $-NR^7R^8$ o un radical cicloalifático saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo como miembro del anillo, que puede estar condensado con un sistema cíclico cicloalifático mono- o bicíclico saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo como miembro del anillo,

R^2 , R^3 , R^4 , R^5 y R^6 , idénticos o diferentes, representan cada uno hidrógeno, halógeno, ciano, nitro, un radical alifático lineal o ramificado, saturado o insaturado, un radical alcoxi lineal o ramificado, un radical alquiltio lineal o ramificado, hidroxilo, trifluorometilo, un radical cicloalifático saturado o insaturado, un radical alquilcarbonilo, un fenilcarbonilo o un grupo $-NR^9R^{10}$,

R^7 y R^8 , idénticos o diferentes, representan cada uno hidrógeno o un radical alifático, lineal o ramificado, saturado o insaturado, opcionalmente al menos monosustituido,

o

R^7 y R^8 junto con el átomo puente de nitrógeno forman un anillo heterocíclico saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo más como miembro del anillo, que puede estar condensado con un sistema cíclico cicloalifático mono- o bicíclico saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo como miembro del anillo,

R^9 y R^{10} , idénticos o diferentes, representan cada uno hidrógeno o un radical alifático, lineal o ramificado, saturado o insaturado, opcionalmente al menos monosustituido,

o

R^8 y R^{10} junto con el átomo puente de nitrógeno forman un anillo heterocíclico saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo más como miembro del anillo, que puede estar condensado con un sistema cíclico cicloalifático mono- o bicíclico saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo como miembro del anillo,

A y B, idénticos o diferentes, representan cada uno un radical alifático, lineal o ramificado, saturado o insaturado, opcionalmente al menos monosustituido,

o

A y B, junto con el átomo de carbono al que están unidos, forman un anillo cicloalquilo saturado o insaturado, pero no aromático, opcionalmente al menos monosustituido,

y

n es 0, 1, 2, 3 ó 4;

opcionalmente en forma de uno de sus estereoisómeros, preferiblemente enantiómeros o diasterómeros, su racemato o en forma de una mezcla de al menos dos de sus estereoisómeros, preferiblemente enantiómeros o diasterómeros, en cualquier razón de mezcla, o una sal de los mismos, preferiblemente una sal fisiológicamente aceptable correspondiente de los mismos, o un solvato correspondiente de los mismos.

Si uno o más de los residuos R^2 - R^{10} , A y B, representan un radical alquilo, un radical alquenilo o un radical alquinilo, que está sustituido por uno o más sustituyentes, cada uno de estos sustituyentes puede seleccionarse preferiblemente del grupo que consiste en hidroxilo, halógeno, alquilo C_1 - C_8 lineal o ramificado, alcoxi C_1 - C_8 lineal o ramificado, perfluoroalquilo C_1 - C_8 lineal o ramificado, perfluoroalcoxi C_1 - C_8 lineal o ramificado, o un radical fenilo opcionalmente al menos monosustituido.

Si dicho radical fenilo está él mismo sustituido por uno o más sustituyentes, cada uno de estos sustituyentes puede seleccionarse preferiblemente del grupo que consiste en flúor, cloro, bromo, alquilo C_1 - C_8 lineal o ramificado, alcoxi C_1 - C_8 lineal o ramificado, alquiltio C_1 - C_8 lineal o ramificado, un radical trifluorometilo, un radical ciano y un radical $NR^{11}R^{12}$, en el que R^{11} y R^{12} , idénticos o diferentes, se definen como R^7 y R^8 .

Si R^1 es un radical cicloalifático saturado o insaturado, que contiene opcionalmente al menos un heteroátomo como miembro del anillo, el cual está sustituido por uno o más sustituyentes y/o si R^1 comprende un sistema cíclico

cicloalifático mono- o bicíclico saturado o insaturado, que contiene opcionalmente al menos un heteroátomo como miembro del anillo, el cual está sustituido por uno o más sustituyentes, a menos que se defina lo contrario, cada uno de estos sustituyentes puede seleccionarse preferiblemente del grupo que consiste en hidroxilo, flúor, cloro, bromo, alquilo C₁-C₆ lineal o ramificado, alcoxi C₁-C₆ lineal o ramificado, perfluoroalquilo C₁-C₆ lineal o ramificado, perfluoroalcoxi C₁-C₆ lineal o ramificado y bencilo, más preferiblemente del grupo que consiste en alquilo C₁-C₆ lineal o ramificado y bencilo.

Los heteroátomos del radical cicloalifático y/o de dicho sistema cíclico cicloalifático mono o bicíclico pueden seleccionarse, independientemente unos de otros, preferiblemente del grupo que consiste en nitrógeno, azufre y oxígeno, se elige más preferiblemente nitrógeno como heteroátomo.

Dicho radical cicloalifático puede contener 0, 1, 2 ó 3 heteroátomos elegidos del grupo mencionado anteriormente, preferiblemente contiene 0, 1 ó 2 heteroátomos elegidos del grupo mencionado anteriormente.

Si R⁷ y R⁸ junto con el átomo puente de nitrógeno forman un anillo heterocíclico saturado o insaturado, que contiene al menos un heteroátomo más como miembro del anillo, el cual está sustituido por uno o más sustituyentes y/o condensado con un sistema cíclico cicloalifático mono o bicíclico saturado o no saturado, que contiene opcionalmente al menos un heteroátomo como miembro del anillo, que está sustituido por uno o más sustituyentes, a menos que se defina lo contrario, cada uno de estos sustituyentes puede seleccionarse preferiblemente del grupo que consiste en hidroxilo, flúor, cloro, bromo, alquilo C₁-C₆ lineal o ramificado, alcoxi C₁-C₆ lineal o ramificado, perfluoroalquilo C₁-C₆ lineal o ramificado, perfluoroalcoxi C₁-C₆ lineal o ramificado y bencilo, más preferiblemente del grupo que consiste en alquilo C₁-C₆ lineal o ramificado y bencilo.

Si el anillo heterocíclico contiene uno o más heteroátomos adicionales y/o si uno o ambos anillos mono o bicíclicos contienen uno o más heteroátomos, estos heteroátomos pueden seleccionarse, independientemente unos de otros, preferiblemente del grupo que consiste en nitrógeno, azufre y oxígeno, más preferiblemente se elige el nitrógeno como heteroátomo.

Dicho anillo heterocíclico puede contener 0, 1, 2 ó 3 heteroátomos adicionales elegidos del grupo mencionado anteriormente, preferiblemente contiene 0 ó 1 heteroátomos elegidos del grupo mencionado anteriormente.

Si A es un radical alifático, es decir, un radical alquilo, alqueno o alquino, sustituido por uno o más sustituyentes, cada uno de estos sustituyentes puede seleccionarse preferiblemente del grupo que consiste en hidroxilo, halógeno, alquilo C₁-C₆ lineal o ramificado, alcoxi C₁-C₆ lineal o ramificado, perfluoroalquilo C₁-C₆ lineal o ramificado, perfluoroalcoxi C₁-C₆ lineal o ramificado o un radical fenilo opcionalmente al menos monosustituido.

Si dicho radical fenilo está él mismo sustituido por uno o más sustituyentes, cada uno de los sustituyentes puede seleccionarse preferiblemente del grupo que consiste en flúor, cloro, bromo, alquilo C₁-C₆ lineal o ramificado, alcoxi C₁-C₆ lineal o ramificado, alquiltio C₁-C₆ lineal o ramificado, un radical trifluorometilo, un radical ciano y un radical NR¹³R¹⁴, en el que R¹³ y R¹⁴, idénticos o diferentes se definen como R⁷ y R⁸.

Si B es un radical alifático, es decir, un radical alquilo, un radical alqueno o un radical alquino, el cual está sustituido por uno o más sustituyentes, cada uno de estos sustituyentes puede seleccionarse preferiblemente del grupo que consiste en hidroxilo, halógeno, alquilo C₁-C₆ lineal o ramificado, alcoxi C₁-C₆ lineal o ramificado, perfluoroalquilo C₁-C₆ lineal o ramificado, perfluoroalcoxi C₁-C₆ lineal o ramificado o un radical fenilo opcionalmente al menos monosustituido.

Si dicho radical fenilo está él mismo sustituido por uno o más sustituyentes, cada uno de estos sustituyentes puede seleccionarse preferiblemente del grupo que consiste en flúor, cloro, bromo, alquilo C₁-C₆ lineal o ramificado, alcoxi C₁-C₆ lineal o ramificado, alquiltio C₁-C₆ lineal o ramificado, un radical trifluorometilo, un radical ciano y un radical NR¹⁵R¹⁶, en el que R¹⁵ y R¹⁶, idénticos o diferentes se definen como R⁷ y R⁸.

Si A y B, junto con el átomo de carbono al que están unidos, forman un anillo cicloalquilo saturado o insaturado, pero no aromático, el cual está sustituido por uno o más sustituyentes, cada uno de estos sustituyentes puede seleccionarse preferiblemente del grupo que consiste en hidroxilo, halógeno, alquilo C₁-C₆ lineal o ramificado, alcoxi C₁-C₆ lineal o ramificado, perfluoroalquilo C₁-C₆ lineal o ramificado, perfluoroalcoxi C₁-C₆ lineal o ramificado o un radical fenilo opcionalmente al menos monosustituido.

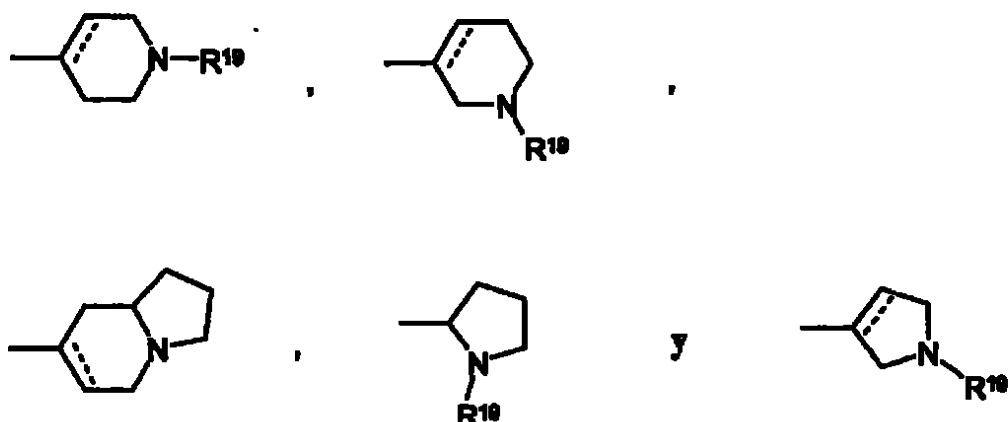
Si dicho radical fenilo está él mismo sustituido por uno o más sustituyentes, cada uno de estos sustituyentes puede seleccionarse preferiblemente del grupo que consiste en flúor, cloro, bromo, alquilo C₁-C₆ lineal o ramificado, alcoxi C₁-C₆ lineal o ramificado, alquiltio C₁-C₆ lineal o ramificado, un radical trifluorometilo, un radical ciano

y un radical $\text{NR}^{17}\text{R}^{18}$, en el que R^{17} y R^{18} , idénticos o diferentes se definen como R^7 y R^8 .

Si uno de los sustituyentes R^2 , R^3 , R^4 , R^5 y R^6 representan un radical alifático lineal o ramificado, un radical alcoxi lineal o ramificado o un radical alquiltio lineal o ramificado, la cadena de carbono puede tener preferiblemente 1-6, más preferiblemente 1-3 átomos de carbono.

Los expertos en la técnica, entenderán que el término "condensado" indica que los anillos condensados comparten más de un átomo. El término "anulado" o "fusionado" también puede usarse para este tipo de enlace.

Se prefieren derivados de sulfonamidas de fórmula general (Ia), en la que R^1 representa un radical $-\text{NR}^7\text{R}^8$ o un radical cicloalifático de 5 ó 6 miembros saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo como miembro del anillo, que puede estar condensado con un sistema cíclico cicloalifático mono o bicíclico saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo como miembro del anillo, en el cual los anillos del sistema cíclico tienen 5 ó 6 miembros, más preferiblemente R^1 representa un radical $-\text{NR}^7\text{R}^8$ o un radical seleccionado del grupo que consiste en



en los que, si está presente, la línea de puntos representa un enlace químico opcional y R^{10} representa hidrógeno, un radical alquilo $\text{C}_1\text{-C}_6$ lineal o ramificado o un radical bencilo, preferiblemente hidrógeno o un radical alquilo $\text{C}_1\text{-C}_2$, y $\text{R}^2\text{-R}^6$, R^9 , R^{10} , A, B y n se definen como anteriormente.

También se prefieren derivados de sulfonamidas de fórmula general (Ia), en la que R^2 , R^3 , R^4 , R^5 y R^6 , idénticos o diferentes, representan cada uno hidrógeno, F, Cl, Br, ciano, nitro, un radical alquilo $\text{C}_1\text{-C}_6$ lineal o ramificado, un radical alquenilo $\text{C}_2\text{-C}_6$ lineal o ramificado o un radical alquinilo $\text{C}_2\text{-C}_6$ lineal o ramificado, un radical alcoxi $\text{C}_1\text{-}$

C_8 lineal o ramificado, un radical alquiltio C_1-C_8 lineal o ramificado, hidroxilo, trifluorometilo, un radical cicloalifático C_{3-8} saturado o insaturado, un radical alquilcarbonilo C_1-C_8 lineal o ramificado, fenilcarbonilo o un grupo $-NR^8R^{10}$,

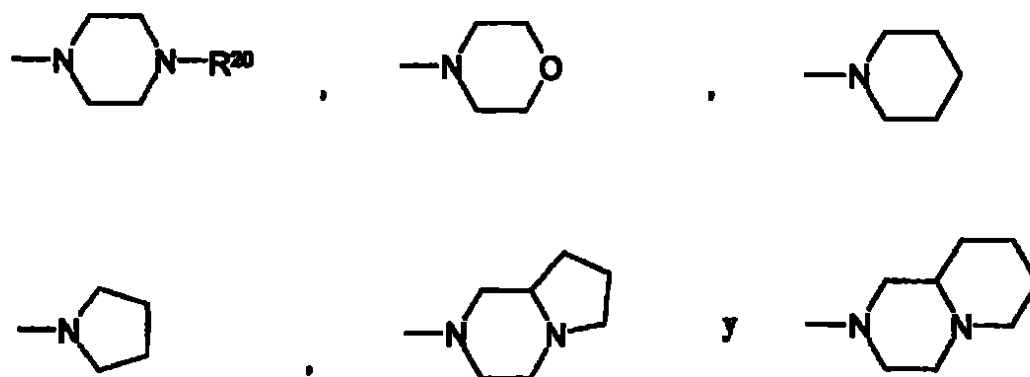
más preferiblemente R^2 , R^3 , R^4 , R^5 y R^6 idénticos o diferentes, representan cada uno H, F, Cl, NO_2 , NH_2 o un radical alquilo C_{1-2} y R^1 , R^7-R^{10} , A, B y n se definen como anteriormente.

Además, también se prefieren derivados de sulfonamidas de fórmula general (Ia), en la que R^7 y R^8 , idénticos o diferentes, representan cada uno hidrógeno un radical alquilo C_1-C_{10} lineal o ramificado, opcionalmente al menos monosustituido, un radical alquenilo C_2-C_{10} lineal o ramificado, opcionalmente al menos monosustituido, un radical alquinilo C_2-C_{10} lineal o ramificado, opcionalmente al menos monosustituido, con la condición, de que R^8 y R^9 no sean al mismo tiempo hidrógeno, y si uno de ellos R^8 y R^9 , es un radical alifático C_1-C_4 , lineal o ramificado, saturado o insaturado, opcionalmente al menos monosustituido, el otro es un radical alifático lineal o ramificado, saturado o insaturado, opcionalmente al menos monosustituido con al menos cinco átomos de carbono,

o R^7 y R^8 junto con el átomo puente de nitrógeno forman un anillo heterocíclico de 5 ó 6 miembros, saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo adicional como miembro del anillo, el cual puede estar condensado con un sistema cíclico cicloalifático mono o bicíclico saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo como miembro del anillo, en el que los anillos del sistema cíclico tienen 5, 6 ó 7 miembros y R^1-R^6 , R^9 , R^{10} , A, B y n se definen como anteriormente.

Se prefieren particularmente derivados de sulfonamidas de fórmula general (Ia), en la que R^7 y R^8 , idénticos o diferentes, representan hidrógeno o un radical alquilo C_1-C_{10} lineal o ramificado, con la condición, de que R^8 y R^9 no sean al mismo tiempo hidrógeno, y si uno de ellos R^8 o R^9 , representa un radical alifático C_1-C_4 , lineal o ramificado, saturado o insaturado, opcionalmente al menos monosustituido, el otro de ellos representa un radical alifático lineal o ramificado, saturado o insaturado, opcionalmente al menos monosustituido con al menos cinco átomos de carbono, o

R^7 y R^8 junto con el átomo puente de nitrógeno forman un radical seleccionado del grupo que consiste en



en los que R^{20} , si está presente, representa hidrógeno, un radical alquilo C_1-C_8 lineal o ramificado o un radical bencilo, preferiblemente hidrógeno, o un radical alquilo C_1-C_2 , y R^1-R^8 , R^9 , R^{10} , A, B y n se definen como anteriormente.

5 Además, también se prefieren derivados de sulfonamidas de fórmula general (Ia), en la que R^9 y R^{10} , idénticos o diferentes, representan cada uno hidrógeno, un radical alquilo C_1-C_{10} lineal o ramificado, opcionalmente al menos monosustituido, un radical alquenilo C_2-C_{10} lineal o ramificado, opcionalmente al menos monosustituido o un radical alquinilo C_2-C_{10} lineal o ramificado, opcionalmente al menos monosustituido,

10 o

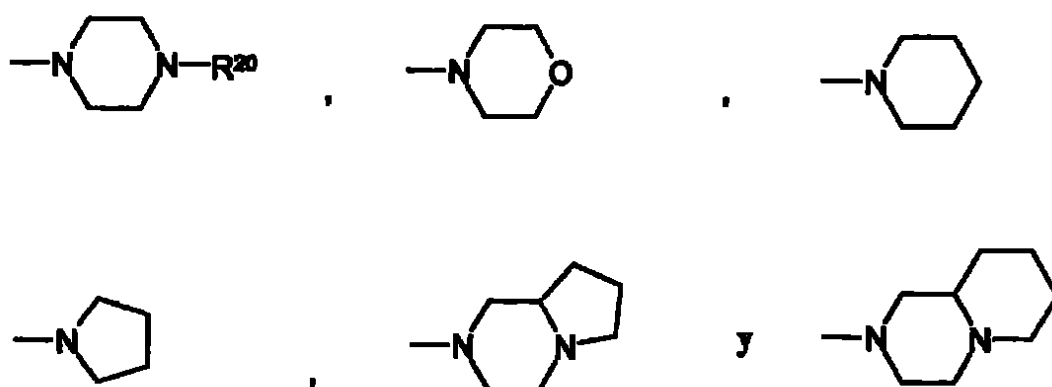
R^9 y R^{10} junto con el átomo puente de nitrógeno forman un anillo heterocíclico de 5 ó 6 miembros saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo más como miembro del anillo, que puede estar condensado con un sistema cíclico cicloalifático mono- o bicíclico saturado o insaturado, opcionalmente al menos monosustituido, que contiene

15 opcionalmente al menos un heteroátomo como miembro del anillo, en el que los anillos del sistema cíclico tienen 5, 6 ó 7 miembros y R^1-R^8 , A, B y n se definen como anteriormente.

Se prefieren particularmente derivados de sulfonamidas de la fórmula general (Ia), en la que R^9 y R^{10} , idénticos o diferentes, representan cada uno hidrógeno o un radical alquilo C_1-C_{10} lineal o ramificado, o

20

R^9 y R^{10} , junto con el átomo puente de nitrógeno forman un radical seleccionado del grupo que consiste en



en los que R^{20} , si está presente, representa hidrógeno, un radical alquilo C_1-C_6 lineal o ramificado o un radical bencilo, preferiblemente hidrógeno, o un radical alquilo C_1-C_2 , y R^1-R^8 , A, B y n se definen como anteriormente.

5 Además, se prefieren derivados de sulfonamidas de fórmula general (Ia), en la que A y B, idénticos o diferentes, representan cada uno un radical alquilo C_1-C_6 lineal o ramificado, un radical alquenilo C_2-C_6 lineal o ramificado o un radical alquinilo C_2-C_6 lineal o ramificado, más preferiblemente A y B, idénticos o diferentes, representan cada uno un radical alquilo C_1-C_6 lineal o ramificado, o

10 A y B, junto con el átomo de carbono al que están unidos, forman un anillo cicloalquilo saturado o insaturado, pero no aromático, opcionalmente al menos monosustituido, más preferiblemente A y B, junto con el átomo de carbono al que están unidos, forman un anillo cicloalquilo C_3-C_6 , incluso más preferiblemente A y B, junto con el átomo de carbono al que están unidos, forman un anillo ciclohexilo y R^1-R^{10} y n se definen como anteriormente.

15

Además, se prefieren derivados de sulfonamidas de fórmula general (Ia), en la que n es 0, 1, 2, 3 ó 4; preferiblemente n es 0 ó 1; más preferiblemente n es 0 y R^1 a R^{10} y A y B se definen como anteriormente.

20 Aquellos compuestos más preferidos de fórmula general (Ia) se seleccionan del grupo que consiste en

[1] 1-ciclohexanosulfonil-3-(1-metil-1,2,3,6-tetrahidropiridin-4-il)-5-nitro-1H-indol,

[2] 5-cloro-1-ciclohexanosulfonil-3-(1-metil-1,2,3,6-tetrahidropiridin-4-il)-1H-indol,

[3] 5-amino-1-ciclohexanosulfonil-3-(1-metil-1,2,3,6-tetrahidropiridin-4-il)-1H-indol,

y

25 [4] clorhidrato de 1-ciclohexanosulfonil-5-fluoro-3-(1,2,3,5,8,8a-hexahidro-indolizin-7-il)-1H-indol,

y sus correspondientes sales y solvatos.

También se prefieren derivados de sulfonamidas de fórmula general (Ib), en la que R^2 , R^3 , R^4 , R^5 y R^6 , idénticos o diferentes, representan cada uno hidrógeno, F, Cl, Br, ciano, nitro, un radical alquilo C_{1-8} lineal o ramificado, un radical alquenilo C_{2-8} lineal o ramificado, un radical alquinilo C_{2-8} lineal o ramificado, un radical alcoxi C_{1-8} lineal o ramificado, un radical alquiltio C_{1-8} lineal o ramificado, hidroxilo, trifluorometilo, un radical cicloalifático C_{3-8} saturado o insaturado, un radical alquilcarbonilo C_1-C_8 lineal o ramificado, fenilcarbonilo o un grupo $-NR^8R^{10}$,

preferiblemente R^2 , R^3 , R^4 , R^5 y R^6 idénticos o diferentes, representan cada uno H, F, Cl, NO_2 , NH_2 o un radical alquilo C_{1-2} y R^1 , R^7-R^{10} , A, B y n se definen como anteriormente.

Además, también se prefieren derivados de sulfonamidas de fórmula general (Ib), en la que R^7 y R^8 , idénticos o diferentes, representan cada uno hidrógeno, un radical alquilo C_1-C_4 lineal o ramificado, opcionalmente al menos monosustituido, y R^1-R^6 , R^9 , R^{10} , A, B y n se definen como anteriormente.

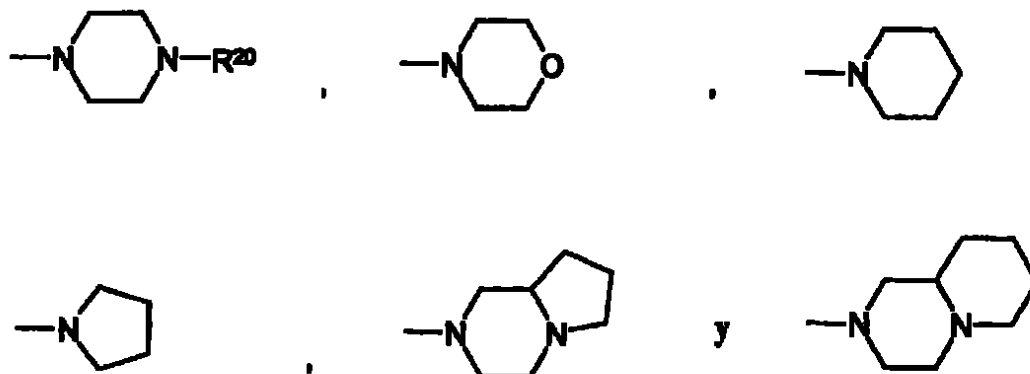
Se prefieren particularmente derivados de sulfonamidas de fórmula general (Ib), en la que R^7 y R^8 , idénticos o diferentes, representan cada uno hidrógeno o un radical alquilo C_1-C_2 , con la condición de que R^7 y R^8 no sean al mismo tiempo hidrógeno, y R^1-R^6 , R^9 , R^{10} , A, B y n se definen como anteriormente.

Además, también se prefieren derivados de sulfonamidas de fórmula general (Ib), en la que R^9 y R^{10} , idénticos o diferentes, representan cada uno hidrógeno, un radical alquilo C_1-C_{10} lineal o ramificado, opcionalmente al menos monosustituido, un radical alquenilo C_2-C_{10} lineal o ramificado, opcionalmente al menos monosustituido o un radical alquinilo C_2-C_{10} lineal o ramificado, opcionalmente al menos monosustituido, o

R^9 y R^{10} junto con el átomo puente de nitrógeno forman un anillo heterocíclico de 5 ó 6 miembros saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo más como miembro del anillo, que puede estar condensado con un sistema cíclico cicloalifático mono- o bicíclico saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo como miembro del anillo, en el que los anillos del sistema cíclico tienen 5, 6 ó 7 miembros y R^1-R^8 , A, B y n se definen como anteriormente.

Se prefieren particularmente derivados de sulfonamidas de fórmula general (Ib), en la que R^9 y R^{10} , idénticos o diferentes, representan cada uno hidrógeno o un radical alquilo C_1-C_{10} lineal o ramificado, o

R^9 y R^{10} , junto con el nitrógeno de puente forman un radical seleccionado del grupo que consiste en



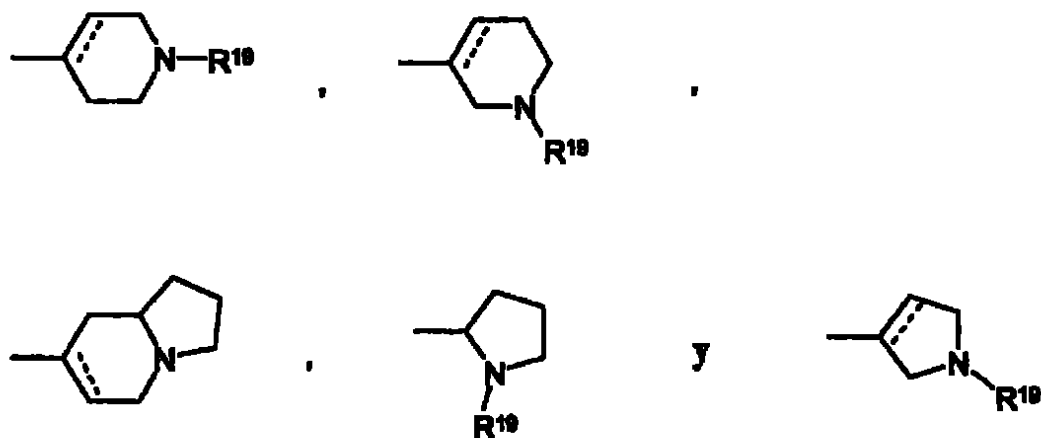
en los que R^{20} , si está presente, representa hidrógeno, un radical alquilo C_1-C_8 lineal o ramificado o un radical bencilo, preferiblemente hidrógeno, o un radical alquilo C_1-C_2 , y R^1-R^8 , A, B y n se definen como anteriormente.

Además, se prefieren derivados de sulfonamidas de fórmula general (Ib), en la que A y B, idénticos o diferentes, representan cada uno un radical alquilo C_1-C_8 lineal o ramificado, un radical alquenilo C_1-C_8 lineal o ramificado o un radical alquinilo C_1-C_8 lineal o ramificado, preferiblemente un radical alquilo C_1-C_8 lineal o ramificado, o A y B, junto con el átomo de carbono al que están unidos, forman un anillo cicloalquilo saturado o insaturado, pero no aromático, opcionalmente al menos monosustituido, más preferiblemente A y B, junto con el átomo de carbono al que están unidos, forman un anillo cicloalquilo C_3-C_8 , incluso más preferiblemente A y B, junto con el átomo de carbono al que están unidos, forman un anillo ciclohexilo y R^1-R^{10} y n se definen como anteriormente.

Además, se prefieren derivados de sulfonamidas de fórmula general (Ib), en la que n es 0, 1, 2, 3 ó 4; preferiblemente n es 0 ó 1; más preferiblemente n es 0 y R^1 a R^{10} y A y B se definen como anteriormente.

Se prefieren derivados de sulfonamidas de fórmula general (Ic), en la que R^1 representa un radical $-NR^7R^8$ o un radical cicloalifático de 5 ó 6 miembros saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo como miembro del anillo, que puede estar condensado con un sistema cíclico cicloalifático mono o bicíclico saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo como miembro del anillo, en el cual los anillos del sistema cíclico tienen 5 ó 6 miembros,

más preferiblemente R^1 representa un radical $-NR^7R^8$ o un radical seleccionado del grupo que consiste en



en los que, si está presente, la línea de puntos representa un enlace químico opcional y R^{10} representa hidrógeno, un radical alquilo C_1-C_8 lineal o ramificado o un radical bencilo, preferiblemente hidrógeno o un radical alquilo C_1-C_2 , y R^2-R^6 , R^9 , R^{10} , A, B y n se definen como anteriormente.

También se prefieren derivados de sulfonamidas de fórmula general (lc), en la que R^2 , R^3 , R^4 , R^5 y R^6 , idénticos o diferentes, representan cada uno hidrógeno, F, Cl, Br, ciano, nitro, un radical alquilo C_1-C_8 lineal o ramificado, un radical alquenilo C_2-C_8 lineal o ramificado, un radical alquinilo C_2-C_8 lineal o ramificado, un radical alcoxi C_1-8 lineal o ramificado, un radical alquiltio C_1-8 lineal o ramificado, hidroxilo, trifluorometilo, un radical cicloalifático C_3-8 saturado o insaturado, un radical alquilcarbonilo C_1-C_8 lineal o ramificado, fenilcarbonilo o un grupo $-NR^9R^{10}$,

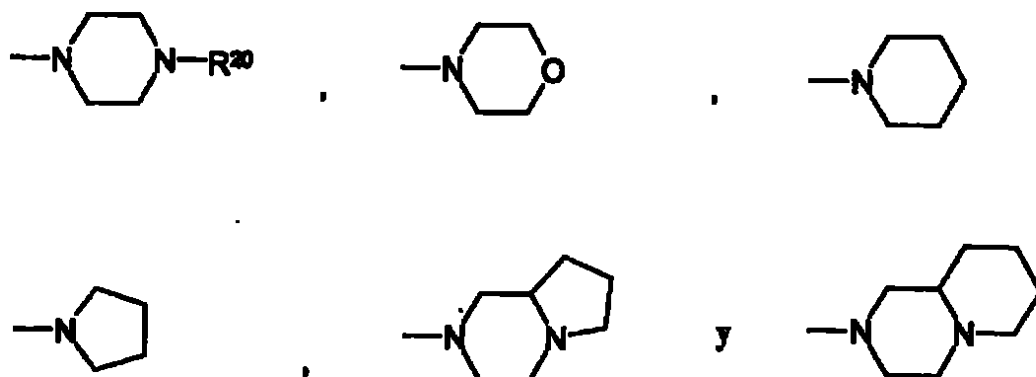
más preferiblemente R^2 , R^3 , R^4 , R^5 y R^6 idénticos o diferentes, representan cada uno H, F, Cl, NO_2 , NH_2 o un radical alquilo C_{1-2} y R^1 , R^7-R^{10} , A, B y n se definen como anteriormente.

Además, también se prefieren derivados de sulfonamidas de fórmula general (lc), en la que R^7 y R^8 , idénticos o diferentes, representan cada uno hidrógeno un radical alquilo C_1-C_{10} lineal o ramificado, opcionalmente al menos monosustituido, un radical alquenilo C_2-C_{10} lineal o ramificado, opcionalmente al menos monosustituido, un radical alquinilo C_2-C_{10} lineal o ramificado, opcionalmente al menos monosustituido, o R^7 y R^8 junto con el átomo puente de nitrógeno forman un anillo heterocíclico de 5 ó 6 miembros, saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo adicional como miembro del anillo, el cual puede estar condensado con un sistema cíclico cicloalifático mono o bicíclico saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo como miembro del anillo, en el que los anillos

del sistema cíclico tienen 5, 6 ó 7 miembros y R^1 - R^6 , R^8 , R^{10} , A, B y n se definen como anteriormente.

Se prefieren particularmente derivados de sulfonamidas de fórmula general (Ic), en la que R^7 y R^8 , idénticos o diferentes, representan hidrógeno o un radical alquilo C_1 - C_{10} lineal o ramificado, o

R^7 y R^8 junto con el átomo puente de nitrógeno forman un radical seleccionado del grupo que consiste en



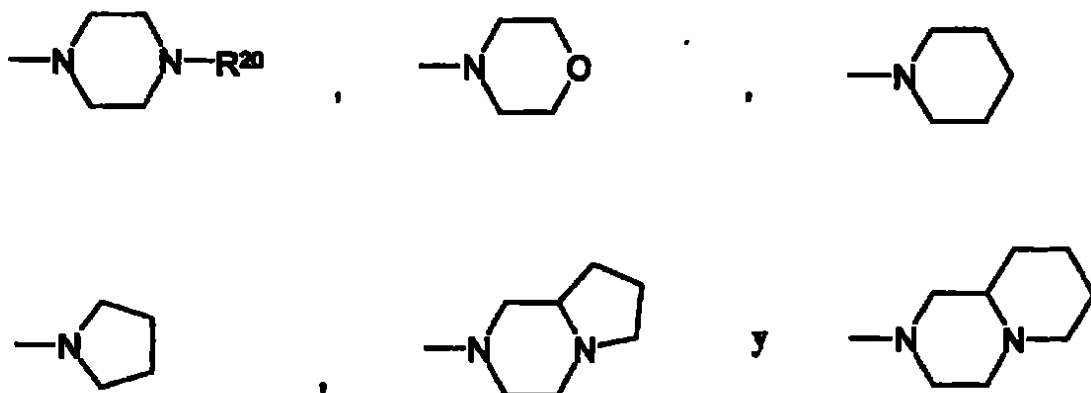
en los que R^{20} , si está presente, representa hidrógeno, un radical alquilo C_1 - C_8 lineal o ramificado o un radical bencilo, preferiblemente hidrógeno, o un radical alquilo C_1 - C_2 , y R^1 - R^6 , R^8 , R^{10} , A, B y n se definen como anteriormente.

Además, también se prefieren derivados de sulfonamidas de fórmula general (Ic), en la que R^9 y R^{10} , idénticos o diferentes, representan cada uno hidrógeno, un radical alquilo C_1 - C_{10} lineal o ramificado, opcionalmente al menos monosustituido, un radical alquenilo C_2 - C_{10} lineal o ramificado, opcionalmente al menos monosustituido o un radical alquínilo C_2 - C_{10} lineal o ramificado, opcionalmente al menos monosustituido, o

R^9 y R^{10} junto con el átomo puente de nitrógeno forman un anillo heterocíclico de 5 ó 6 miembros saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo más como miembro del anillo, que puede estar condensado con un sistema cíclico cicloalifático mono- o bicíclico saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo como miembro del anillo, en el que los anillos del sistema cíclico tienen 5, 6 ó 7 miembros y R^1 - R^8 , A, B y n se definen como anteriormente.

Se prefieren particularmente derivados de sulfonamidas de fórmula general (Ic), en la que R^9 y R^{10} , idénticos o diferentes, representan cada uno hidrógeno o un radical alquilo C_1 - C_{10} lineal o ramificado, o

R^9 y R^{10} , junto con el átomo puente de nitrógeno forman un radical seleccionado del grupo que consiste en



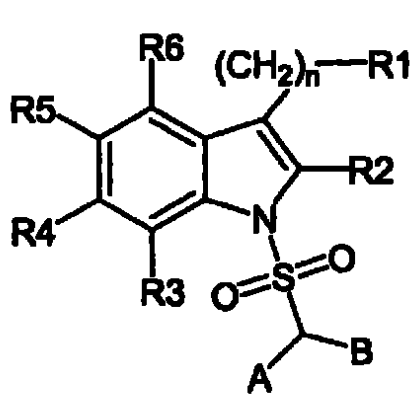
en los que R^{20} , si está presente, representa hidrógeno, un radical alquilo C_1-C_6 lineal o ramificado o un radical bencilo, preferiblemente hidrógeno, o un radical alquilo C_1-C_2 , y R^1-R^8 , A, B y n se definen como anteriormente.

Además, se prefieren derivados de sulfonamidas de fórmula general (Ic), en la que A y B, idénticos o diferentes, representan cada uno un radical alquilo C_1-C_6 lineal o ramificado, un radical alquenilo C_2-C_6 lineal o ramificado o un radical alquinilo C_2-C_6 lineal o ramificado, más A y B, idénticos o diferentes, representan cada uno un radical alquilo C_1-C_6 lineal o ramificado, o

A y B, junto con el átomo de carbono al que están unidos, forman un anillo cicloalquilo saturado o insaturado, pero no aromático, opcionalmente al menos monosustituido, más preferiblemente A y B, junto con el átomo de carbono al que están unidos, forman un anillo cicloalquilo C_3-C_6 , incluso más preferiblemente A y B, junto con el átomo de carbono al que están unidos, forman un anillo ciclohexilo y R^1-R^{10} y n se definen como anteriormente.

Además, se prefieren derivados de sulfonamidas de fórmula general (Ic), en la que n es 0, 1, 2, 3 ó 4; preferiblemente n es 0 ó 1; más preferiblemente n es 0 y R^1 a R^{10} y A y B se definen como anteriormente.

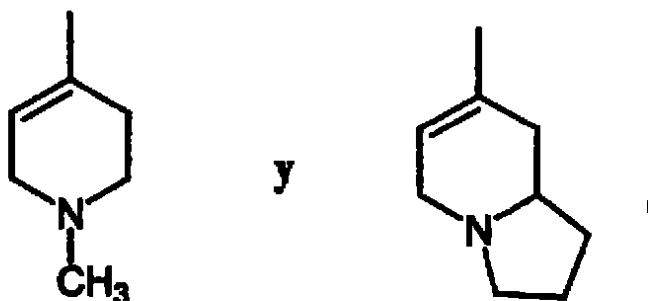
Otro aspecto de la presente invención son los compuestos de fórmula general (Ic),



(Ic),

en la que

- 5 R^1 representa un radical cicloalifático de 5 ó 6 miembros insaturado, que contiene opcionalmente al menos un átomo de nitrógeno como miembro del anillo, que puede estar sustituido por un grupo metilo y/o que puede estar condensado con un anillo cicloalifático de 5 miembros, más preferiblemente R^1 representa un radical - NR^7R^8 o un resto seleccionado del grupo que consiste en



- 10 R^2 , R^3 , R^4 y R^6 representan cada uno hidrógeno,
 R^5 representa H, flúor, cloro, nitro o un grupo - NR^9R^{10} ,
 R^9 y R^{10} representan cada uno hidrógeno

- A y B, junto con el átomo de carbono al que están unidos, forman un anillo cicloalquilo C_3 - C_8 , saturado o insaturado, pero no aromático, más preferiblemente
 15 forman un anillo ciclohexilo,

y

n es 0;

- opcionalmente en forma de uno de sus estereoisómeros, preferiblemente enantiómeros o diastereómeros, su racemato o en forma de una mezcla de al menos
 20 dos de sus estereoisómeros, preferiblemente enantiómeros o diastereómeros, en cualquier razón de mezcla, o una sal de los mismos, preferiblemente las sales

fisiológicamente aceptables correspondientes de los mismos o los solvatos correspondientes de los mismos.

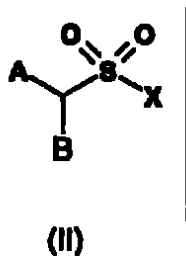
Aquellos compuestos más preferidos de fórmula general (Ic) se seleccionan del grupo que consiste en

- 5 [1] 1-ciclohexanosulfonil-3-(1-metil-1,2,3,6-tetrahidropiridin-4-il)-5-nitro-1H-Indol,
 [2] 5-cloro-1-ciclohexanosulfonil-3-(1-metil-1,2,3,6-tetrahidropiridin-4-il)-1H-indol,
 [3] 5-amino-1-ciclohexanosulfonil-3-(1-metil-1,2,3,6-tetrahidropiridin-4-il)-1H-indol,
 y
 [4] clorhidrato de 1-ciclohexanosulfonil-5-fluoro-3-(1,2,3,5,8,8a-hexahidro-indolizin-
 10 7-il)-1H-indol,
 y sus correspondientes sales y solvatos.

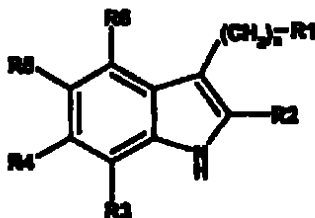
La presente invención se refiere igualmente a las sales, preferiblemente a las sales fisiológicamente aceptables de los compuestos de fórmula general (Ia) y/o (Ib), y/o de fórmula general (Ic), en particular las sales de adición de ácidos minerales más
 15 preferiblemente de ácido clorhídrico, ácido bromhídrico, ácido fosfórico, ácido sulfúrico, ácido nítrico y las sales de ácidos orgánicos más preferiblemente de ácido cítrico, ácido maleico, ácido fumárico, ácido tartárico o sus derivados, ácido p-toluensulfónico, ácido metanosulfónico, ácido camforsulfónico, etc.

A continuación la expresión derivados de sulfonamidas de fórmula general (I)
 20 se refiere a uno o más compuestos de fórmula general (Ia) y/o a uno o más compuestos de fórmula general (Ib), y/o a uno o más compuestos de fórmula general (Ic) respectivamente, y opcionalmente en forma de uno de sus estereoisómeros, preferiblemente enantiómeros o diasterómeros, su racemato o en forma de una mezcla de al menos dos de sus estereoisómeros, preferiblemente enantiómeros o
 25 diasterómeros, en cualquier razón de mezcla, o una sal de los mismos preferiblemente una sal fisiológicamente aceptable correspondiente de los mismos, o un solvato correspondiente de los mismos.

Otro aspecto de la presente invención consiste en un procedimiento para la preparación de los nuevos derivados de fórmula general (I), en la que R^1 - R^{10} , A, B y n
 30 tienen el significado dado anteriormente, según el cual al menos un compuesto de fórmula general (II),



en la que A y B tienen el significado dado anteriormente y X es un grupo saliente aceptable, preferiblemente un átomo de halógeno, más preferiblemente cloro; se hace reaccionar con al menos un indol sustituido de fórmula general (III)



(III)

5

en la que R^1 - R^5 y n tienen el significado dado anteriormente, o uno de sus derivados adecuadamente protegido, y, si fuera necesario, se eliminan los grupos protectores para obtener el derivado de sulfonamidas de fórmula (I) correspondiente, que puede purificarse y/o aislarse mediante métodos convencionales conocidos en la técnica anterior.

10

La reacción se lleva a cabo preferiblemente en presencia de una base fuerte adecuada, por ejemplo, diisopropilamina de litio, butillitio, hidruro de sodio, o bis(trimetilsilil)amida de sodio en un disolvente inerte, preferiblemente tetrahidrofurano, hexano o dimetilformamida. Las temperaturas de reacción más adecuadas varían desde -100°C hasta la temperatura ambiente y el tiempo de reacción comprende preferiblemente desde 5 minutos hasta 24 horas. Las condiciones más preferidas son hidruro de sodio en dimetilformamida a aproximadamente 0°C .

15

El derivado de sulfonamida de fórmula general (I) resultante puede purificarse y/o aislarse de acuerdo con métodos convencionales conocidos en la técnica anterior.

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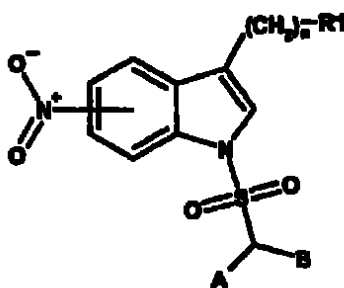
Preferiblemente, los derivados de sulfonamida de fórmula general (I) pueden aislarse evaporando el medio de reacción, añadiendo agua y si fuera necesario ajustando el pH para que se obtenga un sólido que pueda aislarse por filtración; o bien el derivado de sulfonamida puede extraerse con un disolvente no miscible en agua preferiblemente cloroformo y purificarse por cromatografía o recristalización de un disolvente adecuado.

25

Los compuestos de fórmula general (II) están disponibles comercialmente o pueden prepararse según métodos estándar conocidos en la técnica anterior, por ejemplo por métodos similares a los descritos en la bibliografía [KHANNA, V.; TAMILSELVAN, P.; KALRA, S.J.S.; IQBAL, J.; Tetrahedron 1994, 35 (32), 5935-5938; L.N. Aristarkhova et al., *J. Org. Chem. USSR*, 1970, 6, 2454-2458; E.E. Gilbert, *Synthesis*, 1969, 1, 3]. Los compuestos de fórmula general (III) también pueden prepararse según métodos estándar conocidos en la técnica anterior, por ejemplo, métodos similares a los descritos en la bibliografía. Substituted aromatic 5-HT1f agonist, el documento WO 9846570. Piperidine-indole compounds having 5-HT6 affinity, el documento US 6.133.287.

Las descripciones bibliográficas respectivas se incorporan como referencia y forman parte de la descripción.

Otro aspecto de la presente invención consiste en un procedimiento para la preparación de los nuevos derivados de sulfonamida de fórmula general (I), en el que uno o más de R^2 , R^3 , R^4 , R^5 o R^6 se reducen a un grupo amino mediante la reducción del grupo nitro de los derivados de fórmula general (IV) mediante métodos conocidos en la técnica anterior, por ejemplo BRATTON, L.D.; ROTH, B.D.; TRIVEDI, B.K.; UNANGST, P.C.; *J. Heterocycl Chem*, 2000, 37 (5), 1103-1108. FANGHAENEL, E.; CHTCHEGLOV, D.; *J. Prakt Chem / Chem-Ztg*, 1996, 338 (8), 731-737. KUYPER, L.F.; BACCANARI, D.P.; JONES, M.L.; HUNTER, R.N.; TANSIK, R.L.; JOYNER, S.S.; BOYTOS, C.M.; RUDOLPH, S.K.; KNICK, V.; WILSON, H.R.; CADDELL, J.M.; FRIEDMAN, H.S.; et al.; *J. Med Chem*, 1996, 39 (4), 892-903.



(IV)

y los otros R^1 - R^6 , A, B y n tienen el significado mencionado anteriormente, o uno de sus derivados adecuadamente protegidos, y, si fuera necesario, se eliminan los grupos protectores para obtener la amina de fórmula general (I) correspondiente, que puede purificarse y/o aislarse por medio de métodos convencionales conocidos en la técnica anterior.

Las descripciones bibliográficas respectivas se incorporan como referencia y forman parte de la descripción.

Las sales, preferiblemente las sales farmacéuticamente aceptables de los compuestos de fórmula general (I) pueden prepararse mediante métodos convencionales conocidos en la técnica anterior, preferiblemente por reacción con un ácido mineral, más preferiblemente por reacción con ácido clorhídrico, ácido bromhídrico, ácido fosfórico, ácido sulfúrico, ácido nítrico o por reacción con ácidos orgánicos más preferiblemente por reacción con ácido cítrico, ácido maleico, ácido fumárico, ácido tartárico o sus derivados, ácido p-toluensulfónico, ácido metanosulfónico, ácido canforsulfónico etc., en un disolvente apropiado preferiblemente metanol, etanol, dietiléter, acetato de etilo, acetonitrilo o acetona y obteniéndose las sales resultantes con las técnicas habituales de precipitación o cristalización de las sales correspondientes.

Las sales fisiológicamente aceptables preferidas de los derivados de sulfonamida de fórmula general (I) son las sales de adición de ácidos minerales, más preferiblemente de ácido clorhídrico, ácido bromhídrico, ácido fosfórico, ácido sulfúrico o ácido nítrico y las sales de adición de ácidos orgánicos, más preferiblemente ácido cítrico, ácido maleico, ácido fumárico, ácido tartárico o sus derivados, ácido p-toluensulfónico, ácido metanosulfónico, ácido canforsulfónico, etc.

Los solvatos, preferiblemente los solvatos fisiológicamente aceptables, más preferiblemente hidratos, de los derivados de sulfonamida de fórmula general (I) o de las sales fisiológicamente aceptables correspondientes pueden prepararse por métodos conocidos en la técnica anterior.

Durante algunas de las secuencias sintéticas descritas o en la preparación de los reactivos adecuados utilizados puede ser necesario y/o deseable proteger grupos sensibles o reactivos en algunas de las moléculas utilizadas. Esto puede llevarse a cabo mediante el uso de grupos protectores convencionales preferiblemente aquellos descritos en la bibliografía [Protective groups in Organic Chemistry, ed J. F.W. McOmie, Plenum Press, 1973; T.W. Greene & P.G.M. Wuts, Protective Groups in Organic Chemistry, John Wiley & Sons, 1991]. Los grupos protectores pueden eliminarse en el estadio posterior adecuado por métodos conocidos en la técnica anterior. Las descripciones bibliográficas respectivas se incorporan como referencia y forman parte de la descripción.

Si los derivados de sulfonamida de fórmula general (I) se obtienen en forma de mezcla de estereoisómeros, preferiblemente enantiómeros o diasterómeros, dichas

mezclas pueden separarse mediante procedimientos estándar conocidos en la técnica anterior, por ejemplo métodos cromatográficos o cristalización con agentes quirales.

Otro aspecto de la presente invención es un medicamento que comprende al menos un derivado de 1-sulfonilindol de fórmula general (I), opcionalmente en forma de uno de sus estereoisómeros, preferiblemente enantiómeros o diasterómeros, su racemato o en forma de una mezcla de al menos dos de sus estereoisómeros, preferiblemente enantiómeros o diasterómeros, en cualquier razón de mezcla, o una sal fisiológicamente aceptable correspondiente de los mismos o un solvato correspondiente de los mismos, y opcionalmente uno o más adyuvantes farmacéuticamente aceptables.

Este medicamento es adecuado para la regulación del receptor 5-HT₆, para la profilaxis y/o el tratamiento de un trastorno o enfermedad relacionada con la ingestión de alimentos, preferiblemente para la regulación del apetito, para el mantenimiento, incremento o reducción del peso corporal, para la profilaxis y/o el tratamiento de la obesidad, bulimia, anorexia, caquexia o diabetes de tipo II (diabetes mellitus insulino independiente), preferiblemente diabetes de tipo II que es causada por la obesidad, para la profilaxis y/o el tratamiento de trastornos del tracto gastrointestinal, preferiblemente el síndrome del intestino irritable, para la mejora de la cognición, para la profilaxis y/o el tratamiento de trastornos del sistema nervioso central, ansiedad, pánico, depresión, preferiblemente trastornos bipolares, trastornos cognitivos de la memoria, procesos de demencia senil, trastornos neurodegenerativos, preferiblemente enfermedad de Alzheimer, enfermedad de Parkinson, enfermedad de Huntington y/o esclerosis múltiple, esquizofrenia, psicosis, hiperquinesia infantil (ADHD, déficit de atención / trastorno de hiperactividad) y otros trastornos mediados por el receptor 5-HT₆ de la serotonina en humanos y/o animales, preferiblemente en mamíferos, más preferiblemente en humanos.

Otro aspecto de la presente invención es un medicamento que comprende al menos un derivado de 1-sulfonilindol de fórmula general (Ia), opcionalmente en forma de uno de sus estereoisómeros, preferiblemente enantiómeros o diasterómeros, su racemato o en forma de una mezcla de al menos dos de sus estereoisómeros, preferiblemente enantiómeros o diasterómeros, en cualquier razón de mezcla, o una sal fisiológicamente aceptable correspondiente de los mismos o un solvato correspondiente de los mismos, y opcionalmente uno o más adyuvantes farmacéuticamente aceptables.

Este medicamento es adecuado para la regulación del receptor 5-HT₆, para la profilaxis y/o el tratamiento de un trastorno o enfermedad relacionada con la ingestión de alimentos, preferiblemente para la regulación del apetito, para el mantenimiento, incremento o reducción del peso corporal, para la profilaxis y/o el tratamiento de la

5 obesidad, bulimia, anorexia, caquexia o diabetes de tipo II (diabetes mellitus insulino independiente), preferiblemente diabetes de tipo II que es causada por la obesidad, para la profilaxis y/o el tratamiento de trastornos del tracto gastrointestinal, preferiblemente el síndrome del intestino irritable, para la mejora de la cognición, para la profilaxis y/o el tratamiento de trastornos del sistema nervioso central, ansiedad,

10 pánico, depresión, preferiblemente trastornos bipolares, trastornos cognitivos de la memoria, procesos de demencia senil, trastornos neurodegenerativos, preferiblemente enfermedad de Alzheimer, enfermedad de Parkinson, enfermedad de Huntington y/o esclerosis múltiple, esquizofrenia, psicosis o hiperquinesia infantil (ADHD, déficit de atención / trastorno de hiperactividad) y otros trastornos mediados por el receptor 5-

15 HT₆ de la serotonina en humanos y/o animales, preferiblemente en mamíferos, más preferiblemente en humanos,

más adecuado para la regulación del receptor 5-HT₆, para la profilaxis y/o el tratamiento de un trastorno o enfermedad relacionada con la ingestión de alimentos, preferiblemente para la regulación del apetito, para el mantenimiento, incremento o

20 reducción del peso corporal, para la profilaxis y/o el tratamiento de la obesidad, bulimia, anorexia, caquexia o diabetes de tipo II (diabetes mellitus insulino independiente), preferiblemente diabetes de tipo II que es causada por la obesidad, para la profilaxis y/o el tratamiento de trastornos del tracto gastrointestinal, preferiblemente el síndrome del intestino irritable, en humanos y/o animales,

25 preferiblemente en mamíferos, más preferiblemente en humanos.

Otro aspecto de la presente invención es un medicamento que comprende al menos un derivado de 1-sulfonilindol de fórmula general (Ib), opcionalmente en forma de uno de sus estereoisómeros, preferiblemente enantiómeros o diasterómeros, su racemato o en forma de una mezcla de al menos dos de sus estereoisómeros,

30 preferiblemente enantiómeros o diasterómeros, en cualquier razón de mezcla, o una sal fisiológicamente aceptable correspondiente de los mismos o un solvato correspondiente de los mismos, y opcionalmente uno o más adyuvantes farmacéuticamente aceptables.

Este medicamento es adecuado para la regulación del receptor 5-HT₆, para la

35 profilaxis y/o el tratamiento de un trastorno o enfermedad relacionada con la ingestión

de alimentos, preferiblemente para la regulación del apetito, para el mantenimiento, incremento o reducción del peso corporal, para la prevención y/o el tratamiento de la obesidad, bulimia, anorexia, caquexia o diabetes de tipo II (diabetes mellitus insulino independiente), preferiblemente diabetes de tipo II que es causada por la obesidad,

5 para la profilaxis y/o el tratamiento de trastornos del tracto gastrointestinal, preferiblemente el síndrome del intestino irritable, para la mejora de la cognición, para la profilaxis y/o el tratamiento de trastornos del sistema nervioso central, ansiedad, pánico, depresión, preferiblemente trastornos bipolares, trastornos cognitivos de la memoria, procesos de demencia senil, trastornos neurodegenerativos, preferiblemente

10 enfermedad de Alzheimer, enfermedad de Parkinson, enfermedad de Huntington y/o esclerosis múltiple, esquizofrenia, psicosis o hiperquinesia infantil (ADHD, déficit de atención / trastorno de hiperactividad) y otros trastornos mediados por el receptor 5-HT₆ de la serotonina en humanos y/o animales, preferiblemente en mamíferos, más preferiblemente en humanos,

15 más adecuado para la mejora de la cognición, para la profilaxis y/o el tratamiento de trastornos del sistema nervioso central, ansiedad, pánico, depresión, preferiblemente trastornos bipolares, trastornos cognitivos de la memoria, procesos de demencia senil, trastornos neurodegenerativos, preferiblemente enfermedad de Alzheimer, enfermedad de Parkinson, enfermedad de Huntington y/o esclerosis

20 múltiple, esquizofrenia, psicosis o hiperquinesia infantil (ADHD, déficit de atención / trastorno de hiperactividad) en humanos y/o animales, preferiblemente en mamíferos, más preferiblemente en humanos.

Otro objeto de la presente invención es un medicamento compuesto por al menos un derivado de 1-sulfonilindol de fórmula general (Ic), opcionalmente en forma

25 de uno de sus estereoisómeros, preferiblemente enantiómeros o diasterómeros, su racemato o en forma de una mezcla de al menos dos de sus estereoisómeros, preferiblemente enantiómeros o diasterómeros, en cualquier razón de mezcla, o una sal fisiológicamente aceptable correspondiente de los mismos o un solvato correspondiente de los mismos, y opcionalmente uno o más adyuvantes

30 farmacéuticamente aceptables.

Este medicamento es adecuado para la regulación del receptor 5-HT₆, para la profilaxis y/o el tratamiento de un trastorno o enfermedad relacionada con la ingestión de alimentos, preferiblemente para la regulación del apetito, para el mantenimiento, incremento o reducción del peso corporal, para la profilaxis y/o el tratamiento de la

35 obesidad, bulimia, anorexia, caquexia o diabetes de tipo II (diabetes mellitus insulino

independiente), preferiblemente diabetes de tipo II que es causada por la obesidad, para la profilaxis y/o el tratamiento de trastornos del tracto gastrointestinal, preferiblemente el síndrome del intestino irritable, para la mejora de la cognición, para la profilaxis y/o el tratamiento de trastornos del sistema nervioso central, ansiedad, pánico, depresión, preferiblemente trastornos bipolares, trastornos cognitivos de la memoria, procesos de demencia senil, trastornos neurodegenerativos, preferiblemente enfermedad de Alzheimer, enfermedad de Parkinson, enfermedad de Huntington y/o esclerosis múltiple, esquizofrenia, psicosis o hiperquinesia infantil (ADHD, déficit de atención / trastorno de hiperactividad) y otros trastornos mediados por el receptor 5-HT₆ de la serotonina en humanos y/o animales, preferiblemente en mamíferos, más preferiblemente en humanos.

El medicamento obtenido según la presente invención es particularmente adecuado para su administración a mamíferos, incluido el ser humano. El medicamento puede administrarse preferiblemente a todos los grupos de edad, es decir, niños, adolescentes y adultos.

Otro aspecto de la presente invención es el uso de al menos un derivado de sulfonamida de fórmula general (I), opcionalmente en forma de uno de sus estereoisómeros, preferiblemente enantiómeros o diasterómeros, su racemato o en forma de una mezcla de al menos dos de sus estereoisómeros, preferiblemente enantiómeros o diasterómeros, en cualquier razón de mezcla, o una sal fisiológicamente aceptable correspondiente de los mismos o un solvato correspondiente de los mismos, para la fabricación de un medicamento para la regulación del receptor 5-HT₆, para la profilaxis y/o el tratamiento de un trastorno o enfermedad relacionada con la ingestión de alimentos, preferiblemente para la regulación del apetito, para el mantenimiento, incremento o reducción del peso corporal, para la profilaxis y/o el tratamiento de la obesidad, bulimia, anorexia, caquexia o diabetes de tipo (diabetes mellitus insulino independiente), preferiblemente diabetes de tipo II que es causada por la obesidad, para la profilaxis y/o el tratamiento de trastornos del tracto gastrointestinal, preferiblemente el síndrome del intestino irritable, para la mejora de la cognición, para la profilaxis y/o el tratamiento de trastornos del sistema nervioso central, ansiedad, pánico, depresión, preferiblemente trastornos bipolares, trastornos cognitivos de la memoria, procesos de demencia senil, trastornos neurodegenerativos, preferiblemente enfermedad de Alzheimer, enfermedad de Parkinson, enfermedad de Huntington y/o esclerosis múltiple, esquizofrenia, psicosis o hiperquinesia infantil (ADHD, déficit de atención / trastorno de

hiperactividad) y otros trastornos mediados por el receptor 5-HT₆ de la serotonina en humanos y/o animales, preferiblemente en mamíferos, más preferiblemente en humanos.

Otro aspecto de la presente invención es el uso de al menos un derivado de sulfonamida de fórmula general (Ia) anterior, opcionalmente en forma de uno de sus estereoisómeros, preferiblemente enantiómeros o diasterómeros, su racemato o en forma de una mezcla de al menos dos de sus estereoisómeros, preferiblemente enantiómeros o diasterómeros, en cualquier razón de mezcla, o una sal fisiológicamente aceptable correspondiente de los mismos o un solvato correspondiente de los mismos, para la fabricación de un medicamento para la regulación del receptor 5-HT₆, para la profilaxis y/o el tratamiento de un trastorno o enfermedad relacionada la ingestión de alimentos, preferiblemente para la regulación del apetito, para el mantenimiento, incremento o reducción del peso corporal, para la profilaxis y/o el tratamiento de la obesidad, bulimia, anorexia, caquexia o diabetes de tipo II (diabetes mellitus insulino independiente), preferiblemente diabetes de tipo II que es causada por la obesidad, para la profilaxis y/o el tratamiento de trastornos del tracto gastrointestinal, preferiblemente el síndrome del intestino irritable, para la mejora de la cognición, para la profilaxis y/o el tratamiento de trastornos del sistema nervioso central, ansiedad, pánico, depresión, preferiblemente trastornos bipolares, trastornos cognitivos de la memoria, procesos de demencia senil, trastornos neurodegenerativos, preferiblemente enfermedad de Alzheimer, enfermedad de Parkinson, enfermedad de Huntington y/o esclerosis múltiple, esquizofrenia, psicosis o hiperquinesia infantil (ADHD, déficit de atención / trastorno de hiperactividad) y otros trastornos mediados por el receptor 5-HT₆ de la serotonina en humanos y/o animales, preferiblemente en mamíferos, más preferiblemente en humanos,

preferiblemente para la regulación del receptor 5-HT₆, para la profilaxis y/o el tratamiento de un trastorno o enfermedad relacionada con la ingestión de alimentos, preferiblemente para la regulación del apetito, para el mantenimiento, incremento o reducción del peso corporal, para la profilaxis y/o el tratamiento de la obesidad, bulimia, anorexia, caquexia o diabetes de tipo II (diabetes mellitus insulino independiente), preferiblemente diabetes de tipo II que es causada por la obesidad, para la profilaxis y/o el tratamiento de trastornos del tracto gastrointestinal, preferiblemente el receptor del síndrome del intestino irritable en humanos y/o animales, preferiblemente en mamíferos, más preferiblemente en humanos.

Otro aspecto de la presente invención es el uso de al menos un derivado de sulfonamida de fórmula general (Ib) anterior, opcionalmente en forma de uno de sus estereoisómeros, preferiblemente enantiómeros o diasterómeros, su racemato o en forma de una mezcla de al menos dos de sus estereoisómeros, preferiblemente enantiómeros o diasterómeros, en cualquier razón de mezcla, o una sal fisiológicamente aceptable correspondiente de los mismos o un solvato correspondiente de los mismos, para la fabricación de un medicamento para la regulación del receptor 5-HT₆, para la profilaxis y/o el tratamiento de un trastorno o enfermedad relacionada la ingestión de alimentos, preferiblemente para la regulación del apetito, para el mantenimiento, incremento o reducción del peso corporal, para la profilaxis y/o el tratamiento de la obesidad, bulimia, anorexia, caquexia o diabetes de tipo II (diabetes mellitus insulino independiente), preferiblemente diabetes de tipo II que es causada por la obesidad, para la profilaxis y/o el tratamiento de trastornos del tracto gastrointestinal, preferiblemente el síndrome del intestino irritable, para la mejora de la cognición, para la profilaxis y/o el tratamiento de trastornos del sistema nervioso central, ansiedad, pánico, depresión, preferiblemente trastornos bipolares, trastornos cognitivos de la memoria, procesos de demencia senil, trastornos neurodegenerativos, preferiblemente enfermedad de Alzheimer, enfermedad de Parkinson, enfermedad de Huntington y/o esclerosis múltiple, esquizofrenia, psicosis o hiperquinesia infantil (ADHD, déficit de atención / trastorno de hiperactividad) y otros trastornos mediados por el receptor 5-HT₆ de la serotonina en humanos y/o animales, preferiblemente en mamíferos, más preferiblemente en humanos,

preferiblemente para la fabricación de un medicamento para la mejora de la cognición, para la profilaxis y/o el tratamiento de trastornos del sistema nervioso central, ansiedad, pánico, depresión, preferiblemente trastornos bipolares, trastornos cognitivos de la memoria, procesos de demencia senil, trastornos neurodegenerativos, preferiblemente enfermedad de Alzheimer, enfermedad de Parkinson, enfermedad de Huntington y/o esclerosis múltiple, esquizofrenia, psicosis o hiperquinesia infantil (ADHD, déficit de atención / trastorno de hiperactividad) en animales, preferiblemente en mamíferos, más preferiblemente en humanos,

Otro aspecto de la presente invención es el uso de al menos un derivado de sulfonamida de fórmula general (Ic) anterior, opcionalmente en forma de uno de sus estereoisómeros, preferiblemente enantiómeros o diasterómeros, su racemato o en forma de una mezcla de al menos dos de sus estereoisómeros, preferiblemente enantiómeros o diasterómeros, en cualquier razón de mezcla, o una sal

fisiológicamente aceptable correspondiente de los mismos o un solvato correspondiente de los mismos, para la fabricación de un medicamento para la regulación del receptor 5-HT₂, para la profilaxis y/o el tratamiento de un trastorno o enfermedad relacionada la ingestión de alimentos, preferiblemente para la regulación del apetito, para el mantenimiento, incremento o reducción del peso corporal, para la profilaxis y/o el tratamiento de la obesidad, bulimia, anorexia, caquexia o diabetes de tipo II (diabetes mellitus insulino independiente), preferiblemente diabetes de tipo II que es causada por la obesidad, para la profilaxis y/o el tratamiento de trastornos del tracto gastrointestinal, preferiblemente el síndrome del intestino irritable, para la mejora de la cognición, para la profilaxis y/o el tratamiento de trastornos del sistema nervioso central, ansiedad, pánico, depresión, preferiblemente trastornos bipolares, trastornos cognitivos de la memoria, procesos de demencia senil, trastornos neurodegenerativos, preferiblemente enfermedad de Alzheimer, enfermedad de Parkinson, enfermedad de Huntington y/o esclerosis múltiple, esquizofrenia, psicosis o hiperquinesia infantil (ADHD, déficit de atención / trastorno de hiperactividad) y otros trastornos mediados por el receptor 5-HT₂ de la serotonina en humanos y/o animales, preferiblemente en mamíferos, más preferiblemente en humanos.

La preparación de las composiciones farmacéuticas correspondientes, así como de los medicamentos formulados puede llevarse a cabo mediante métodos convencionales conocidos en la técnica anterior, por ejemplo a partir de los índices de "Pharmaceutics: The Science of Dosage Forms", segunda edición, Aulton, M.E. (ED. Churchill Livingstone, Edinburgh (2002); "Encyclopedia of Pharmaceutical Technology", segunda edición, Swarbrick, J. y Bollen J.C. (Eds.), Marcel Dekker, Inc. Nueva York (2002); "Modern Pharmaceutics", cuarta edición, Banker G.S. y Rhodes C.T. (Eds.) Marcel Dekker, Inc. Nueva York 2002 y "The Theory and Practice of Industrial Pharmacy", Lachman L., Lieberman H. and Kanig J. (Eds.), Lea & Febiger, Filadelfia (1986). Las respectivas descripciones de la bibliografía se incorporan en el presente documento como referencia y forman parte de la descripción.

Las composiciones farmacéuticas, así como los medicamentos formulados, preparados según la presente invención, pueden comprender, además al menos un derivado de sulfonamida de fórmula general (I), opcionalmente en forma de uno de sus estereoisómeros, preferiblemente enantiómeros o diasterómeros, su racemato o en forma de una mezcla de al menos dos de sus estereoisómeros, preferiblemente enantiómeros o diasterómeros, en cualquier razón de mezcla, o una sal fisiológicamente aceptable correspondiente de los mismos o un solvato

correspondiente de los mismos, otras sustancias auxiliares convencionales conocidas en la técnica anterior, preferiblemente excipientes, cargas, disolventes, diluyentes, tintes, agentes de recubrimiento, agentes para formar una matriz y/o aglutinantes. Tal y como saben los expertos en la técnica, la elección de las sustancias auxiliares, y de la cantidad de las mismas, dependerá de la vía de administración buscada, por ejemplo rectal, intravenosa, intraperitoneal, intramuscular, intranasal, oral, bucal o tópica.

Los medicamentos adecuados para la administración oral son, por ejemplo, comprimidos, comprimidos recubiertos, cápsulas o multiparticulados, preferiblemente gránulos o grageas, sometidos opcionalmente a compresión en comprimidos, cargados en cápsulas o suspendidos en disoluciones, suspensiones o líquidos adecuados.

Los medicamentos adecuados para la administración parenteral, tópica o inhalada pueden elegirse preferiblemente del grupo consistente en disoluciones, suspensiones, preparaciones anhidras de rápida reconstitución y también aerosoles.

Los medicamentos adecuados para su uso oral o percutáneo pueden liberar los compuestos de sulfonamida de fórmula general (I) de una forma sostenida, generalmente se conoce en la técnica anterior la preparación de estos medicamentos de liberación sostenida.

Se conocen de la técnica anterior las formulaciones de liberación sostenida más adecuadas, así como los materiales y métodos para la preparación de las mismas, por ejemplo, a partir de los índices de "Modified-Release Drug Delivery Technology", Rathbone, J.JI, Hadgraft, J. y Roberts, M.S. (Eds.), Marcel Dekker, Inc., Nueva York (2002); "Handbook of Pharmaceutical Controlled Release Technology", Wise, D.L. (Ed.), Marcel Dekker, Inc. Nueva York, (2000); "Controlled Drug Delivery", Vol. I, Basic Concepts, Bruck, S.D. (Ed.), CRD Press Inc., Boca Raton (1983) y de Takada, K. and Yoshikawa, H., "Oral Drug Delivery", Encyclopedia of Controlled Drug Delivery, Matlowitz, E. (Ed.), John Wiley & Sons, Inc., Nueva York (1999), Vol. 2, 728-742; Fix, J., "Oral drug delivery, small intestine and colon", Encyclopedia of Controlled Drug Delivery, Matlowitz, E. (Ed.), John Wiley & Sons, Inc., Nueva York (1999), Vol. 2, 698-728. Las referencias bibliográficas respectivas se incorporan como referencia al presente documento y forman parte de la descripción.

Los medicamentos de la presente invención también pueden tener al menos un recubrimiento entérico, que se disuelve según el valor de pH. Debido a dicho recubrimiento, el medicamento puede pasar por el estómago sin disolverse y los

compuestos de fórmula general I se liberan sólo en el tracto intestinal. El recubrimiento entérico se disuelve preferiblemente a un pH de entre 5 y 7,5. También se conocen en la técnica anterior los materiales y métodos adecuados para preparar recubrimientos entéricos.

- 5 Normalmente, las composiciones farmacéuticas y los medicamentos comprenden desde un 1 hasta un 60% en peso de uno o más derivados de sulfonamida de fórmula general (I) y desde un 40 hasta un 99% en peso de uno o más excipientes.

- 10 La cantidad de sustancia medicinal a administrar al paciente varía en función del peso del paciente, de la vía de administración, la indicación y la gravedad del trastorno. Habitualmente, se administran desde 1 mg hasta 2 g de al menos un derivado de sulfonamida de fórmula general (I) por paciente y día. La dosis diaria total puede administrarse al paciente en una o más dosis.

15 Métodos Farmacéuticos

UNIÓN AL RECEPTOR DE LA SEROTONINA 5-HT₂

- La membranas celulares de células HEK-293 que expresan el receptor recombinante humano 5HT₂ fueron suministradas por Receptor Biology. En dichas
20 membranas la concentración de receptor es 2,18 pmol/mg de proteína y la concentración de proteína es 9,17 mg/ml. El protocolo experimental sigue el método de B. L. Roth et al. [B. L. Roth, S. C. Craigo, M. S. Choudhary, A. Uluer, F. J. Monsma, Y. Shen, H. Y. Meltzer, D. R. Sibley: Binding of Typical and Atypical Antipsychotic Agents to 5-Hydroxytryptamine-6 and Hydroxytryptamine-7 Receptors. *The Journal of Pharmacology and Experimental Therapeutics*, 1994, 268, 1403] con ligeras
25 modificaciones. Se diluye la membrana comercial (dilución 1:40) con el tampón de unión: Tris-HCl 50 mM, MgCl₂ 10 mM, EDTA 0,5 mM (pH 7,4). El radioligando usado es [³H]-LSD a una concentración de 2,7 nM con un volumen final de 200 µl. Se inicia la incubación añadiendo 100 µl de suspensión de membrana, (≈ 22,9 µg de proteína de
30 membrana), y se prolonga durante 60 minutos a una temperatura de 37 °C. Se finaliza la incubación por filtración rápida en un colector de células de Brandel a través de filtros de fibra de vidrio de la marca registrada Schleicher & Schuell GF 3362 pretratados con una disolución de polietilenimina al 0,5 %. Se lavan los filtros tres veces con tres mililitros de tampón Tris-HCl 50 mM, pH 7,4. Se transfieren los filtros a
35 viales y se añaden a cada vial 5 ml de la mezcla de centelleo líquido Ecoscint H. Se

deja que los viales alcancen el equilibrio durante varias horas antes del recuento con un contador de centelleo Wallac Winspectral 1414. Se determina la unión no específica en presencia de serotonina 100 μ M. Se realizan las pruebas por triplicado. Se calcularon las constantes de inhibición (K_i , nM) por un análisis de regresión no lineal usando el programa EBDA/LIGAND descrito en [Munson y Rodbard, *Analytical Biochemistry*, 1980, 107, 220].

MEDIDAS DE LA INGESTIÓN DE COMIDA (MODELOS DE COMPORTAMIENTO):

Se usan ratas macho W (200-270 g) obtenidas de Harlan, S.A. Las ratas se aclimatan a los alojamientos durante al menos 5 días antes de que se sometan a cualquier experimento. Durante este periodo los animales se alojan (en grupos de cinco) en jaulas traslúcidas, y se les da agua y comida a voluntad. Al menos 24 horas antes de que comience las pruebas, los animales se destinan en alojamientos individuales.

Entonces, se determina el efecto agudo de los derivados de sulfonamida de fórmula (I) usados de manera experimental sobre la ingestión de comida en ratas en condiciones de ayunas según se indica a continuación:

Las ratas se mantienen en ayunas durante 23 horas en sus jaulas individuales de origen. Después de este periodo, se trata a las ratas vía oral o intraperitoneal con una composición que comprende un derivado de sulfonamida de fórmula general (I) o una composición correspondiente (vehículo) sin dicho derivado de sulfonamida. Inmediatamente después de esto, se deja a la rata con alimentos pesados previamente y se mide la ingesta de comida acumulada después de 1, 2, 4 y 6 horas.

Dicho método de medida de la ingestión de comida se describe también en la bibliografía (Kask et al., *European Journal of Pharmacology* 414 (2001), 215-224 y Turnbull et al., *Diabetes*, Vol. 51, Agosto 2002). Las partes respectivas de las descripciones se incorporan en el presente documento como referencia y forman parte de la descripción.

La preparación de nuevos compuestos según la invención se indica en los siguientes ejemplos. Se describe también la afinidad por el receptor de serotonina 5HT₂, así como las fórmulas galénicas aplicables a los compuestos de la invención. Los ejemplos indicados a continuación, se dan solamente a modo de ejemplo y no limitan el alcance de la invención.

Ejemplos:

Ejemplo 1.- Preparación de 1-ciclohexanosulfonil-3-(1-metil-1,2,3,6-tetrahidropiridin-4-il)-5-nitro-1H-indol

Se añadieron 468 mg (9,8 mMol) de hidruro de sodio al 50% en aceite a 0°C a una disolución de 1,0 g (3,9 mMol) de 3-(1-metil-1,2,3,6-tetrahidropiridin-4-il)-5-nitro-1H-indol en 50 ml de dimetilformamida anhidra y se dejó agitar la mezcla durante 30 minutos. Después, se añadieron 2,14 g de cloruro de ciclohexanosulfonilo, y continuó la agitación durante 3 h a temperatura ambiente. Se añadió agua y se evaporó hasta sequedad. Se trató el crudo resultante con bicarbonato de sodio y se extrajo con cloroformo. Se secó la fase orgánica con sulfato de sodio anhidro y se evaporó hasta sequedad; se purificó el sólido resultante mediante cromatografía, obteniendo 900 mg (57%) de 1-ciclohexanosulfonil-3-(1-metil-1,2,3,6-tetrahidropiridin-4-il)-5-nitro-1H-indol como un sólido amarillo.

Ejemplo 2.- Preparación de 5-cloro-1-ciclohexanosulfonil-3-(1-metil-1,2,3,6-tetrahidropiridin-4-il)-1H-indol

Se obtuvieron 900 mg (74%) del compuesto mencionado a partir de 770 mg (3,12 mMol) de 5-cloro-3-(1-metil-1,2,3,6-tetrahidropiridin-4-il)-1H-indol y 1,7 g (9,36 mMol) de cloruro de ciclohexanosulfonilo, por medio del procedimiento descrito en el ejemplo 1, como un sólido amarillo.

Ejemplo 3.- Preparación de 5-amino-1-ciclohexanosulfonil-3-(1-metil-1,2,3,6-tetrahidropiridin-4-il)-1H-indole

Se añadieron 200 mg de Pd/C al 50% con una humedad del 5% a una disolución de 403 mg (1 mMol) de 1-ciclohexanosulfonil-3-(1-metil-1,2,3,6-tetrahidropiridin-4-il)-5-nitro-1H-indol en 200 ml de etanol. Se hidrogenó la suspensión resultante a 25 psi de sobrepresión durante 20 horas. Después se filtró el catalizador y se evaporó hasta sequedad. Se purificó el crudo resultante mediante cromatografía y se obtuvieron 150 mg (40%) del compuesto mencionado como una crema sólida.

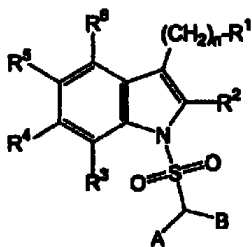
Ejemplo 4.- Preparación de 1-ciclohexanosulfonil-5-fluoro-3-(1,2,3,5,8,8a-hexahidro-indolizin-7-il)-1H-indol

Se obtuvieron 1,95 g (78%) de 1-ciclohexanosulfonil-5-fluoro-3-(1,2,3,5,8,8a-hexahidro-indolizin-7-il)-1H-indol como un aceite a partir de 1,6 g (6,25 mMol) de 5-fluoro-3-(1,2,3,5,8,8a-hexahidro-indolizin-7-il)-1H-indol y 3,42 g (18,76 mMol) de

cloruro de ciclohexanosulfonilo, por medio del procedimiento descrito en el ejemplo 1. Después se añadieron 2 ml de una disolución de etanol / HCl 6N a una disolución de 1,95 g (4,85 mMol) de 1-ciclohexanosulfonil-5-fluoro-3-(1,2,3,5,8,8a-hexahidro-indolizin-7-il)-1H-indol en 20 ml de etanol, haciendo precipitar un sólido que se
5 recristalizó a partir del etanol, obteniendo 1,5 g (71%) del compuesto mencionado como un sólido blanco.

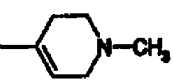
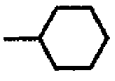
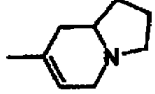
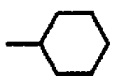
Los rendimientos son indicativos y no se hizo ningún esfuerzo adicional para mejorarlos.

El punto de fusión y los datos espectroscópicos para la identificación de alguno
10 de los compuestos de la presente invención se indican en la tabla siguiente.



EJ	R1	R2	R3	R4	R5	R6	n	A-B	sal	p f °C	IR cm ⁻¹	¹ H-RMN(300MHz), δ (disolvante)
1		H	H	H	NO ₂	H	0		-	155-160	3433, 2938, 2859, 1522, 1371, 1340, 1158, 1128, 988, 612	1.00-1.90 (m, 10H); 2.56 (s, 3H); 2.68 (m, 2H); 2.98 (m, 2H); 3.47 (m, 2H); 3.78 (m, 1H); 6.35 (s, 1H); 7.87 (s, 1H); 8.08 (d, 1H, J=9.2 Hz); 8.26 (dd, 1H, J=9.2 Hz, J'=1.9 Hz); 8.69 (d, 1H, J=1.8 Hz). (DMSO-d ₆)
2		H	H	H	Cl	H	0		-	88-90	3433, 2941, 2858, 2787, 1447, 1364, 1158, 1128, 1116, 614, 557	1.00-1.80 (m, 10H); 2.41 (s, 3H); 2.55 (m, 2H); 2.67 (m, 2H); 3.15 (m, 3H); 6.18 (m, 1H); 7.27 (dd, 1H, J=8.9 Hz, J'=2.0 Hz); 7.32 (s, 1H); 7.79 (d, 1H, J=2.0 Hz); 7.82 (d, 1H, J=1.8 Hz). (CDCl ₃)

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#j.	R1	R2	R3	R4	R5	R6	n		Sal	p.f °C	IR cm ⁻¹	¹ H-RMN(300MHz), δ (disolvente)
3		H	H	H	NH ₂	H	0		-	75 (descomposición)	3376, 2937, 2857, 2784, 1435, 1363, 1342, 1158, 1127, 987, 817, 565	1.00-1.90 (m, 10H), 2.40 (s, 3H), 2.54 (m, 2H); 2.68 (m, 2H); 3.13 (m, 3H); 6.18 (m, 1H); 6.71 (dd, 1H, J=8.8 Hz, J'=2.4 Hz); 7.09 (d, 1H, J=2.2 Hz), 7.23 (s, 1H), 7.67 (d 1H J=8.8 Hz) (CDCl ₃)
4		H	H	H	F	H	0		HCl	263 (descomposición)	3424, 2941, 2499, 2451, 1466, 1445, 1371, 1346, 1188, 1157, 1127, 649, 619	1.18 (m, 3H); 1.38 (m, 2H); 1.64 (m, 1H); 1.73 (m, 5H); 2.01 (m 2H), 2.31 (m, 1H); 2.80 (m, 1H); 3.09 (m, 2H), 3.44 (m, 1H); 3.68 (m, 2H), 3.76 (m, 1H); 4.10 (m, 1H), 6.39 (s, 1H); 7.28 (m, 1H); 7.78 (m, 2H); 7.90 (dd, 1H, J=9.0 Hz, J'=4.6 Hz); (DMSO-d ₆)

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Datos farmacéuticos:

La unión de los nuevos compuestos de fórmula general (I) al receptor 5-HT₂ se determinó como se describe anteriormente.

5 Los resultados de unión para algunos de los compuestos de la presente invención se indican en la tabla siguiente:

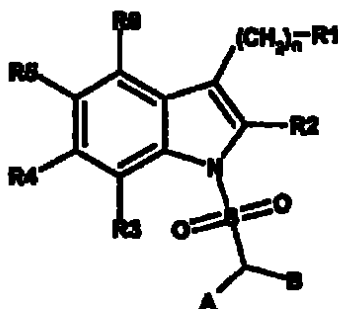
Tabla

Ejemplo	% de inhibición 10 ⁻⁶ M	K _i (nM)
1	59,8 ± 3,0	
2		98,2
3		55,1
4		191

La posología diaria en medicina humana está comprendida entre 1 miligramo y 2 gramos de producto medicinal que puede administrarse en una o varias dosis. Las composiciones se preparan en formas compatibles con la vía de administración utilizada, preferiblemente comprimidos, comprimidos recubiertos, cápsulas, supositorios, disoluciones o suspensiones. Estas composiciones se preparan mediante métodos conocidos y comprenden desde el 1 hasta el 60% en peso del principio activo (compuesto de fórmula general 1) y desde el 40 hasta el 99% en peso del vehículo farmacéutico adecuado compatible con el principio activo y la forma física de la composición utilizada. A título de ejemplo se presenta la fórmula de un comprimido que contiene un producto de la invención:

Ejemplo de fórmula por comprimido:

Ejemplo 1	5 mg
20 Lactosa	60 mg
Celulosa cristalina	25 mg
Povidona K 90	5 mg
Almidón pregelatinizado	3 mg
Dióxido de sílice coloidal	1 mg
25 Estearato de magnesio	1 mg
Peso total por comprimido	100 mg

REIVINDICACIONES**1. Compuesto sulfonamida de fórmula general (Ia)****(Ia)**

en la que

5 R^1 representa un radical $-NR^7R^8$ o un radical cicloalifático saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo como miembro del anillo, que puede estar condensado con un sistema cíclico cicloalifático mono- o bicíclico saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo como

10 miembro del anillo,

R^2 , R^3 , R^4 , R^5 y R^6 , idénticos o diferentes, representan cada uno hidrógeno, halógeno, ciano, nitro, un radical alifático lineal o ramificado, saturado o insaturado, un radical alcoxi lineal o ramificado, un radical alquiltio lineal o ramificado, hidroxilo, trifluorometilo, un radical cicloalifático saturado o insaturado, un radical alquilcarbonilo,

15 un fenilcarbonilo o un grupo $-NR^9R^{10}$,

R^7 y R^8 , idénticos o diferentes, representan cada uno hidrógeno o un radical alifático, lineal o ramificado, saturado o insaturado, opcionalmente al menos monosustituido,

con la condición, de que R^8 y R^9 no sean al mismo tiempo hidrógeno, y si uno de ellos

20 R^8 o R^9 , es un radical alifático C_1-C_4 , lineal o ramificado, saturado o insaturado, opcionalmente al menos monosustituido, el otro es un radical alifático lineal o ramificado, saturado o insaturado, opcionalmente al menos monosustituido con al menos cinco átomos de carbono,

o

25 R^7 y R^8 junto con el átomo puente de nitrógeno forman un anillo heterocíclico saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo más como miembro del anillo, que puede estar condensado con un sistema cíclico cicloalifático mono- o bicíclico saturado o

insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo como miembro del anillo,

R^9 y R^{10} , idénticos o diferentes, representan cada uno hidrógeno o un radical alifático, lineal o ramificado, saturado o insaturado, opcionalmente al menos monosustituido,

o

R^9 y R^{10} junto con el átomo puente de nitrógeno forman un anillo heterocíclico saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo más como miembro del anillo, que puede estar condensado con un sistema cíclico cicloalifático mono- o bicíclico saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo como miembro del anillo,

A y B, idénticos o diferentes, representan cada uno un radical alifático, lineal o ramificado, saturado o insaturado, opcionalmente al menos monosustituido,

o

A y B, junto con el átomo de carbono al que están unidos, forman un anillo cicloalquilo saturado o insaturado, pero no aromático, opcionalmente al menos monosustituido,

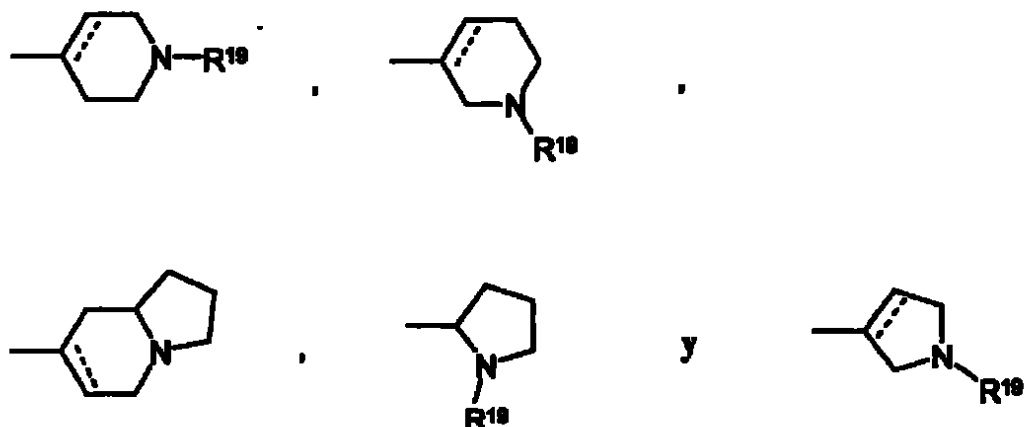
y

n es 0,

opcionalmente en forma de uno de sus estereoisómeros, preferiblemente enantiómeros o diasterómeros, su racemato o en forma de una mezcla de al menos dos de sus estereoisómeros, preferiblemente enantiómeros o diasterómeros, en cualquier razón de mezcla, o una sal de los mismos, preferiblemente una sal fisiológicamente aceptable correspondiente de los mismos, o un solvato correspondiente de los mismos.

2. Compuesto según la reivindicación 1, caracterizado porque R^1 representa un radical $-NR^7R^8$ o un radical cicloalifático de 5 ó 6 miembros saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo como miembro del anillo, que puede estar condensado con un sistema cíclico cicloalifático mono o bicíclico saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo como miembro del anillo, en el cual los anillos del sistema cíclico tienen 5 ó 6 miembros,

preferiblemente un radical $-NR^7R^8$ o un radical seleccionado del grupo que consiste en



en los que, si está presente, la línea de puntos representa un enlace químico opcional y R¹⁹ representa hidrógeno, un radical alquilo C₁-C₆ lineal o ramificado o un radical bencilo, preferiblemente hidrógeno o un radical alquilo C₁-C₂.

- 5 3. Compuesto según las reivindicaciones 1 ó 2, caracterizado porque R², R³, R⁴, R⁵ y R⁶, idénticos o diferentes, representan cada uno hidrógeno, F, Cl, Br, ciano, nitro, un radical alquilo C₁₋₆ lineal o ramificado, un radical alquenilo C₂₋₆ lineal o ramificado, un radical alquinilo C₂₋₆ lineal o ramificado, , un radical alcoxi C₁₋₆ lineal o ramificado, un radical alquiltio C₁₋₆ lineal o ramificado, hidroxilo, trifluorometilo, un radical
- 10 cicloalifático C₃₋₆ saturado o insaturado, un radical alquilcarbonilo C₁₋₆ lineal o ramificado, fenilcarbonilo o un grupo -NR⁹R¹⁰,

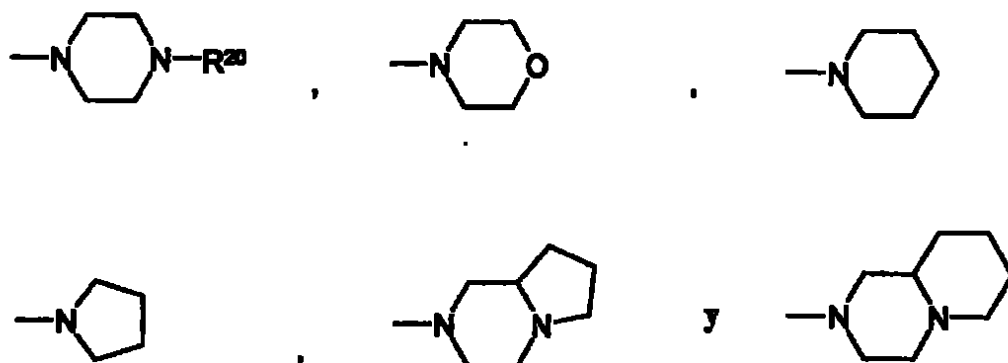
preferiblemente H, F, Cl, NO₂, NH₂ o un radical alquilo C₁₋₂.

4. Compuesto según una o más de las reivindicaciones 1 a 3, caracterizado porque R⁷ y R⁸, idénticos o diferentes, representan cada uno hidrógeno un radical alquilo C₁₋₁₀ lineal o ramificado, opcionalmente al menos monosustituido, un radical alquenilo C₂₋₁₀ lineal o ramificado, opcionalmente al menos monosustituido, o un radical alquinilo C₂₋₁₀ lineal o ramificado, opcionalmente al menos monosustituido, o
- 15 R⁷ y R⁸ junto con el nitrógeno puente forman un anillo heterocíclico de 5 ó 6 miembros, saturado o insaturado, opcionalmente al menos monosustituido, que

- 20 contiene opcionalmente al menos un heteroátomo adicional como miembro del anillo, el cual puede estar condensado con un sistema cíclico cicloalifático mono o bicíclico saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo como miembro del anillo, en el que los anillos del sistema cíclico tienen 5, 6 ó 7 miembros.

- 25 5. Compuesto según la reivindicación 4, caracterizado porque R⁷ y R⁸, idénticos o diferentes, representan cada uno hidrógeno o un radical alquilo C₁₋₁₀ lineal o ramificado, o

R^7 y R^8 junto con el átomo puente de nitrógeno forman un radical seleccionado del grupo que consiste en



5 en los que R^{20} , si está presente, es hidrógeno, un radical alquilo C_1-C_9 lineal o ramificado o un radical bencilo, preferiblemente hidrógeno, o un radical alquilo C_1-C_2 .

6. Compuesto según una o más de las reivindicaciones 1 a 5, caracterizado porque R^9 y R^{10} , idénticos o diferentes, representan cada uno hidrógeno, un radical alquilo C_1-C_{10} lineal o ramificado, opcionalmente al menos monosustituido, un radical alquenilo C_2-C_{10} lineal o ramificado, opcionalmente al menos monosustituido o un radical alquinilo C_2-C_{10} lineal o ramificado, opcionalmente al menos monosustituido, o

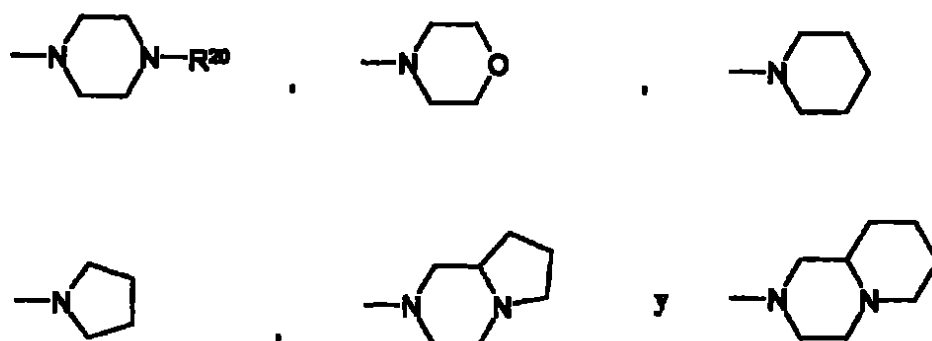
10 R^9 y R^{10} junto con el átomo puente de nitrógeno forman un anillo heterocíclico de 5 ó 6 miembros saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo más como miembro del anillo, que puede estar condensado con un sistema cíclico cicloalifático mono- o bicíclico saturado o insaturado, opcionalmente al menos monosustituido, que contiene

15 opcionalmente al menos un heteroátomo como miembro del anillo, en el que los anillos del sistema cíclico tienen 5, 6 ó 7 miembros.

7. Compuesto según la reivindicación 6, caracterizado porque R^9 y R^{10} , idénticos o diferentes, representan cada uno hidrógeno o un radical alquilo C_1-C_{10} lineal o

20 ramificado, o

R^9 y R^{10} , junto con el átomo puente de nitrógeno forman un radical seleccionado del grupo que consiste en



en los que R^{20} , si está presente, es hidrógeno, un radical alquilo C_1-C_6 lineal o ramificado o un radical bencilo, preferiblemente hidrógeno, o un radical alquilo C_1-C_2 .

8. Compuesto según una o más de las reivindicaciones 1 a 7, caracterizado porque A y B, idénticos o diferentes, representan cada uno un radical alquilo C_1-C_6 lineal o ramificado, un radical alquenilo C_2-C_6 lineal o ramificado o un radical alquinilo C_2-C_6 lineal o ramificado,

preferiblemente un radical alquilo C_1-C_6 lineal o ramificado, o

- A y B, junto con el átomo de carbono al que están unidos, forman un anillo cicloalquilo saturado o insaturado, pero no aromático, opcionalmente al menos monosustituido,

preferiblemente un anillo cicloalquilo C_3-C_6 ,

más preferiblemente forman un anillo ciclohexilo.

9. Compuesto según una o más de las reivindicaciones 1 a 8, caracterizado porque el compuesto se selecciona de un grupo que consiste en

[1] 1-ciclohexanosulfonil-3-(1-metil-1,2,3,6-tetrahidropiridin-4-il)-5-nitro-1H-indol,

[2] 5-cloro-1-ciclohexanosulfonil-3-(1-metil-1,2,3,6-tetrahidropiridin-4-il)-1H-indol,

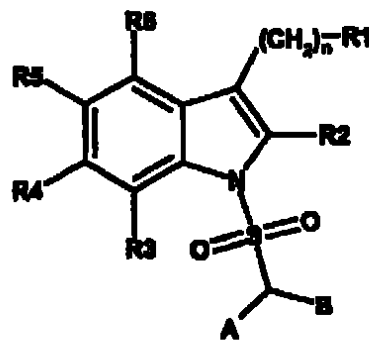
[3] 5-amino-1-ciclohexanosulfonil-3-(1-metil-1,2,3,6-tetrahidropiridin-4-il)-1H-indol,

y

- [4] clorhidrato de 1-ciclohexanosulfonil-5-fluoro-3-(1,2,3,5,8,8a-hexahidro-indolizín-7-il)-1H-indol,

y sus correspondientes sales y solvatos.

10. Compuesto sulfonamida de fórmula general (Ib)



(1b)

en la que

R^1 es un radical $-NR^7R^8$,

R^2 , R^3 , R^4 , R^5 y R^6 , idénticos o diferentes, representan cada uno hidrógeno, halógeno, ciano, nitro, un radical alifático lineal o ramificado, saturado o insaturado, un radical alcoxi lineal o ramificado, un radical alquiltio lineal o ramificado, hidroxilo, trifluorometilo, un radical cicloalifático saturado o insaturado, un radical alquilcarbonilo, un fenilcarbonilo o un grupo $-NR^9R^{10}$,

R^7 y R^8 , idénticos o diferentes, representan cada uno hidrógeno o un radical alifático C_{1-4} , lineal o ramificado, saturado o insaturado, opcionalmente al menos monosustituido,

R^9 y R^{10} , idénticos o diferentes, representan cada uno hidrógeno o un radical alifático, lineal o ramificado, saturado o insaturado, opcionalmente al menos monosustituido,

o

R^9 y R^{10} junto con el átomo puente de nitrógeno forman un anillo heterocíclico saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo más como miembro del anillo, que puede estar condensado con un sistema cíclico cicloalifático mono- o bicíclico saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo como miembro del anillo,

A y B, idénticos o diferentes, representan cada uno un radical alifático, lineal o ramificado, saturado o insaturado, opcionalmente al menos monosustituido,

o

A y B, junto con el átomo de carbono al que están unidos, forman un anillo cicloalquilo saturado o insaturado, pero no aromático, opcionalmente al menos monosustituido,

y

n es 0;

opcionalmente en forma de uno de sus estereoisómeros, preferiblemente enantiómeros o diastereómeros, su racemato o en forma de una mezcla de al menos dos de sus estereoisómeros, preferiblemente enantiómeros o diastereómeros, en cualquier razón de mezcla, o una sal de los mismos, preferiblemente una sal fisiológicamente aceptable correspondiente de los mismos, o un solvato correspondiente de los mismos

11. Compuesto según la reivindicación 10, caracterizado porque R^2 , R^3 , R^4 , R^5 y R^6 , idénticos o diferentes, representan cada uno hidrógeno, F, Cl, Br, ciano, nitro, un radical alquilo C_1-C_6 lineal o ramificado, un radical alquenilo C_2-C_6 lineal o ramificado, un radical alquinilo C_2-C_6 lineal o ramificado, un radical alcoxi C_1-C_6 lineal o ramificado, un radical alquiltio C_1-C_6 lineal o ramificado, hidroxilo, trifluorometilo, un radical cicloalifático C_3-C_6 saturado o insaturado, un radical alquilcarbonilo C_1-C_6 lineal o ramificado, fenilcarbonilo o un grupo $-NR^9R^{10}$,

preferiblemente H, F, Cl, NO_2 , NH_2 o un radical alquilo C_1-C_2 .

12. Compuesto según la reivindicación 10 ó 11, caracterizado porque R^7 y R^8 , idénticos o diferentes, en la que R^7 y R^8 , idénticos o diferentes, representan cada uno hidrógeno, un radical alquilo C_1-C_4 lineal o ramificado, opcionalmente al menos monosustituido,

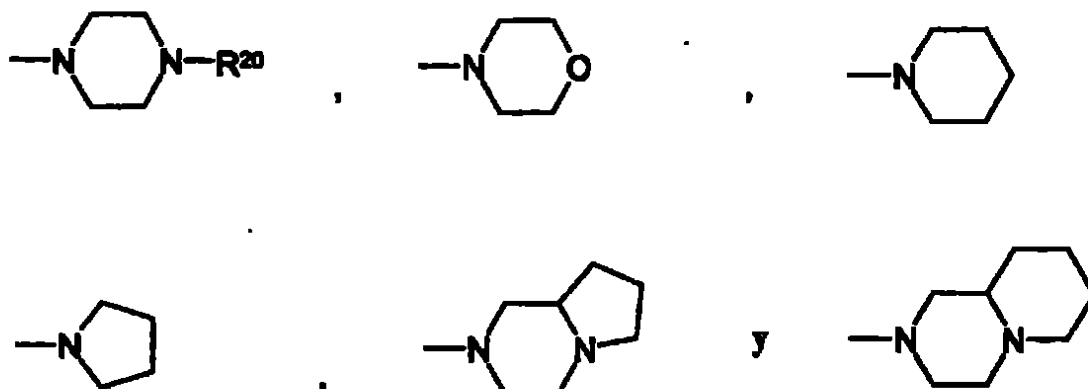
preferiblemente hidrógeno o un radical alquilo C_1-C_2 , con la condición de que R^7 y R^8 no sean al mismo tiempo hidrógeno.

13. Compuesto según una o más de las reivindicaciones 10 a 12, caracterizado porque R^9 y R^{10} , idénticos o diferentes, representan cada uno hidrógeno, un radical alquilo C_1-C_{10} lineal o ramificado, opcionalmente al menos monosustituido, un radical alquenilo C_2-C_{10} lineal o ramificado, opcionalmente al menos monosustituido o un radical alquinilo C_2-C_{10} lineal o ramificado, opcionalmente al menos monosustituido, o

R^9 y R^{10} junto con el átomo puente de nitrógeno forman un anillo heterocíclico de 5 ó 6 miembros saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo más como miembro del anillo, que puede estar condensado con un sistema cíclico cicloalifático mono- o bicíclico saturado o insaturado, opcionalmente al menos monosustituido, que contiene opcionalmente al menos un heteroátomo como miembro del anillo, en el que los anillos del sistema cíclico tienen 5, 6 ó 7 miembros

14. Compuesto según la reivindicación 13, caracterizado porque R^9 y R^{10} , idénticos o diferentes, representan cada uno hidrógeno o un radical alquilo C_1-C_{10} lineal o ramificado, o

5 R^9 y R^{10} , junto con el átomo puente de nitrógeno forman un radical seleccionado del grupo que consiste en



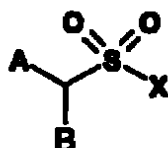
en los que R^{20} , si está presente, representa hidrógeno, un radical alquilo C_1-C_8 lineal o ramificado o un radical bencilo, preferiblemente hidrógeno, o un radical alquilo C_1-C_2

10 15. Compuesto según una o más de las reivindicaciones 10 a 14, caracterizado porque A y B, junto con el átomo de carbono al que están unidos, forman un anillo cicloalquilo saturado o insaturado, pero no aromático, opcionalmente al menos monosustituido,

preferiblemente un anillo cicloalquilo C_3-C_8 ,

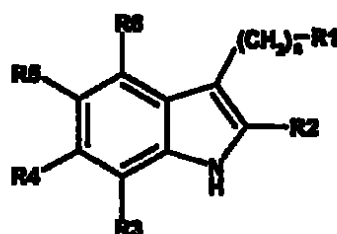
más preferiblemente un anillo ciclohexilo.

15 16. Procedimiento para la obtención de un derivado de sulfonamida de fórmula general (Ia) y/o (Ib), según una o más de las reivindicaciones 1 a 15, caracterizado porque al menos un compuesto de fórmula general (II), o uno de sus derivados convenientemente protegidos,



(II)

20 en la que A y B tienen la significación según una o más de las reivindicaciones 1 a 15, y X es un grupo saliente aceptable, preferiblemente un átomo de halógeno, más preferiblemente cloro, se hace reaccionar con al menos un indol sustituido de fórmula general (III),



(III)

en la que R^1 - R^6 y n tienen el significado según una o más de las reivindicaciones 1-15, o uno de sus derivados convenientemente protegidos, y, si fuera necesario, se eliminan los grupos protectores.

- 5 17. Procedimiento para la obtención de un derivado de sulfonamida de fórmula general (Ia) y/o (Ib), según una o más de las reivindicaciones 1 a 15, en la que uno o más sustituyentes R^2 , R^3 , R^4 , R^5 o R^6 representan un grupo nitro, caracterizado porque se reduce un derivado de sulfonamida de fórmula general (Ia) y/o (Ib) correspondiente a un derivado de sulfonamida de fórmula general (Ia) y/o (Ib) correspondiente, en la
- 10 que R^2 , R^3 , R^4 , R^5 o R^6 representan un grupo amino.

18. Procedimiento para la preparación de las sales, preferiblemente las sales fisiológicamente aceptables de los compuestos de fórmula general (Ia) y/o (Ib), según una o más de las reivindicaciones 1 a 15, que consiste en hacer reaccionar al menos un compuesto de fórmula general (Ia) y/o al menos un compuesto de fórmula general
- 15 (Ib) con un ácido mineral o con un ácido orgánico en un disolvente adecuado.

19. Medicamento que comprende al menos un compuesto según una o más de las reivindicaciones 1 a 9 y opcionalmente uno o más de los excipientes farmacológicamente aceptables.

- 20 20. Medicamento según la reivindicación 19 para la regulación del receptor 5-HT₆, para la profilaxis y/o el tratamiento de un trastorno o enfermedad relacionada con la ingestión de alimentos, preferiblemente para la regulación del apetito, para el mantenimiento, incremento o reducción del peso corporal, para la profilaxis y/o el tratamiento de la obesidad, bulimia, anorexia, caquexia o diabetes de tipo II (diabetes mellitus insulino independiente), preferiblemente diabetes de tipo II que es causada
- 25 por la obesidad, para la profilaxis y/o el tratamiento de trastornos del tracto gastrointestinal, preferiblemente el síndrome del intestino irritable, para la mejora de la cognición, para la profilaxis y/o el tratamiento de trastornos del sistema nervioso central, ansiedad, pánico, depresión, preferiblemente trastornos bipolares, trastornos cognitivos de la memoria, procesos de demencia senil, trastornos neurodegenerativos,

preferiblemente enfermedad de Alzheimer, enfermedad de Parkinson, enfermedad de Huntington y/o esclerosis múltiple, esquizofrenia, psicosis o hiperquinesia infantil (ADHD, déficit de atención / trastorno de hiperactividad),

5 preferiblemente para la regulación del receptor 5-HT₆, para la profilaxis y/o el
tratamiento de un trastorno o enfermedad relacionada con la ingestión de alimentos,
preferiblemente para la regulación del apetito, para el mantenimiento, incremento o
reducción del peso corporal, para la profilaxis y/o el tratamiento de la obesidad,
bulimia, anorexia, caquexia o diabetes de tipo II (diabetes mellitus insulino
independiente), preferiblemente diabetes de tipo II que es causada por la obesidad,
10 para la profilaxis y/o el tratamiento de trastornos del tracto gastrointestinal,
preferiblemente el síndrome del intestino irritable

21. Uso de al menos un compuesto según una o más de las reivindicaciones 1 a 9,
para la preparación de un medicamento para la regulación del receptor 5-HT₆.

15 22. Uso de al menos un compuesto según una o más de las reivindicaciones 1 a
9, para la preparación de un medicamento para profilaxis y/o el tratamiento de un
trastorno o enfermedad relacionada con la ingestión de alimentos.

23. Uso de al menos un compuesto según una o más de las reivindicaciones 1 a
9, para la preparación de un medicamento para la regulación del apetito.

20 24. Uso de al menos un compuesto según una o más de las reivindicaciones 1 a
9, para la preparación de un medicamento para el mantenimiento, incremento o
reducción del peso corporal.

25 25. Uso de al menos un compuesto según una o más de las reivindicaciones 1 a
9, para la preparación de un medicamento para la profilaxis y/o el tratamiento de la
obesidad.

25 26. Uso de al menos un compuesto según una o más de las reivindicaciones 1 a
9, para la preparación de un medicamento para la profilaxis y/o el tratamiento de la
bulimia.

30 27. Uso de al menos un compuesto según una o más de las reivindicaciones 1 a
9, para la preparación de un medicamento para la profilaxis y/o el tratamiento de la
anorexia.

28. Uso de al menos un compuesto según una o más de las reivindicaciones 1 a
9, para la preparación de un medicamento para la profilaxis y/o el tratamiento de la
caquexia.

35 29. Uso de al menos un compuesto según una o más de las reivindicaciones 1 a
9, para la preparación de un medicamento para la profilaxis y/o el tratamiento de la

diabetes de tipo II (diabetes mellitus insulino independiente), preferiblemente diabetes tipo II que es causada por la obesidad.

30. Uso de al menos un compuesto según una o más de las reivindicaciones 1 a 9, para la preparación de un medicamento para la profilaxis y/o el tratamiento de los trastornos del tracto gastrointestinal.

31. Uso de al menos un compuesto según una o más de las reivindicaciones 1 a 9, para la preparación de un medicamento para la profilaxis y/o el tratamiento del síndrome de Intestino Irritable.

32. Uso de al menos un compuesto según una o más de las reivindicaciones 1 a 9, para la preparación de un medicamento para la profilaxis y/o el tratamiento de la ansiedad.

33. Uso de al menos un compuesto según una o más de las reivindicaciones 1 a 9, para la preparación de un medicamento para la profilaxis y/o el tratamiento de la depresión.

34. Uso de al menos un compuesto según una o más de las reivindicaciones 1 a 9, para la preparación de un medicamento para la profilaxis y/o el tratamiento de los trastornos bipolares.

35. Uso de al menos un compuesto según una o más de las reivindicaciones 1 a 9, para la preparación de un medicamento para la profilaxis y/o el tratamiento de los trastornos cognitivos de la memoria.

36. Uso de al menos un compuesto según una o más de las reivindicaciones 1 a 9, para la preparación de un medicamento para la profilaxis y/o el tratamiento de los procesos de demencia senil.

37. Uso de al menos un compuesto según una o más de las reivindicaciones 1 a 9, para la preparación de un medicamento para la profilaxis y/o el tratamiento de enfermedad de Alzheimer.

38. Uso de al menos un compuesto según una o más de las reivindicaciones 1 a 9, para la preparación de un medicamento para la profilaxis y/o el tratamiento de enfermedad de Parkinson.

39. Uso de al menos un compuesto según una o más de las reivindicaciones 1 a 9, para la preparación de un medicamento para la profilaxis y/o el tratamiento de enfermedad de Huntington.

40. Uso de al menos un compuesto según una o más de las reivindicaciones 1 a 9, para la preparación de un medicamento para la profilaxis y/o el tratamiento de la esclerosis múltiple.

41. Uso de al menos un compuesto según una o más de las reivindicaciones 1 a 9, para la preparación de un medicamento para la profilaxis y/o el tratamiento de las demencias en las que predomina un déficit de la cognición.

5 42. Uso de al menos un compuesto según una o más de las reivindicaciones 1 a 9, para la preparación de un medicamento para la profilaxis y/o el tratamiento de la psicosis.

43. Uso de al menos un compuesto según una o más de las reivindicaciones 1 a 9, para la preparación de un medicamento para la profilaxis y/o el tratamiento de la hiperquinesia infantil (ADHD, déficit de atención / trastorno de hiperactividad).

10 44. Uso de al menos un compuesto según una o más de las reivindicaciones 1 a 9, para la preparación de un medicamento para la profilaxis y/o el tratamiento de los trastornos del sistema nervioso central.

15 45. Uso de al menos un compuesto según una o más de las reivindicaciones 1 a 9, para la preparación de un medicamento para la profilaxis y/o el tratamiento de la esquizofrenia.

46. Uso de al menos un compuesto según una o más de las reivindicaciones 1 a 9, para la preparación de un medicamento para la mejora de la cognición.

20 47. Medicamento que comprende al menos un compuesto según una o más de las reivindicaciones 9 a 15, y opcionalmente al menos uno o más excipientes farmacológicamente aceptables.

25 48. Medicamento según la reivindicación 47 para la regulación del receptor 5-HT₆, para la profilaxis y/o el tratamiento de un trastorno o enfermedad relacionada con la ingestión de alimentos, preferiblemente para la regulación del apetito, para el mantenimiento, incremento o reducción del peso corporal, para la profilaxis y/o el tratamiento de la obesidad, bulimia, anorexia, caquexia o diabetes de tipo II (diabetes mellitus insulino independiente), preferiblemente diabetes de tipo II que es causada por la obesidad, para la profilaxis y/o el tratamiento de trastornos del tracto gastrointestinal, preferiblemente el síndrome del intestino irritable, para la mejora de la cognición, para la profilaxis y/o el tratamiento de trastornos del sistema nervioso
30 central, ansiedad, pánico, depresión, preferiblemente trastornos bipolares, trastornos cognitivos de la memoria, procesos de demencia senil, trastornos neurodegenerativos, preferiblemente enfermedad de Alzheimer, enfermedad de Parkinson, enfermedad de Huntington y/o esclerosis múltiple, esquizofrenia, psicosis, hiperquinesia Infantil (ADHD, déficit de atención / trastorno de hiperactividad)

preferiblemente para la mejora de la cognición, para la profilaxis y/o el tratamiento de trastornos del sistema nervioso central, ansiedad, pánico, depresión, preferiblemente trastornos bipolares, trastornos cognitivos de la memoria, procesos de demencia senil, trastornos neurodegenerativos, preferiblemente enfermedad de Alzheimer, enfermedad de Parkinson, enfermedad de Huntington y esclerosis múltiple, esquizofrenia, psicosis o hiperquinesia infantil (ADHD, déficit de atención / trastorno de hiperactividad).

49. Uso de al menos un compuesto según una o más de las reivindicaciones 10 a 15, para la preparación de un medicamento para la regulación del receptor 5-HT₆.

50. Uso de al menos un compuesto según una o más de las reivindicaciones 9 a 15, para la preparación de un medicamento para profilaxis y/o el tratamiento de un trastorno o enfermedad relacionada con la ingestión de alimentos.

51. Uso de al menos un compuesto según una o más de las reivindicaciones 10 a 15, para la preparación de un medicamento para la regulación del apetito.

52. Uso de al menos un compuesto según una o más de las reivindicaciones 10 a 15, para la preparación de un medicamento para el mantenimiento, incremento o reducción del peso corporal.

53. Uso de al menos un compuesto según una o más de las reivindicaciones 10 a 15, para la preparación de un medicamento para la profilaxis y/o el tratamiento de la obesidad.

54. Uso de al menos un compuesto según una o más de las reivindicaciones 10 a 15, para la preparación de un medicamento para la profilaxis y/o el tratamiento de la bulimia.

55. Uso de al menos un compuesto según una o más de las reivindicaciones 10 a 15, para la preparación de un medicamento para la profilaxis y/o el tratamiento de la anorexia.

56. Uso de al menos un compuesto según una o más de las reivindicaciones 10 a 15, para la preparación de un medicamento para la profilaxis y/o el tratamiento de la caquexia.

57. Uso de al menos un compuesto según una o más de las reivindicaciones 10 a 15, para la preparación de un medicamento para la profilaxis y/o el tratamiento de la diabetes de tipo II (diabetes mellitus insulino independiente), preferiblemente diabetes tipo II que es causada por la obesidad.

58. Uso de al menos un compuesto según una o más de las reivindicaciones 10 a 15, para la preparación de un medicamento para la profilaxis y/o el tratamiento de los trastornos del tracto gastrointestinal.

5 59. Uso de al menos un compuesto según una o más de las reivindicaciones 10 a 15, para la preparación de un medicamento para la profilaxis y/o el tratamiento del síndrome de intestino irritable.

60. Uso de al menos un compuesto según una o más de las reivindicaciones 10 a 15, para la preparación de un medicamento para la profilaxis y/o el tratamiento de la ansiedad.

10 61. Uso de al menos un compuesto según una o más de las reivindicaciones 10 a 15, para la preparación de un medicamento para la profilaxis y/o el tratamiento de la depresión.

15 62. Uso de al menos un compuesto según una o más de las reivindicaciones 10 a 15, para la preparación de un medicamento para la profilaxis y/o el tratamiento de los trastornos bipolares.

63. Uso de al menos un compuesto según una o más de las reivindicaciones 10 a 15, para la preparación de un medicamento para la profilaxis y/o el tratamiento de los trastornos cognitivos de la memoria.

20 64. Uso de al menos un compuesto según una o más de las reivindicaciones 10 a 15, para la preparación de un medicamento para la profilaxis y/o el tratamiento de los procesos de demencia senil.

65. Uso de al menos un compuesto según una o más de las reivindicaciones 10 a 15, para la preparación de un medicamento para la profilaxis y/o el tratamiento de la enfermedad de Alzheimer.

25 66. Uso de al menos un compuesto según una o más de las reivindicaciones 10 a 15, para la preparación de un medicamento para la profilaxis y/o el tratamiento de la enfermedad de Parkinson.

30 67. Uso de al menos un compuesto según una o más de las reivindicaciones 10 a 15, para la preparación de un medicamento para la profilaxis y/o el tratamiento de la enfermedad de Huntington.

68. Uso de al menos un compuesto según una o más de las reivindicaciones 10 a 15, para la preparación de un medicamento para la profilaxis y/o el tratamiento de la esclerosis múltiple.

69. Uso de al menos un compuesto según una o más de las reivindicaciones 10 a 15, para la preparación de un medicamento para la profilaxis y/o el tratamiento de las demencias en las que predomina un déficit de cognición.

5 70. Uso de al menos un compuesto según una o más de las reivindicaciones 10 a 15, para la preparación de un medicamento para la profilaxis y/o el tratamiento de la psicosis.

71. Uso de al menos un compuesto según una o más de las reivindicaciones 10 a 15, para la preparación de un medicamento para la profilaxis y/o el tratamiento de la hiperquinesia infantil (ADHD, déficit de atención / trastorno de hiperactividad).

10 72. Uso de al menos un compuesto según una o más de las reivindicaciones 10 a 15, para la preparación de un medicamento para la profilaxis y/o el tratamiento de los trastornos del sistema nervioso central.

15 73. Uso de al menos un compuesto según una o más de las reivindicaciones 10 a 15, para la preparación de un medicamento para la profilaxis y/o el tratamiento de la esquizofrenia.

74. Uso de al menos un compuesto según una o más de las reivindicaciones 10 a 15, para la preparación de un medicamento para la mejora de la cognición.

RESUMEN

La presente invención se refiere a nuevos derivados de sulfonamidas, de fórmula general (1a, 1b, 1c), (I), (Ia, Ib, Ic), opcionalmente en forma de uno de sus estereoisómeros, preferiblemente enantiómeros o diasterómeros, su racemato o en
5 forma de una mezcla de al menos dos de sus estereoisómeros, preferiblemente enantiómeros o diasterómeros, en cualquier razón de mezcla, o sus sales, preferiblemente sus sales de los mismos fisiológicamente aceptables, correspondientes o solvatos correspondientes; a los procedimientos para su preparación, a su aplicación como medicamentos en medicina humana y/o veterinaria
10 y a las composiciones farmacéuticas que los contienen. Los nuevos compuestos de la presente invención pueden utilizarse en la industria farmacéutica como intermedios para preparar medicamentos.

PATENT COOPERATION TREATY

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From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

To:

DAVILA BAZ, A.
Clarke, Modet & Co.
C/Goya, 11
E-28001 Madrid
ESPAGNE

RECEIVED
14 OCT. 2005
CLARKE MODET & CO.

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (PCT Rule 71.1)

Date of mailing
(day/month/year)

11.10.2005

Applicant's or agent's file reference
ET0027PCT

425/2005

IMPORTANT NOTIFICATION

International application No.
PCT/EP2004/008518

International filing date (day/month/year)
29.07.2004

Priority date (day/month/year)
30.07.2003

Applicant

LABORATORIOS DEL DR. ESTEVE S.A. et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the International preliminary report on patentability and its annexes, if any, established on the International application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the International preliminary report on patentability. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:



European Patent Office
D-80298 Munich
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Authorized Officer

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference ET0027PCT	FOR FURTHER ACTION See Form PCT/PEA/16	
International application No. PCT/EP2004/008516	International filing date (day/month/year) 29.07.2004	Priority date (day/month/year) 30.07.2003
International Patent Classification (IPC) or national classification and IPC A61K31/04, C07D208/40, A61P3/04, A61P25/00, C07D401/04, C07D471/04		
Applicant LABORATORIOS DEL DR. ESTEVE S.A. et al.		
1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36. 2. This REPORT consists of a total of 5 sheets, including this cover sheet. 3. This report is also accompanied by ANNEXES, comprising: a. ☒ sent to the applicant and to the International Bureau a total of 19 sheets, as follows: ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 807 of the Administrative Instructions). ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box. b. ☐ (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).		
4. This report contains indications relating to the following items: ☒ Box No. I Basis of the opinion ☐ Box No. II Priority ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability ☐ Box No. IV Lack of unity of invention ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement ☐ Box No. VI Certain documents cited ☐ Box No. VII Certain defects in the international application ☒ Box No. VIII Certain observations on the international application		
Date of submission of the demand 28.02.2005	Date of completion of this report 11.10.2005	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80299 Munich Tel. +49 89 2369 - 0 Tlx 623656 epmu d Fax: +49 89 2369 - 4465	Authorized Officer Seymour, L. Telephone No. +49 89 2369-8694 	

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language, which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the elements* of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-48 as originally filed

Claims, Numbers

1-74 received on 02.08.2005 with letter of 30.05.2005

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/figs
- ☐ the sequence listing *(specify)*:
- ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/figs
- ☐ the sequence listing *(specify)*:
- ☐ any table(s) related to sequence listing *(specify)*:

* If item 4 applies, some or all of these sheets may be marked "superseded."

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-74
	No: Claims	
Inventive step (IS)	Yes: Claims	1-74
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-74
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

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Re Item V

1. The following documents are referred to in this communication:

D1: WO-A-02 051837 D2: WO-A-01 12629 D3: WO-A-02 060871

2. Novelty (Article 33(2) PCT)

The compounds of D1 differ from the present compounds owing to the definition of R_6 , which may not be a non-aromatic ring.

The compounds of D2 differ from the present compounds owing to the $-SO_2-Ar$ substituent at position 1 of the indole ring.

The compounds of D3 differ from the present compounds e.g. owing to the benzenesulfonic acid substituent at position 5 of the indole ring.

3. The present application is considered as involving an inventive step (Article 33(3) PCT).

The problem underlying the present application lies in the provision of further indole derivatives effective in the treatment of disorders related to the $5-HT_6$ receptor.

Document D1 discloses $5-HT_6$ receptor ligands, which differ from the present compounds in that the substituent at position 1 of the indole ring is $-SO_2-Ar$ rather than the present $-SO_2-CH(A)(B)$ wherein A and B form a saturated or unsaturated, but not aromatic cycloalkyl ring. D1 itself teaches that the Ar group may be replaced by C_1-C_6 alkyl (see D1, claim 1), but not with cycloalkyl. In D2 and D3 there is also no hint that the aryl group of D1 may be exchanged for a cycloalkyl group as a solution to the above-mentioned problem.

Representative data for the present compounds is given on page 47 of the description. It is therefore credible that the above-mentioned problem has actually been solved.

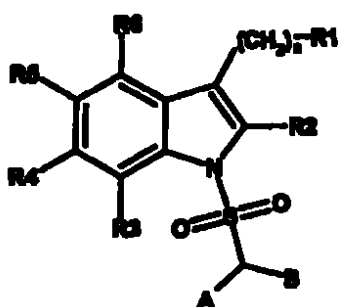
Re Item VIII

1. Although claims 1 and 10 have been drafted as separate independent claims, they appear to relate effectively to the same subject-matter. The aforementioned claims therefore lack conciseness and as such do not meet the requirements of Article 6 PCT.
2. The reason for the proviso found in claim 1 is not clear (Article 6 PCT; see also Rule 5.1(a)(ii) PCT).
3. The optional features in the claims, i.e. the definitions following the term "preferably" (see e.g. claims 2, 3, 11, 12, 15, 48), have no limiting effect on said claims. For the sake of clarity (Article 6 PCT) these preferred embodiments should therefore be claimed in separate dependent claims (Rule 6.4 PCT).
4. Claims 1 and 10 lack conciseness (Article 6 PCT) since the formulae Ia and Ib include a linker $(CH_2)_n$ although $n = 0$ i.e. the linker does not exist.
5. The description is not in conformity with the claims as required by Rule 5.1(a)(iii) PCT (see reference in description to formula Ic).

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CLAIMS

1.- Sulfonamide compounds of general formula (Ia),



(Ia)

wherein

R^1 represents a $-NR^7R^8$ radical or a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing cycloaliphatic radical, which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system,

R^2 , R^3 , R^4 , R^5 and R^6 , identical or different, each represent hydrogen, halogen, cyano, nitro, a saturated or unsaturated, linear or branched aliphatic radical, a linear or branched alkoxy radical, a linear or branched alkylthio radical, hydroxy, trifluoromethyl, a saturated or unsaturated cycloaliphatic radical, an alkylcarbonyl radical, a phenylcarbonyl or a $-NR^9R^{10}$ group,

R^7 and R^8 , identical or different, each represent hydrogen or a saturated or unsaturated, optionally at least mono-substituted linear or branched aliphatic radical,

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with the proviso that R^a and R^b are not hydrogen at the same time, and if one of them, R^a or R^b , is a saturated or unsaturated, linear or branched, optionally at least mono-substituted C_1 - C_4 aliphatic radical, the other one is a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical with at least five carbon atoms,

or

R^7 and R^8 , together with the bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted, optionally at least one further heteroatom as a ring member containing heterocyclic ring which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system,

R^9 and R^{10} , identical or different, each represent hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

or

R^9 and R^{10} , together with the bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted, optionally at least one further heteroatom as a ring member containing heterocyclic ring which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system,

A and B, together with the carbon atom to which they are bonded, form a saturated or unsaturated, but not aromatic, optionally at least mono-substituted cycloalkyl ring,

and

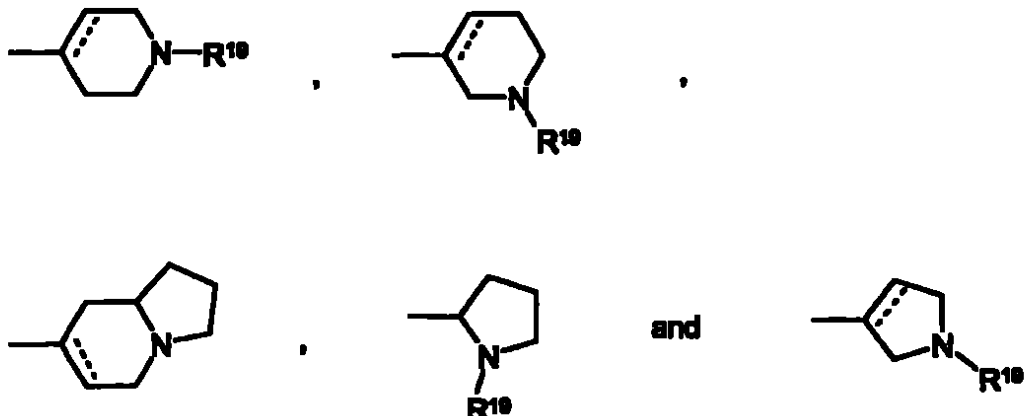
141

n is 0,

optionally in form of one of their stereoisomers, preferably enantiomers or diastereomers, their racemate or in form of a mixture of at least two of their stereoisomers, preferably enantiomers or diastereomers, in any mixing ratio, or a salt thereof, preferably a corresponding physiologically acceptable salt thereof or a corresponding solvate thereof.

2. The compounds according to claim 1, characterized in that R^1 represents a NR^7R^8 radical or a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing 5- or 6-membered cycloaliphatic radical, which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system, whereby the rings of the ring system are 5- or 6-membered,

preferably a NR^7R^8 radical or a radical chosen from the group consisting of



wherein, if present, the dotted line represents an optional chemical bond, and R^{10} represents hydrogen, a linear or branched C_1-C_8 alkyl radical or a benzyl radical, preferably hydrogen or a C_1-C_2 alkyl radical.

3.- The compounds according to claim 1 or 2, characterized in that R^2 , R^3 , R^4 , R^5 and R^6 , identical or different, each represent hydrogen, F, Cl, Br, cyano, nitro, a linear or branched C_{1-8} alkyl radical, a linear or branched C_{2-8} alkenyl radical, a linear or branched C_{2-8} alkynyl radical, a linear or branched C_{1-8} alkoxy, a linear or branched C_{1-8} alkylthio, hydroxy, trifluoromethyl, a saturated or unsaturated C_{3-8} cycloaliphatic radical, a linear or branched C_{1-8} alkylcarbonyl radical, phenylcarbonyl or an $-NR^9R^{10}$ group,

preferably H, F, Cl, NO_2 , NH_2 or a C_{1-2} alkyl radical.

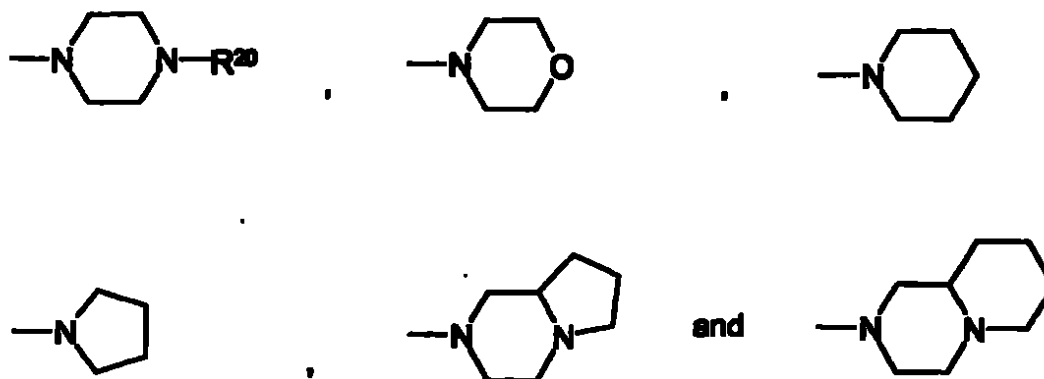
4.- The compounds according to one or more of claims 1 to 3, characterized in that R^7 and R^8 , identical or different, each represent hydrogen, a linear or branched, optionally at least mono-substituted C_{1-10} alkyl radical, a linear or branched, optionally at least mono-substituted, C_{2-10} alkenyl radical, or a linear or branched, optionally at least mono-substituted, C_{2-10} alkynyl radical or

R^7 and R^8 , together with the bridging nitrogen form a saturated or unsaturated, optionally at least mono-substituted, optionally at least one further heteroatom as a ring member containing 5- or 6-membered heterocyclic ring which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system, whereby the rings of the ring system are 5- 6- or 7-membered.

5.- The compounds according to claim 4, characterized in that R^7 and R^8 , identical or different, each represent hydrogen or a linear or branched C_{1-10} alkyl radical or

R^7 and R^8 , together with the bridging nitrogen atom form a radical chosen from the group consisting of

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wherein R^{20} , if present, is hydrogen, a linear or branched C_1 - C_6 alkyl radical or a benzyl radical, preferably hydrogen, or a C_1 - C_2 alkyl radical.

5

6.-

The compounds according to one or more of claims 1 to 5, characterized in that R^9 and R^{10} , identical or different, each represent hydrogen, a linear or branched, optionally at least mono-substituted C_1 - C_{10} alkyl radical, a linear or branched, optionally at least mono-substituted C_2 - C_{10} alkenyl radical or a linear or branched, optionally at least mono-substituted C_2 - C_{10} alkynyl radical or

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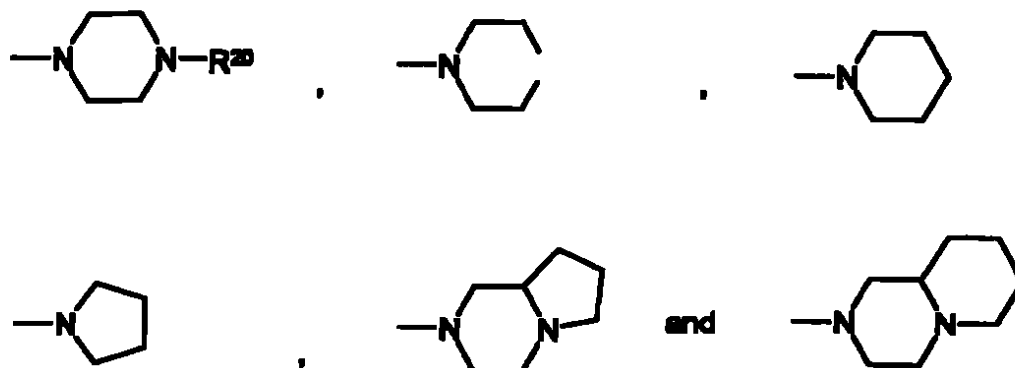
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R^9 and R^{10} , together with the bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted, optionally at least one further heteroatom as a ring member containing 5- or 6-membered heterocyclic ring, which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system whereby the rings of the ring system are 5- 6- or 7-membered.

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7.- The compounds according to claim 6, characterized in that R^9 and R^{10} , identical or different, each represent hydrogen or a linear or branched C_1 - C_{10} alkyl radical, or

R^9 and R^{10} , together with the bridging nitrogen atom form a radical chosen from a group consisting of



wherein R^{20} , if present, is hydrogen, a linear or branched $\text{C}_1\text{—C}_6$ alkyl radical or a benzyl radical, preferably hydrogen, or a $\text{C}_1\text{—C}_2$ alkyl radical.

5 8.- The compounds according to one or more of claims 1-7, characterized in that
(.) A and B, together with the carbon atom to which they are bonded, form a $\text{C}_3\text{—C}_6$ cycloalkyl ring, preferably a cyclohexyl ring.

10 9.- The compounds according to one or more of claims 1-8, characterized in that
the compound is selected from a group consisting of

[1] 1-Cyclohexanesulfonyl-3-(1-methyl-1,2,3,6-tetrahydropyridine-4-yl)-5-nitro-1H-Indole,

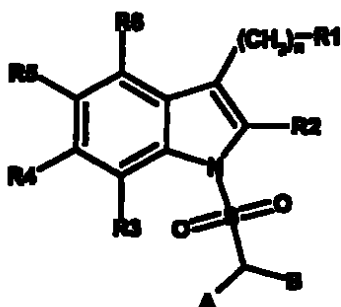
15 [2] 5-Chloro-1-cyclohexanesulfonyl-3-(1-methyl-1,2,3,6-tetrahydropyridine-4-yl)-1H-Indole,

(.) [3] 5-Amino-1-cyclohexanesulfonyl-3-(1-methyl-1,2,3,6-tetrahydropyridine-4-yl)-1H-Indole and

20 [4] 1-Cyclohexanesulfonyl-5-fluoro-3-(1,2,3,5,8,8a-hexahydro-Indolizine-7-yl)-1H-Indole hydrochloride

and their corresponding salts and solvates.

10.- Sulfonamide compounds of general formula (Ib),



(Ib)

wherein

R^1 is a $-NR^7R^8$ radical,

R^2, R^3, R^4, R^5 and R^6 , identical or different, each represent hydrogen, halogen, cyano, nitro, a saturated or unsaturated, linear or branched aliphatic radical, a linear or branched alkoxy radical, a linear or branched alkylthio radical, hydroxy, trifluoromethyl, a saturated or unsaturated cycloaliphatic radical, an alkylcarbonyl radical, a phenylcarbonyl or a $-NR^9R^{10}$ group,

R^7 and R^8 , identical or different, each represent hydrogen or a saturated or unsaturated, optionally at least mono-substituted linear or branched C_{1-4} aliphatic radical,

R^9 and R^{10} , identical or different, each represent hydrogen or a saturated or unsaturated, linear or branched, optionally at least mono-substituted aliphatic radical,

or

R^9 and R^{10} , together with the bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted, optionally at least one further heteroatom as a ring member containing heterocyclic ring which may be condensed with a saturated or unsaturated, optionally at least mono-

substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system,

A and B, together with the carbon atom to which they are bonded, form a saturated or unsaturated, but not aromatic, optionally at least mono-substituted cycloalkyl ring,

and

n is 0;

optionally in form of one of its stereoisomers, preferably enantiomers or diastereomers, their racemate or in form of a mixture of at least two of their stereoisomers, preferably enantiomers or diastereomers, in any mixing ratio, or a salt thereof, preferably a corresponding physiologically acceptable salt thereof or a corresponding solvate thereof.

11.- The compounds according to claim 10, characterized in that R^2 , R^3 , R^4 , R^5 and R^6 , identical or different, each represent hydrogen, F, Cl, Br, cyano, nitro, a linear or branched C_1-C_6 alkyl radical, a linear or branched C_2-C_6 alkenyl radical, a linear or branched C_2-C_6 alkynyl radical, a linear or branched C_1-C_6 alkoxy, a linear or branched C_1-C_6 -alkylthio, hydroxy, trifluoromethyl, a saturated or unsaturated C_3-C_6 cycloaliphatic radical, a linear or branched C_1-C_6 -alkylcarbonyl radical, phenylcarbonyl or an $-NR^9R^{10}$ group,

preferably H, F, Cl, NO_2 , NH_2 or a C_1-C_2 alkyl radical.

12.- The compounds according to claim 10 or 11, characterized in that R^7 and R^8 , identical or different, wherein R^7 and R^8 , identical or different, each represent hydrogen, a linear or branched, optionally at least mono-substituted C_1-C_4 alkyl radical,

preferably hydrogen or a C_1-C_2 alkyl radical, with the proviso that R^7 and R^8 are not hydrogen at the same time.

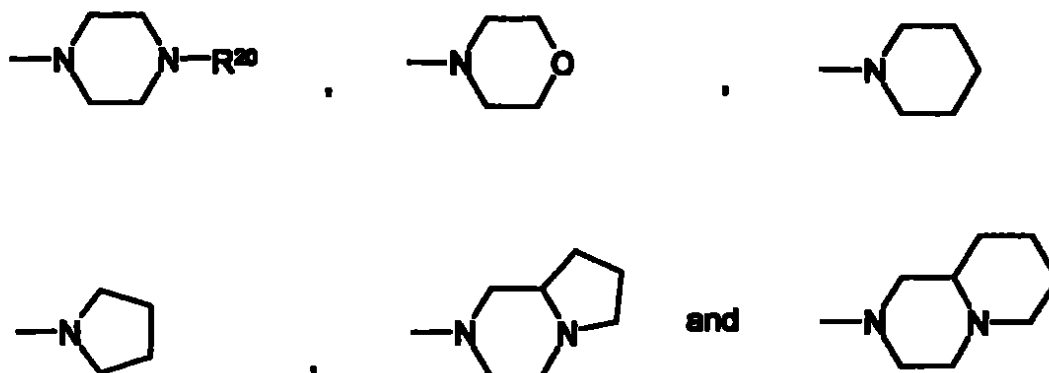
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13.- The compounds according to one or more of claims 10 to 12, characterized in that R^9 and R^{10} , identical or different, each represent hydrogen, a linear or branched, optionally at least mono-substituted C_1-C_{10} alkyl radical, a linear or branched, optionally at least mono-substituted C_2-C_{10} alkenyl radical, or a linear or branched, optionally at least mono-substituted C_2-C_{10} alkynyl radical or

R^9 and R^{10} , together with the bridging nitrogen atom form a saturated or unsaturated, optionally at least mono-substituted, optionally at least one further heteroatom as a ring member containing 5- or 6-membered heterocyclic which may be condensed with a saturated or unsaturated, optionally at least mono-substituted, optionally at least one heteroatom as a ring member containing mono- or bicyclic cycloaliphatic ring system, whereby the rings of the ring system are 5- 6- or 7-membered.

14.- The compounds according to claim 13, characterized in that R^9 and R^{10} , identical or different, each represent hydrogen or a linear or branched C_1-C_{10} alkyl radical, or

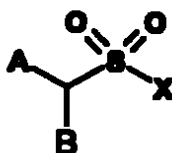
R^9 and R^{10} , together with the bridging nitrogen atom form a radical chosen from a group consisting of



wherein R^{20} , if present, represents hydrogen, a linear or branched C_1-C_6 alkyl radical or a benzyl radical, preferably hydrogen, or a C_1-C_2 alkyl radical.

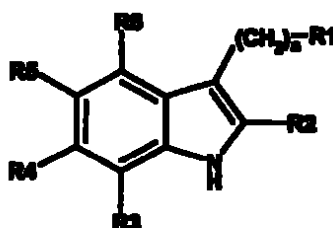
15.- The compounds according to one or more of claims 10 to 14, characterized in that A and B, together with the carbon atom to which they are bonded, form a C₃-C₈ cycloalkyl ring, preferably a cyclohexyl ring.

16.- A process for obtaining a sulfonamide derivative of general formula (Ia) and/or (Ib), according to one or more of claims 1 to 15, characterized in that at least one compound of general formula (II), or one of its suitably protected derivatives,



(II)

wherein A and B have the meaning according to one or more of claims 1 to 15 and X is an acceptable leaving group, preferably an halogen atom, more preferably chlorine, is reacted with at least one substituted indole of general formula (III)



(III)

wherein R¹-R⁶ and n have the meaning according to one or more of claims 1 to 15, or one of their suitable protected derivatives, and, if necessary, the protective groups are removed.

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- 17.- A process for obtaining a sulfonamide derivative of general formula (Ia) and/or (Ib) according to one or more of claims 1-15, wherein one or more substituents R^2 , R^3 , R^4 , R^5 or R^6 represent a nitro group, characterized in that a sulfonamide derivative of corresponding general formula (Ia) and/or (Ib) is reduced to a sulfonamide derivative of corresponding general formula (Ia) and/or (Ib), wherein one or more substituents R^2 , R^3 , R^4 , R^5 or R^6 represent an amino group.
- 18.- A process for preparing the salts, preferably the physiologically acceptable salts of the compounds of general formula (Ia) and/or (Ib), according to one or more of claims 1 to 15, consisting of reacting at least one compound of the general formula (Ia) and/or at least one compound of the general formula (Ib) with a mineral acid or organic acid in a suitable solvent.
- 19.- A medicament comprising at least one compound according to one or more of claims 1 to 9 and optionally one or more pharmacologically acceptable excipients.
- 20.- A medicament according to claim 19, for 5-HT₆ receptor regulation, for the prophylaxis and/or treatment of a disorder or disease related to food intake, preferably for the regulation of appetite, for the maintenance, increase or reduction of body weight, for the prophylaxis and/or treatment of obesity, bulimia, anorexia, cachexia or type II diabetes (non insulin dependent diabetes mellitus), preferably type II diabetes caused by obesity, for the prophylaxis and/or treatment of gastrointestinal tract disorders, preferably irritable bowel syndrome, for cognitive enhancement, for the prophylaxis and/or treatment of disorders of the central nervous system, anxiety, panic disorders, depression, preferably bipolar disorders, cognitive memory disorders, senile dementia processes, neurodegenerative disorders, preferably Alzheimer's disease, Parkinson's disease, Huntington's disease and/or multiple sclerosis, schizophrenia, psychosis or infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder),

preferably for 5-HT₆ receptor regulation, for the prophylaxis and/or treatment of a disorder or disease related to food intake, preferably for the regulation of appetite, for the maintenance, increase or reduction of body weight, for the prophylaxis and/or treatment of obesity, bulimia, anorexia, cachexia or type II diabetes (non insulin dependent diabetes mellitus), preferably type II diabetes caused by obesity, for the prophylaxis and/or treatment of gastrointestinal tract disorders, preferably irritable bowel syndrome.

- 10 21. - The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for 5-HT₆ receptor regulation.
- 15 22.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of a disorder or disease related to food intake.
- 23.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the regulation of appetite.
- 20 24.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the maintenance, increase or reduction of body weight.
- 25 25.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of obesity.
- 26.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of bulimia.
- 30 27.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament the prophylaxis and/or treatment of anorexia.

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- 28.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of cachexia.
- 29.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of type II diabetes (non insulin dependent diabetes mellitus), preferably type II diabetes caused by obesity.
- 30.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of gastrointestinal tract disorders.
- 31.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of irritable bowel syndrome.
- 32.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of anxiety.
- 33.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of depression.
- 34.- The use of at least one compound according to one more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of bipolar disorders.
- 35.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of cognitive memory disorders.

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- 36.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of senile dementia processes.
- 5 37.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of Alzheimer's Disease.
- 10 38.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of Parkinson's Disease.
- 15 39.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of Huntington's Disease.
- 20 40.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of Multiple Sclerosis.
- 41.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of dementias in which a cognitive deficit predominates.
- 25 42.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of psychosis.
- 30 43.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder).

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44.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of disorders of the central nervous system.

5 45.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for the prophylaxis and/or treatment of schizophrenia.

10 46.- The use of at least one compound according to one or more of claims 1 to 9 for the manufacture of a medicament for cognitive enhancement.

47. A medicament comprising at least one compound according to one or more of claims 9 to 15 and optionally at least one or more of pharmacologically acceptable excipients.

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48.- A medicament according to claim 47 for 5-HT₆ receptor regulation, for the prophylaxis and/or treatment of a disorder or disease related to food intake, preferably for the regulation of appetite, for the maintenance, increase or reduction of body weight, for the prophylaxis and/or treatment of obesity, bulimia, anorexia, cachexia or type II diabetes (non insulin dependent diabetes mellitus), preferably type II diabetes caused by obesity, for the prophylaxis and/or treatment of gastrointestinal tract disorders, preferably irritable bowel syndrome, for cognitive enhancement, for the prophylaxis and/or treatment of disorders of the central nervous system, anxiety, panic disorders, depression, preferably bipolar disorders, cognitive memory disorders, senile dementia processes, neurodegenerative disorders, preferably Alzheimer's disease, Parkinson's disease, Huntington's disease and/or multiple sclerosis, schizophrenia, psychosis or infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder),

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preferably for cognitive enhancement, for the prophylaxis and/or treatment of disorders of the central nervous system, anxiety, panic disorders, depression, preferably bipolar disorders, cognitive memory disorders, senile dementia processes, neurodegenerative disorders, preferably Alzheimer's disease,

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Parkinson's disease, Huntington's disease and multiple sclerosis, schizophrenia, psychosis or infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder).

- 5 49.- The use of at least one compound according to one or more of claims 10 to 15
for the manufacture of a medicament for 5-HT₆ receptor regulation.
- 10 50.- The use of at least one compound according to one or more of claims 9 to 15
for the manufacture of a medicament for the prophylaxis and/or treatment of a
disorder or disease related to food intake.
- 15 51.- The use of at least one compound according to one or more of claims 10 to 15
for the manufacture of a medicament for the regulation of appetite.
- 20 52.- The use of at least one compound according to one or more of claims 10 to 15
for the manufacture of a medicament for the maintenance, increase or
reduction of body weight.
- 25 53.- The use of at least one compound according to one or more of claims 10 to 15
for the manufacture of a medicament for the prophylaxis and/or treatment of
obesity.
- 30 54.- The use of at least one compound according to one or more of claims 10 to 15
for the manufacture of a medicament for the prophylaxis and/or treatment of
bulimia.
- 35 55.- The use of at least one compound according to one or more of claims 10 to 15
for the manufacture of a medicament for the prophylaxis and/or treatment of
anorexia.
- 40 56.- The use of at least one compound according to one or more of claims 10 to 15
for the manufacture of a medicament for the prophylaxis and/or treatment of
cachexia.

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57.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of type II diabetes (non-insulin-dependent diabetes mellitus), preferably type II diabetes caused by obesity.

58.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of gastrointestinal tract disorders.

59.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of irritable bowel syndrome.

60.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of anxiety.

61.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of depression.

62.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of bipolar disorders.

63.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of cognitive memory disorders.

64.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of senile dementia processes.

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- 65.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of Alzheimer's Disease.
- 5 66.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of Parkinson's Disease.
- 10 67.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of Huntington's Disease.
- () 68.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of Multiple Sclerosis.
- 15 69.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of dementias in which a cognitive deficit predominates.
- 20 70.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of psychosis.
- 25 71.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of infantile hyperkinesia (ADHD, attention deficit / hyperactivity disorder).
- 30 72.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of disorders of the central nervous system.

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- 73.- The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for the prophylaxis and/or treatment of schizophrenia.
- 5 74. - The use of at least one compound according to one or more of claims 10 to 15 for the manufacture of a medicament for cognitive enhancement.

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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference ET0027PCT	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, Item 5 below.	
International application No. PCT/EP2004/008516	International filing date (day/month/year) 29/07/2004	(Earliest) Priority Date (day/month/year) 30/07/2003
Applicant LABORATORIOS DEL DR. ESTEVE S.A.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.

2. ☐ Certain claims were found unsearchable (See Box II).

3. ☐ Unity of invention is lacking (see Box III).

4. With regard to the title,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

1-SULFONYLINDOLE DERIVATIVES, THEIR PREPARATION AND THEIR USE AS 5-HT₆ LIGANDS

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regards to the drawings,

- a. the figure of the drawings to be published with the abstract is Figure No. _____

☐ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

- b. ☐ none of the figures is to be published with the abstract.

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 A61K31/404 C07D209/40 A61P3/04 A61P25/00 C07D401/04 C07D471/04		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC 7 C07D		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, WPI Data, PAJ, BEILSTEIN Data, CHEM ABS Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 02/051837 A (WYETH CORP) 4 July 2002 (2002-07-04) claims 1,12,13,20	1-74
Y	WO 01/12629 A (NPS ALLELIX CORP) 22 February 2001 (2001-02-22) claims 1,10,12	1-74
Y	WO 02/060871 A (FLAUGH MICHAEL EDWARD ; GILLIG JAMES RONALD (US); HEINZ LAWRENCE JOSEP) 8 August 2002 (2002-08-08) claims 1,12,14; example 12	1-74
☐ Further documents are listed in the continuation of box C. ☒ Patent family members are listed in annex.		
* Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "A" document member of the same patent family		
Date of the actual completion of the international search 18 November 2004		Date of mailing of the international search report 25/11/2004
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 851 epo nl Fax (+31-70) 340-3018		Authorized officer Seymour, L

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP2004/008516

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 02051837	A	04-07-2002	BR 0116323 A	14-10-2003
			CA 2432654 A1	04-07-2002
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			JP 2004526699 T	02-09-2004
			WO 02060871 A2	08-08-2002
			US 2004102481 A1	27-05-2004

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference
(if desired) (12 characters maximum) ET0027PCT

Box No. I TITLE OF INVENTION

1-sulfonylindole derivatives, their preparation and their use in medicaments

Box No. II APPLICANT

☐ This person is also inventor

Name and address: (Family name followed by given names; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

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E-08041 Barcelona
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Applicant's registration No. with the Office

State (that is, country) of nationality:
ES

State (that is, country) of residence:
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This person is applicant for the purposes of: ☐ all designated States ☒ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: (Family name followed by given names; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

MERCE VIDAL, Ramon
C/Casanova 264 4° 1a
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This person is:

- ☐ applicant only
☒ applicant and inventor
☐ inventor only (if this check-box is marked, do not fill in below.)

Applicant's registration No. with the Office

State (that is, country) of nationality:
ES

State (that is, country) of residence:
ES

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: ☐ agent ☐ common representative

Name and address: (Family name followed by given names; for a legal entity, full official designation. The address must include postal code and name of country.)

DAVILA BAZ, A.,
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Teleprinter No.

Agent's registration No. with the Office

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

If none of the following sub-boxes is used, this sheet should not be included in the request.

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

CODONY SOLER, Xavier
C/Lepanto 71-77 2° 1a
E-08301 Mataro (Barcelona)
SPAIN

This person is:

- ☐ applicant only
- ☒ applicant and inventor
- ☐ inventor only (If this check-box is marked, do not fill in below.)

Applicant's registration No. with the Office

State (that is, country) of nationality:

ES

State (that is, country) of residence:

ES

This person is applicant for the purposes of:

☐ all designated States☐ all designated States except the United States of America☒ the United States of America only☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

DORDAL ZUERAS, Alberto
C/Maladeta 26, 3° 3a
E-08016 Barcelona
SPAIN

This person is:

- ☐ applicant only
- ☒ applicant and inventor
- ☐ inventor only (If this check-box is marked, do not fill in below.)

Applicant's registration No. with the Office

State (that is, country) of nationality:

ES

State (that is, country) of residence:

ES

This person is applicant for the purposes of:

☐ all designated States☐ all designated States except the United States of America☒ the United States of America only☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

This person is:

- ☐ applicant only
- ☐ applicant and inventor
- ☐ inventor only (If this check-box is marked, do not fill in below.)

Applicant's registration No. with the Office

State (that is, country) of nationality:

State (that is, country) of residence:

This person is applicant for the purposes of:

☐ all designated States☐ all designated States except the United States of America☐ the United States of America only☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

This person is:

- ☐ applicant only
- ☐ applicant and inventor
- ☐ inventor only (If this check-box is marked, do not fill in below.)

Applicant's registration No. with the Office

State (that is, country) of nationality:

State (that is, country) of residence:

This person is applicant for the purposes of:

☐ all designated States☐ all designated States except the United States of America☐ the United States of America only☐ the States indicated in the Supplemental Box

Further applicants and/or (further) inventors are indicated on another continuation sheet.

Box No. V DESIGNATIONS

The filing of this request constitutes under Rule 4.9(a), the designation of all Contracting States bound by the PCT on the international filing date, for the grant of every kind of protection available and, where applicable, for the grant of both regional and national patents.

However,

- ☐ DE Germany is not designated for any kind of national protection
- ☐ KR Republic of Korea is not designated for any kind of national protection
- ☐ RU Russian Federation is not designated for any kind of national protection

(The check-boxes above may be used to exclude (irrevocably) the designations concerned in order to avoid the ceasing of the effect, under the national law, of an earlier national application from which priority is claimed. See the Notes to Box No. V as to the consequences of such national law provisions in these and certain other States.)

Box No. VI PRIORITY CLAIM

The priority of the following earlier application(s) is hereby claimed:

Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is:		
		national application: country or Member of WTO	regional application:* regional Office	international application: receiving Office
item (1) July 30, 2003 (30/07/2003)	P200301808	ES		
item (2)				
item (3)				

- ☐ Further priority claims are indicated in the Supplemental Box.

The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (only if the earlier application was filed with the Office which for the purposes of this international application is the receiving Office) identified above as:

- ☐ all items ☐ item (1) ☐ item (2) ☐ item (3) ☐ other, see Supplemental Box

* Where the earlier application is an ARIPO application, indicate at least one country party to the Paris Convention for the Protection of Industrial Property or one Member of the World Trade Organisation for which that earlier application was filed (Rule 4.10(b)(ii)):

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) (if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):

ISA /

Request to use results of earlier search; reference to that search (if an earlier search has been carried out by or requested from the International Searching Authority):

Date (day/month/year) Number Country (or regional Office)

Box No. VIII DECLARATIONS

The following declarations are contained in Boxes Nos. VIII (i) to (v) (mark the applicable check-boxes below and indicate in the right column the number of each type of declaration):

Number of
declarations

- | | | |
|---|--|---|
| ☐ Box No. VIII (i) | Declaration as to the identity of the inventor | : |
| ☐ Box No. VIII (ii) | Declaration as to the applicant's entitlement, as at the international filing date, to apply for and be granted a patent | : |
| ☐ Box No. VIII (iii) | Declaration as to the applicant's entitlement, as at the international filing date, to claim the priority of the earlier application | : |
| ☐ Box No. VIII (iv) | Declaration of inventorship (only for the purposes of the designation of the United States of America) | : |
| ☐ Box No. VIII (v) | Declaration as to non-prejudicial disclosures or exceptions to lack of novelty | : |

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Box No. IX CHECK LIST; LANGUAGE OF FILING

This international application contains:

(a) in paper form, the following number of sheets:

request (including declaration sheets) : 4
description (excluding sequence listing and/or tables related thereto) : 48
claims : 21
abstract : 1
drawings : 1

Sub-total number of sheets : 74

sequence listing :
tables related thereto :

(for both, actual number of sheets if filed in paper form, whether or not also filed in computer readable form; see (c) below)

Total number of sheets : 74

(b) ☐ only in computer readable form (Section 801(a)(i))

(i) ☐ sequence listing
(ii) ☐ tables related thereto

(c) ☐ also in computer readable form (Section 801(a)(ii))

(i) ☐ sequence listing
(ii) ☐ tables related thereto

Type and number of carriers (diskette, CD-ROM, CD-R or other) on which are contained the

☐ sequence listing :
☐ tables related thereto :

(additional copies to be indicated under items 9(ii) and/or 10(ii), in right column)

This international application is accompanied by the following item(s) (mark the applicable check-boxes below and indicate in right column the number of each item):

- | | |
|---|-----|
| 1. ☒ fee calculation sheet | : 1 |
| 2. ☐ original separate power of attorney | : |
| 3. ☐ original general power of attorney | : |
| 4. ☒ copy of general power of attorney, reference number, if any: | : 1 |
| 5. ☐ statement explaining lack of signature | : |
| 6. ☐ priority document(s) identified in Box No. VI as item(s): | : |
| 7. ☐ translation of international application into (language): | : |
| 8. ☐ separate indications concerning deposited microorganism or other biological material | : |
| 9. ☐ sequence listing in computer readable form (indicate type and number of carriers) | : |
| (i) ☐ copy submitted for the purposes of international search under Rule 13ter only (and not as part of the international application) : | : |
| (ii) ☐ (only where check-box (b)(i) or (c)(i) is marked in left column) additional copies including, where applicable, the copy for the purposes of international search under Rule 13ter : | : |
| (iii) ☐ together with relevant statement as to the identity of the copy or copies with the sequence listing mentioned in left column : | : |
| 10. ☐ tables in computer readable form related to sequence listing (indicate type and number of carriers) | : |
| (i) ☐ copy submitted for the purposes of international search under Section 802(b-quater) only (and not as part of the international application) : | : |
| (ii) ☐ (only where check-box (b)(ii) or (c)(ii) is marked in left column) additional copies including, where applicable, the copy for the purposes of international search under Section 802(b-quater) : | : |
| (iii) ☐ together with relevant statement as to the identity of the copy or copies with the tables mentioned in left column : | : |
| 11. ☐ other (specify): | : |

Figure of the drawings which should accompany the abstract:

Language of filing of the international application:

English

Box No. X SIGNATURE OF APPLICANT, AGENT OR COMMON REPRESENTATIVE

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).

Madrid,

A. Davila Baz

For receiving Office use only

1. Date of actual receipt of the purported international application:	2. Drawings: ☐ received: ☐ not received:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:	
4. Date of timely receipt of the required corrections under PCT Article 11(2):	
5. International Searching Authority (if two or more are competent): ISA /	6. ☐ Transmittal of search copy delayed until search fee is paid

For International Bureau use only

Date of receipt of the record copy by the International Bureau:

SUPERINDUSTRIA Y COMERCIO
 Radicación : 86807747 00000000 Folios: 164
 Fecha (NND): 2006-01-27 17:44:25
 Trámite : 011 PCT-PATENT 379 FASE INICI 411 PRESENTAR
 Dependencia: 2020 DIVISION DE NUEVAS CREACIONES

REQUISITOS NECESARIOS PARA PRESENTACION Y AGILIZACION DE TRAMITE

	USUARIO	RADICADOR
PATENTE DE INVENCION	()	()
- Indicación de que se solicita la concesión de una patente.	()	()
- Datos de identificación del solicitante o de la persona que se presenta la solicitud.	()	()
- Descripción de la invención.	()	()
- Dibujos de ser estos pertinentes.	()	()
- Comprobante de Pago de las tasas establecidas.	()	()
COMPLETA ()	INCOMPLETA ()	()
DISEÑO INDUSTRIAL ()		
- Indicación de que se solicita el registro de Diseño Industrial	()	()
- Datos de identificación del solicitante o de la persona que presenta la solicitud.	()	()
- Representación gráfica o fotográfica del Diseño Industrial o muestra del Material que incorpora el diseño.	()	()
- Comprobante de pago de las tasas establecidas	()	()
COMPLETA ()	INCOMPLETA ()	()
ESQUEMA DE TRAZADO ()		
- Indicación de que solicita el registro de un Esquema de trazado.	()	()
- Datos de identificación del solicitante o de la persona que presenta La solicitud.	()	()
- Representación gráfica del esquema de trazado	()	()
- Comprobante de pago de las tasas establecidas.	()	()
COMPLETA ()	INCOMPLETA ()	()

Firma Responsable:

Fecha:

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REPUBLICA DE COLOMBIA
SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

Bogotá,
2020

Doctor(a)
RODRIGUEZ DILIA MARIA
Apoderado(a) y/o Representante de
LABORATORIOS DEL DR ESTEVE S.A

2752

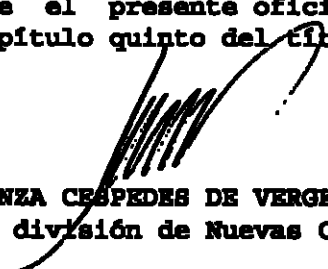
REFERENCIA	Radicación No.	6 7747
	Solicitud internacional	EP2004/008516
	Fecha inicio fase nacional	28/02/2006
	Trámite	11
	Evento	379
	Actuación	430
	Oficio No.	3357

Como resultado del examen de forma, realizado con fundamento en el artículo 38 de la Decisión 486 de la Comisión de la Comunidad Andina, artículo 27 del Tratado de Cooperación en Materia de Patentes (PCT), regla 51 bis del Reglamento y Circular Única de la Superintendencia de Industria y Comercio, se le comunica que:

1. La solicitud no contiene la traducción de los anexos del reporte de examen preliminar internacional (Art. 36.2.b) del tratado PCT.
2. La solicitud no contiene la copia del documento en que consta la cesión del derecho a la patente del inventor al solicitante o a su causante. (Art. 26-k) Decisión 486.

En cumplimiento de lo dispuesto por el artículo 39 de la Decisión 486, se le requiere para que dentro del término de dos meses siguientes a la fecha de notificación del presente oficio, complete los requisitos anteriormente enunciados. En caso de no dar cumplimiento al presente requerimiento, la solicitud se considerará abandonada y perderá su prelación.

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 la división de Nuevas Creaciones

El anterior requerimiento fue notificado por fijación en lista de
fecha 24 MAR. 2006
jramos