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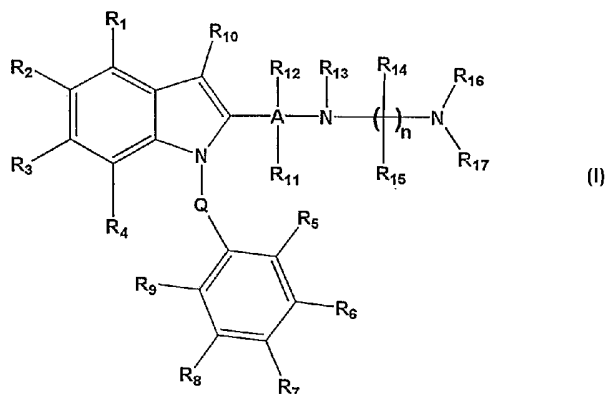
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(54) Title: SUBSTITUTED INDOLES WITH SEROTONIN RECEPTOR AFFINITY, PROCESS FOR THEIR PREPARATION AND PHARMACEUTICAL COMPOSITIONS CONTAINING THEM



(57) Abstract: The present invention relates to the compounds represented by general formula (I) as shown below.



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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

Substituted indoles with serotonin receptor affinity, process for their preparation and pharmaceutical compositions containing them

Field of Invention:

The present invention relates to the compounds described by general formula (I), including the stereoisomers, radioisotopes, N-oxides, polymorphs, pharmaceutically acceptable salts, pharmaceutically acceptable solvates, bio-active metabolites or any suitable combination of the above chemical forms of compounds defined by general formula (I).

The present invention also includes the process for preparing such compounds of general formula (I). These processes also include some additional steps that may be required to obtain the stereoisomers, the radioisotopes, the N-oxides, the polymorphs, the pharmaceutically acceptable salts, the pharmaceutically acceptable solvates, bio-active metabolites and also includes any suitable combination of the above.

There are variety of methods to administer the compounds of general formula (I), and such suitable pharmaceutically acceptable dosage forms and the use of such compounds and compositions in either therapy or diagnosis also form the part of this invention.

Background of the Invention

The compounds of this invention are useful in modulating the function of G-protein-coupled receptors (GPCRs). Majority of drugs exerts their action by interacting with GPCRs, which results into pharmacologically beneficial effect. The mode and general functioning of GPCRs is well understood and can be found in the literature. (References : Bohm S. K., and et. al., Biochem. J. (1997), 322, 1 – 18; McConlogue, Karen, and Nigel W. Bunnett., G-Protein-Coupled Receptors in Gastrointestinal Physiology. II. Regulation of neuropeptide receptors in enteric neurons. Am. J. Physiol. 274 (Gastrointest. Liver Physiol. 37): G792–G796, 1998.)

The compounds of general formulae (I), are useful in treating neuropsychiatric diseases which involve receptors, modulated by ligands such as 5-HT (Serotonin), melatonin and dopamine, in order to obtain the desired therapeutic effect.

International Patent Publications WO 04/000205, WO 04/000845, WO 04/000849, (Suven Lifesciences Limited) describes a few of related prior art. These PCT applications and the references reported therein are all incorporated herein.

The compounds of general formula (I) are useful in treating the psychotic, affective, vegetative and psychomotor symptoms of schizophrenia and the extrapyramidal motor side effects of other antipsychotic drugs; neurodegenerative disorders like Alzheimer's disease, Parkinson's and Huntington's chorea and

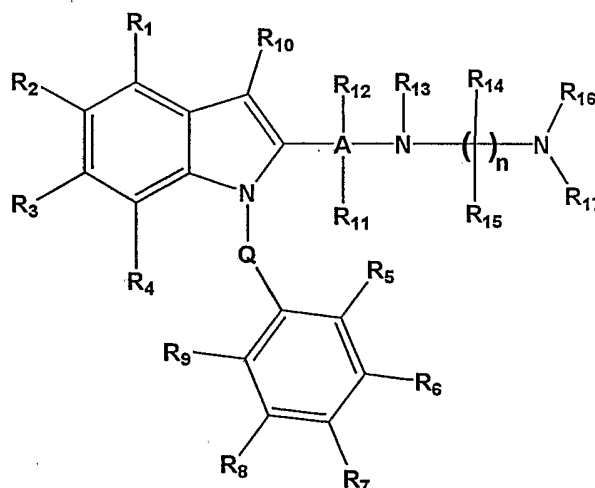
chemotherapy-induced vomiting; and in modulation of eating behavior and thus are useful in reducing the morbidity and mortality associated with excess weight.

International Patent Publication WO 03/066056 A1 reports that antagonism of 5-HT₆ receptor could promote neuronal growth within the central nervous system of a mammal.

Summary of the Invention:

The present invention relates to the compounds of general formula (I), their stereoisomers, their radioisotopes, their N-oxides, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates, their useful bio-active metabolites and also includes any suitable combination of the above.

The compounds of general formula (I) are defined as follows,



General Formula (I)

wherein A may be either a -CR₁₁R₁₂-, -C=O-, -SO₂-, -(CO)NH- or -C=S group.

Q may be either a -CR₁₁R₁₂-, -C=O-, -SO₂-, -(CO)NH- or -C=S group,

R₁, R₂, R₃, R₄, R₅, R₆, R₇, R₈, R₉, R₁₀, R₁₁, R₁₂, R₁₄ and R₁₅ may be same or different and each independently represent hydrogen, halogen, oxo, thio, perhaloalkyl, hydroxy, amino, nitro, cyano, formyl, amidino, guanidino, substituted or unsubstituted groups selected from linear or branched (C₁-C₁₂)alkyl, (C₂-C₁₂)alkenyl, (C₂-C₁₂)alkynyl, (C₃-C₇)cycloalkyl, (C₃-C₇)cycloalkenyl, bicycloalkyl, bicycloalkenyl, (C₁-C₁₂)alkoxy, cyclo(C₃-C₇)alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heterocyclalkyl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, heterocyclalkyloxy, acyl, acyloxy, acylamino, monoalkylamino, dialkylamino, arylamino, diarylamino, aralkylamino, alkoxycarbonyl, aryloxy carbonyl, aralkoxycarbonyl, heterocyclalkoxycarbonyl, heteroaryloxy carbonyl, hydroxyalkyl, aminoalkyl, monoalkylaminoalkyl, dialkylaminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl, alkoxycarbonylamino, aryloxy carbonylamino,

aralkyloxycarbonylamino, aminocarbonylamino, alkylaminocarbonylamino, dialkylaminocarbonylamino, alkylamidino, alkylguanidino, dialkylguanidino, hydrazino, hydroxylamino, carboxylic acid and its derivatives, sulfonic acids and its derivatives, phosphoric acid and its derivatives; or the adjacent groups like R₁ and R₂ or R₂ and R₃ or R₃ and R₄ or R₅ and R₆ or R₆ and R₇ or R₇ and R₈ or R₈ and R₉ together with carbon atoms to which they are attached may form a five or a six membered ring, optionally containing one or more double bonds and optionally containing one or more heteroatoms selected from "Oxygen", "Nitrogen", "Sulfur" or "Selenium" and combinations of double bond and heteroatoms; or R₁₁ and R₁₂ together with the carbon atoms to which they are attached may form a three to six membered ring, optionally containing one or more double bonds and optionally containing one or more heteroatoms selected from "Oxygen", "Nitrogen", "Sulfur" or "Selenium" and combinations of double bond and heteroatoms, R₁₃, R₁₆ and R₁₇ may be same or different and each independently represents hydrogen, substituted or unsubstituted groups selected from linear or branched (C₁-C₁₂)alkyl, (C₂-C₁₂)alkenyl, (C₂-C₁₂)alkynyl, (C₃-C₇)cycloalkyl, (C₃-C₇)cycloalkenyl, bicycloalkyl, bicycloalkenyl, aryl, aralkyl, heteroaryl excluding 2-pyridyl and 4-pyridyl, heterocyclalkyl; alternatively R₁₃ along with either R₁₆ or R₁₇ and the two nitrogen atoms may form a 5-, 6- or 7- membered heterocyclic ring, which may be further substituted with R₁₄ and R₁₅, and may have either one, two or three double bonds, "n" is an integer ranging from 1 to 4, wherein the carbon chains which "n" represents may be either linear or branched.

Partial list of such compounds of general formula (I) is as follows:

- 1-Benzenesulfonyl-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(4-Fluorobenzenesulfonyl)-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(4-Isopropylbenzenesulfonyl)-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(4-Methoxybenzenesulfonyl)-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(2-Bromo-4-methoxybenzenesulfonyl)-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(4-Methoxybenzenesulfonyl)-5-methoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(4-Methoxybenzenesulfonyl)-5-methoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole Hydrochloride salt;
- 1-(4-Isopropylbenzenesulfonyl)-5-methoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 3-Chloro-1-(4-isopropylbenzenesulfonyl)-5-methoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(4-Isopropylbenzenesulfonyl)-5-methoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole

- Hydrochloride salt;
 3-Chloro-1-(4-methoxybenzenesulfonyl)-5-methoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
 3-Chloro-1-(4-methoxybenzenesulfonyl)-5-methoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole Hydrochloride salt;
 1-(2-Bromobenzenesulfonyl)-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
 1-(2-Bromobenzenesulfonyl)-3-chloro-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
 N-(1-Benzenesulfonyl-1H-indol-2-yl)methyl-N,N',N'-trimethylethylene-1,2-diamine;
 N-(1-Benzenesulfonyl)-3-bromo-1H-indol-2-yl)methyl-N,N',N'-trimethylethylene-1,2-diamine;
 N-(1-(4-Methylbenzenesulfonyl)-1H-indol-2-yl)methyl-N,N',N'-trimethylethylene-1,2-diamine;
 1-(2-Bromo-4-methoxybenzenesulfonyl-1H-indol-2-yl)methyl-N,N',N'-trimethylethylene-1,2-diamine;
 1-(2-Bromo-4-methoxybenzenesulfonyl-3-chloro-1H-indol-2-yl)methyl-N,N',N'-trimethylethylene-1,2-diamine, hydrochloride;
 [1-Benzenesulfonyl-1H-indol-2-yl]-(4-methylpiperazin-1-yl)methanone;
 [1-(4-Fluorobenzenesulfonyl)-1H-indol-2-yl]-(4-methylpiperazin-1-yl)methanone;
 [1-(4-Isopropylbenzenesulfonyl)-1H-indol-2-yl]-(4-methylpiperazin-1-yl)methanone;
 [1-(4-Methoxybenzenesulfonyl)-1H-indol-2-yl]-(4-methylpiperazin-1-yl)methanone;
 [1-(2-Bromo-4-methoxybenzenesulfonyl)-1H-indol-2-yl]-(4-methylpiperazin-1-yl)methanone;
 [1-(4-Methoxybenzenesulfonyl)-5-methoxy-1H-indol-2-yl]-(4-methylpiperazin-1-yl)methanone;
 [1-(4-Isopropylbenzenesulfonyl)-5-methoxy-1H-indol-2-yl]-(4-methylpiperazin-1-yl)methanone;
 [3-Chloro-1-(4-isopropylbenzenesulfonyl)-5-methoxy-1H-indol-2-yl]-(4-methylpiperazin-1-yl)methanone;
 [3-Chloro-1-(4-Methoxybenzenesulfonyl)-5-methoxy-1H-indol-2-yl]-(4-methylpiperazin-1-yl)methanone;
 [1-(2-Bromobenzenesulfonyl)-1H-indol-2-yl]-(4-methylpiperazin-1-yl)methanone;
 [1-(2-Bromobenzenesulfonyl)-3-chloro-1H-indol-2-yl]-(4-methylpiperazin-1-yl)methanone;
 1-Benzenesulfonyl-1H-indole-2-carboxylic acid (2-dimethylaminoethyl)-N-methylamide;
 1-Benzenesulfonyl-3-bromo-1H-indole-2-carboxylic acid (2-dimethylaminoethyl)-N-methylamide;

- N-(1-(4-Methylbenzenesulfonyl)-3-bromo-1H-indole-2-carboxylic acid (2-dimethylaminoethyl)-N-methylamide;
 1-(2-Bromo-4-methoxybenzenesulfonyl-1H-indole-2-carboxylic acid (2-dimethylaminoethyl)-N-methylamide;
 5 1-(2-Bromo-4-methoxybenzenesulfonyl-3-bromo-1H-indole-2-carboxylic acid (2-dimethylaminoethyl)-N-methylamide;
 (1-Benzenesulfonyl-5-methoxy-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;
 (1-(4'-Fluoro - benzenesulfonyl-5-methyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;
 10 (1-(4'-trifluoromethyl)benzenesulfonyl-5-methoxy-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;
 (1-(3'-trifluoromethyl)benzenesulfonyl-5-methyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;
 (1-(Benzenesulfonyl-5-ethoxy-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;
 15 (1-(4'-Isopropylbenzenesulfonyl-5-ethoxy-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;
 (1-Benzenesulfonyl-5-thiomethyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;
 (1-(4'-Fluorobenzenesulfonyl-5-thiomethyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;
 20 (1-(4'-Isopropylbenzenesulfonyl-5-thiomethyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;
 (1-(3'-trifluoromethyl)benzenesulfonyl-5-thiomethyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;
 25 5-methoxy -1-(Benzenesulfonyl) -2- (4-Methylpiperazine-1-yl)-methyl)-1H-indole;
 5-methoxy -1-(4'-Bromobenzenesulfonyl) -2- (4-Methylpiperazine-1-yl)-methyl)-1H-indole;
 5-methoxy -1-(3'-Trifluoro methylbenzenesulfonyl)-2-(4-methylpiperazine-1-yl)-methyl)-1H-indole;
 30 (1-(4'-Bromo-benzenesulfonyl-5-methyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;
 (1-(4'-Bromobenzenesulfonyl-5-methoxyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;
 (1-(4'-Fluoro-benzenesulfonyl-5-methoxyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;
 35 methanone;
 3-Chloro-5-methoxy-1-(2'-bromobenzenesulfonyl)-2-yl-(4-methylpiperazine-1-yl methyl)-1H-indole;

- (1-(4'-Methoxy)benzenesulfonyl-5-methyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;
(1-(3'-Trifluoromethyl)benzenesulfonyl-5-isopropyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;
- 5 (1-(4'-Isopropyl)benzenesulfonyl-5-isopropyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;
(1-Benzenesulfonyl-5-isopropyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;
(1-(4'-Fluoro)benzenesulfonyl-5-isopropyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;
- 10 (1-Benzenesulfonyl-6,7-dimethyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;
1-Benzenesulfonyl-5-ethyl-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
1-(4-Fluorobenzenesulfonyl)-5-ethyl-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
1-(4-Isopropylbenzenesulfonyl)-5-ethyl-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 15 1-(4-Methoxybenzenesulfonyl)-5-ethyl-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
1-(2-Bromo-4-methoxybenzenesulfonyl)-5-ethyl-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
1-Benzenesulfonyl-5-isopropoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
1-(4-Fluorobenzenesulfonyl)-5-isopropoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-
- 20 indole;
1-(4-Isopropylbenzenesulfonyl)-5-isopropoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
1-(4-Methoxybenzenesulfonyl)-5-isopropoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 25 1-(2-Bromo-4-methoxybenzenesulfonyl)-5-isopropoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
1-Benzenesulfonyl-5-ethylthio-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
1-(4-Fluorobenzenesulfonyl)-5-ethylthio-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
1-(4-Isopropylbenzenesulfonyl)-5-ethylthio-2-(4-methylpiperazin-1-ylmethyl)-1H-
- 30 indole;
1-(4-Methoxybenzenesulfonyl)-5-ethylthio-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
1-(2-Bromo-4-methoxybenzenesulfonyl)-5-ethylthio-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 35 1-Benzenesulfonyl-5-benzyloxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
1-(4-Fluorobenzenesulfonyl)-5-benzyloxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;

- 1-(4-Isopropylbenzenesulfonyl)-5- benzyloxy -2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(4-Methoxybenzenesulfonyl)-5- benzyloxy -2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 5 1-(2-Bromo-4-methoxybenzenesulfonyl)-5- benzyloxy -2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-Benzenesulfonyl-5-cyclopentyloxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(4-Fluorobenzenesulfonyl)-5-cyclopentyloxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 10 1-(4-Isopropylbenzenesulfonyl)-5-cyclopentyloxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(4-Methoxybenzenesulfonyl)-5-cyclopentyloxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(2-Bromobenzenesulfonyl)-5- cyclopentyloxy -2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 15 1-Benzenesulfonyl-3-bromo-5-ethoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(4-Fluorobenzenesulfonyl)-3-bromo-5-ethoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(4-Isopropylbenzenesulfonyl)-3-bromo-5-ethoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 20 1-(4-Methoxybenzenesulfonyl)-3-bromo-5-ethoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(2-Bromobenzenesulfonyl)- 3-bromo-5-ethoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 25 1-Benzenesulfonyl-3-chloro-5-ethoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(4-Fluorobenzenesulfonyl)-3- chloro -5-ethoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(4-Isopropylbenzenesulfonyl)-3- chloro -5-ethoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 30 1-(4-Methoxybenzenesulfonyl)-3- chloro -5-ethoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(2-Bromobenzenesulfonyl)- 3- chloro -5-ethoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- (1-(4'-Bromo-benzenesulfonyl-5-ethyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;
- 35 (1-(2'-Bromo-benzenesulfonyl-5-ethyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;

(1-(4'-trifluoromethylbenzenesulfonyl-5-ethyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;

(1-(4'-trifluoromethylbenzenesulfonyl-5-ethoxyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone; and

- 5 (1-(4'-fluorobenzenesulfonyl-5-ethoxyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;

or a stereoisomer, or a polymorph, or any suitable combination of above such as a nitrogen oxide thereof; a prodrug of the compound or the nitrogen oxide; a pharmaceutically acceptable salt of the compound, the nitrogen oxide, or the
10 prodrug; or a solvate or hydrate of the compound, the nitrogen oxide, the prodrug or the pharmaceutically acceptable salt.

The present invention also relates to the numerous processes for preparing the compounds of general formula (I) their stereoisomers, their radioisotopes, their N-oxides, their polymorphs, their pharmaceutically acceptable salts, their
15 pharmaceutically acceptable solvates, their useful bio-active metabolites and also includes any suitable combination of the above.

In the case of the compounds of general formula (I) where tautomerism may exist, the present invention relates to all of the possible tautomeric forms and the possible mixture thereof.

20 The present invention also relates to the stereoisomers, which as a rule are obtained as racemates that can be separated into the optically active isomers in a manner known per se.

The present invention also relates to radio-labeled isotopes, which are identical to those defined in the general formula (I) but for the fact that one or more
25 atoms are replaced by an atom having an atomic mass or mass number different from the atomic mass or mass number found usually in nature. Examples of isotopes that can be incorporated into compounds of the invention include isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorus, fluorine, chlorine, iodine, bromine and mTecnitium, exemplified by ^2H , ^3H , ^{11}C , ^{13}C , ^{14}C , ^{13}N , ^{15}N , ^{15}O , ^{18}F , $^{99\text{m}}\text{Tc}$, ^{31}P , S,
30 ^{123}I and ^{125}I . Those compounds of general formula (I) as described earlier containing the aforementioned isotopes and/or other isotopes of other atoms are within the scope of this invention.

In the case of the compounds of general formula (I) containing geometric isomerism the present invention relates to all of these geometric isomers.

35 The term "nitrogen oxide" or "N-oxide" refers to the oxidation of at least one of the two nitrogens in the compounds of general formula (I), (e.g., mono- or di-oxide).

The nitrogen mono-oxides may exist as a single positional isomer, a mixture of 2 positional isomers or oxide of aromatic nitrogen.

Suitable pharmaceutically acceptable acid addition salts of compounds of the general formula (I) can be prepared of the aforementioned base compounds of this invention are those which form non-toxic acid addition salts, includes, salts containing pharmacologically acceptable anions, such as the hydrochloride, hydrobromide, hydroiodide, nitrate, sulfate, bisulfate, phosphate, acid phosphate, acetate, lactate, citrate, acid citrate, tartrate, bitartrate, succinate, maleate, fumarate, gluconate, saccharate, benzoate, methanesulfonate, ethanesulfonate, benzenesulfonate, p-toluenesulfonate, palmoate and oxalate. Pharmaceutically acceptable salts forming part of this invention are intended to define but not limited to the above list.

Suitable pharmaceutically acceptable base addition salts of compounds of the general formula (I) can be prepared of the aforementioned acid compounds of this invention are those which form non-toxic base addition salts, includes, salts containing pharmaceutically acceptable cations, such as Lithium, sodium, potassium, calcium and magnesium, salts of organic bases such as lysine, arginine, guanidine, diethanolamine, choline, tromethamine and the like; ammonium or substituted ammonium salts.

Pharmaceutically acceptable salts forming part of this invention are intended to define but not limited to the above list.

In addition, pharmaceutically acceptable salts of the compound of general formula (I) can be obtained by converting derivatives which have tertiary amino groups into the corresponding quarternary ammonium salts in the methods known in the literature by using quarternizing agents. Possible quarternizing agents are, for example, alkyl halides such as methyl iodide, ethyl bromide and n-propyl chloride, including arylalkyl halides such as benzyl chloride or 2-phenylethyl bromide.

In the addition to pharmaceutically acceptable salts, other salts are included in the invention. They may serve as intermediates in the purification of the compounds, in the preparation of other salts, or in the identification and characterization of the compounds or intermediates.

The pharmaceutically acceptable salts of compounds of formula (I) may exist as solvates, such as with water, methanol, ethanol, dimethylformamide, ethyl acetate, and the like. Mixtures of such solvates can also be prepared. The source of such solvate can be from the solvent of crystallization, inherent in the solvent preparation or crystallization, or adventitious to such solvent. Such solvates are

within the scope of this invention.

The invention also encompasses the pharmaceutically acceptable prodrugs of the compounds of general formula (I). A prodrug is a drug which has been chemically modified and may be biologically in-active at the site of action, but which may be degraded or modified by one or more enzymatic or other in-vivo processes to the parent form. This prodrug should have a different pharmacokinetic profile than the parent, enabling easier absorption across the mucosal epithelium, better salt formation, or solubility, and/or improved systemic stability (an increase in the plasma half-life, for example). Typically, such chemical modifications include any-one of the following:

1. ester or amide derivatives which may be cleaved by esterases or lipases;
2. peptides which may be recognized by specific or non-specific proteases;
3. N-glycosyl or O-glycosyl derivatives;
4. derivatives that accumulate at a site of action through membrane selection of a prodrug form or a modified prodrug form; or
5. any combination of 1 to 4, above.

Conventional procedures for the selection and preparation of suitable prodrug derivatives are described, for example, in H. Bundgard, Design of prodrugs, (1985).

Another aspect of the present invention comprises of a pharmaceutical composition, containing at least one of the compounds of general formula (I), their derivatives, their analogs, their derivatives, their stereoisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates thereof as an active ingredient, together with pharmaceutically employed carriers, auxiliaries and the like.

An effective amount of a compound of general formula (I), or their salt can be used to produce a medicament, along with conventional pharmaceutical auxiliaries, carriers and additives.

The present invention also relates to the pharmaceutically acceptable compositions containing them, and the use of these compounds and compositions in medicine.

The present invention provides the compounds of general formula (I), to prepare the medicaments useful in the treatment and/ or prophylaxis of certain disorders such as psychosis, paraphrenia, anxiety, depression, mania, schizophrenia, schizophreniform disorders, migraine headache, drug addiction, convulsive disorders, personality disorders, hypertension, autism, post-traumatic stress syndrome, alcoholism, panic attacks, obsessive-compulsive disorders, chronobiological abnormalities and circadian rhythms, cognitive memory disorders

e.g. Alzheimer's disease and age-related cognitive decline, ADHD (Attention Deficient Disorder/ Hyperactivity Syndrome), amyotrophic lateral sclerosis, withdrawal from drug abuse such as cocaine, ethanol, nicotine and benzodiazepines, panic attacks, and also disorders associated with spinal trauma and / or head injury
5 such as hydrocephalus. Other conditions where there are low endogenous melatonin levels benefits may be obtained in cases of osteoporosis, ischemic stroke, SIDS in young infants, reproduction, glaucoma and sleep disorders.

Compounds of this invention are expected to be of use in the treatment of mild cognitive impairment and other neurodegenerative disorders like Alzheimer's
10 disease, Parkinsonism and Huntington's chorea.

The compounds of this invention could be of use in the treatment of certain GI (Gastrointestinal) disorders such as IBS (Irritable bowel syndrome) or chemotherapy induced emesis.

Also these compounds can help in modulation of eating behavior and thereby
15 reduce morbidity and mortality associated with the excess weight.

The present invention provides a method for the treatment of a human or a animal subject suffering from disorders such as, anxiety, depression, convulsive disorders, obsessive-compulsive disorders, migraine headache, cognitive memory disorders e.g. Alzheimer's disease and age-related cognitive decline, ADHD
20 (Attention Deficient Hyperactivity Disorder), personality disorders, psychosis, paraphrenia, psychotic depression, mania, schizophrenia, schizophreniform disorders, withdrawal from drug abuse such as cocaine, ethanol, nicotine and benzodiazepines, panic attacks, chronobiological abnormalities, circadian rhythms, anxiolytic, osteoporosis, ischemic stroke, lower the risk of SIDS in young infants with
25 low endogenous melatonin levels, reproduction, glaucoma, sleep disorders (including disturbances of Circadian rhythm) and also disorders associated with spinal trauma and /or head injury such as hydrocephalus. Compounds of the invention are further expected to be of use in the treatment of mild cognitive impairment and other neurodegenerative disorders like Alzheimer's disease, Parkinsonism and
30 Huntington's chorea.

Compounds of the present invention may be administered in combination with other pharmaceutical agents, such as apo-B/MTP inhibitors, MCR-4 agonists, CCK-A agonists, monoamine reuptake inhibitors, sympathomimetic agents, adrenergic receptor agonists, dopamine agonists, melanocyte-stimulating hormone receptor
35 analogs, cannabinoid 1 receptor antagonists, melanin concentrating hormone antagonists, leptins, leptin analogs, leptin receptor agonists, galanin antagonists, lipase inhibitors, bombesin agonists, neuropeptide-Y antagonists, thyromimetic

agents, dehydroepiandrosterone or analogs thereof, glucocorticoid receptor agonists or antagonists, orexin receptor antagonists, urocortin binding protein antagonists, glucagon-like peptide-1 receptor agonists, ciliary neurotrophic factors, AGRPs (human agouti-related proteins), ghrelin receptor antagonists, histamine 3 receptor antagonists or reverse agonists, neuromedin U receptor agonists, and the like, in a therapeutically effective amount via a suitable pharmaceutical composition, to achieve the desired effect in mammals as well as humans.

The phrase "pharmaceutically acceptable" indicates that the substance or composition must be compatible chemically and/or toxicologically, with the other ingredients comprising a formulation, and/or the mammal being treated therewith.

The terms "treating", "treat", or "treatment" embrace all the meanings such as preventative, prophylactic and palliative.

The term "compounds of the present invention" (unless specifically identified otherwise) refer to compounds of Formulae (I), nitrogen oxides thereof, prodrugs of the compounds or nitrogen oxides, pharmaceutically acceptable salts of the compounds, nitrogen oxides, and/or prodrugs, and hydrates or solvates of the compounds, nitrogen oxides, salts, is and/or prodrugs, as well as, all stereoisomers (including diastereoisomers and enantiomers), tautomers and isotopically labeled compounds.

Detailed description of the invention:

The present invention relates to compounds of general formula (I), are described in the summary above.

Suitable groups represented by R₁, R₂, R₃, R₄, R₅, R₆, R₇, R₈, R₉, R₁₀, R₁₁, R₁₂, R₁₃, R₁₄, R₁₅, R₁₆ and R₁₇, wherever applicable, may be selected be from the following group: halogen atom such as fluorine, chlorine, bromine or iodine; perhaloalkyl particularly perhalo (C₁-C₆)alkyl such as fluoromethyl, difluoromethyl, trifluoromethyl, trifluoroethyl, fluoroethyl, difluoroethyl and the like; perhaloalkoxy particularly perhalo(C₁-C₆)alkoxy such as fluoromethoxy, difluoromethoxy, trifluoromethoxy and the like; substituted or unsubstituted (C₁-C₁₂)alkyl group, especially, linear or branched (C₁-C₈)alkyl group, such as methyl, ethyl, n-propyl, isopropyl, n-butyl, iso-butyl, t-butyl, n-pentyl, iso-pentyl, hexyl, iso-hexyl, heptyl, octyl and the like; substituted or unsubstituted (C₂-C₁₂)alkenyl group such as ethylene, n-propylene pentenyl, hexenyl, heptynyl, heptadienyl and the like; (C₂-C₁₂)alkynyl substituted or unsubstituted (C₂-C₁₂)alkynyl group such as acetylene and the like; cyclo(C₃-C₇)alkyl group such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, the cycloalkyl group may be substituted; cyclo(C₃-C₇)alkenyl group such as cyclopentenyl, cyclohexenyl, cycloheptynyl, cycloheptadienyl, cycloheptatrienyl

and the like, the cycloalkenyl group may be substituted; (C₁-C₁₂)alkoxy, especially, (C₁-C₆)alkoxy group such as methoxy, ethoxy, propyloxy, butyloxy, iso-propyloxy and the like, which may be substituted; cyclo(C₃-C₇) alkoxy group such as cyclopropyloxy, cyclobutyloxy, cyclopentyloxy, cyclohexyloxy, cycloheptyloxy and the like, the

5 cycloalkoxy group may be substituted; aryl group such as phenyl or naphthyl, the aryl group may be substituted; aralkyl group such as benzyl, phenethyl, C₆H₅CH₂CH₂CH₂, naphthylmethyl and the like, the aralkyl group may be substituted and the substituted aralkyl is a group such as CH₃C₆H₄CH₂, Hal-C₆H₄CH₂, CH₃OC₆H₄CH₂, CH₃OC₆H₄CH₂CH₂ and the like; aralkoxy group such as benzyloxy, phenethyloxy,

10 naphthylmethyloxy, phenylpropyloxy and the like, the aralkoxy group may be substituted; heterocyclyl groups such as aziridinyl, pyrrolidinyl, morpholinyl, piperidinyl, piperazinyl and the like, the heterocyclyl group may be substituted; heteroaryl group such as pyridyl with the exception of 2-pyridyl and 4-pyridyl, thienyl, furyl, pyrrolyl, oxazolyl, imidazolyl, oxadiazolyl, tetrazolyl, benzopyranyl, benzofuranyl

15 and the like, the heteroaryl group may be substituted; heterocyclo(C₁-C₆)alkyl, such as pyrrolidinylalkyl, piperidinylalkyl, morpholinylalkyl, thiomorpholinylalkyl, oxazolylalkyl and the like, the heterocyclo(C₁-C₆)alkyl group may be substituted; heteroaralkyl group such as furanymethyl, pyridinymethyl, oxazolymethyl, oxazolyethyl and the like, the heteroaralkyl group may be substituted; heteroaryloxy,

20 heteroaralkoxy, heterocycloalkoxy, wherein heteroaryl, heteroaralkyl, heterocycloalkyl and heterocyclylalkyl moieties are as defined earlier and may be substituted, such as furan-2-ylmethoxy-; acyl groups such as acetyl, propionyl or benzoyl, the acyl group may be substituted; acyloxy group such as CH₃COO, CH₃CH₂COO, C₆H₅COO and the like which may optionally be substituted, acylamino

25 group such as CH₃CONH, CH₃CH₂CONH, C₃H₇CONH, C₆H₅CONH which may be substituted, (C₁-C₆)monoalkylamino group such as CH₃NH, C₂H₅NH, C₃H₇NH, C₆H₁₃NH and the like, which may be substituted, (C₁-C₆)dialkylamino group such as N(CH₃)₂, CH₃(C₂H₅)N and the like, which may be substituted; arylamino group such as C₆H₅NH, CH₃(C₆H₅)N, C₆H₄(CH₃)NH, NH-C₆H₄-Hal and the like, which may be

30 substituted; arylalkylamino group such as C₆H₅CH₂NH, C₆H₅CH₂CH₂NH, C₆H₅CH₂NCH₃ and the like, which may be substituted; hydroxy(C₁-C₆)alkyl which may be substituted, amino(C₁-C₆)alkyl which may be substituted; mono(C₁-C₆)alkylamino(C₁-C₆)alkyl, di(C₁-C₆)alkylamino(C₁-C₆)alkyl group which may be substituted, alkoxyalkyl group such as methoxymethyl, ethoxymethyl, methoxyethyl,

35 ethoxyethyl and the like, which may be substituted; aryloxyalkyl group such as C₆H₅OCH₂, C₆H₅OCH₂CH₂, naphthyloxymethyl and the like, which may be substituted; aralkoxyalkyl group such as C₆H₅CH₂OCH₂, C₆H₅CH₂OCH₂CH₂ and the

like, which may be substituted; (C₁-C₆)alkylthio, thio(C₁-C₆)alkyl which may be substituted, alkoxycarbonylamino group such as C₂H₅OCONH, CH₃OCONH and the like which may be substituted; aryloxy carbonylamino group as C₆H₅OCONH, C₆H₅OCONCH₃, C₆H₅OCONC₂H₅, C₆H₄CH₃OCONH, C₆H₄(OCH₃)OCONH and the like which may be substituted; aralkoxycarbonylamino group such as C₆H₅CH₂OCONH, C₆H₅CH₂CH₂OCONH, C₆H₅CH₂OCON(CH₃), C₆H₅CH₂OCON(C₂H₅), C₆H₄CH₃CH₂OCONH, C₆H₄OCH₃CH₂OCONH and the like, which may be substituted; aminocarbonylamino group; (C₁-C₆)alkylaminocarbonylamino group, di(C₁-C₆)alkylaminocarbonylamino group; (C₁-C₆)alkylamidino group, (C₁-C₆)alkylguanidino, di(C₁-C₆)alkylguanidino groups, hydrazino and hydroxylamino groups; carboxylic acid or its derivatives such as amides, like CONH₂, alkylaminocarbonyl like CH₃NHCO, (CH₃)₂NCO, C₂H₅NHCO, (C₂H₅)₂NCO, arylaminocarbonyl like PhNHCO, NaphthylNHCO and the like, aralkylaminocarbonyl such as PhCH₂NHCO, PhCH₂CH₂NHCO and the like, heteroarylaminocarbonyl and heteroaralkylamino carbonyl groups where the heteroaryl groups are as defined earlier, heterocyclaminocarbonyl where the heterocycl group is as defined earlier, carboxylic acid derivatives such as esters, wherein the ester moieties are alkoxycarbonyl groups such as unsubstituted or substituted phenoxy carbonyl, naphthyl oxy carbonyl and the like; aralkoxycarbonyl group such as benzyloxy carbonyl, phenethyloxy carbonyl, naphthylmethoxy carbonyl and the like, heteroaryloxy carbonyl, heteroaralkoxy carbonyl, wherein the heteroaryl group is as defined earlier, heterocycloxy carbonyl where heterocycle is as defined earlier and these carboxylic acid derivatives may be substituted; sulfonic acid or its derivatives such as SO₂NH₂, SO₂NHCH₃, SO₂N(CH₃)₂, SO₂NHCF₃, SO₂NHCO(C₁-C₆)alkyl, SO₂NHCOaryl where the aryl group is as defined earlier and the sulfonic acid derivatives may be substituted; phosphoric acid and its derivatives as P(O)(OH)₂, P(O)(OC₁-C₆-alkyl)₂, P(O)(O-aryl)₂ and the like.

Suitable cyclic structures formed by the two adjacent groups, such as R₁ and R₂ or R₂ and R₃ or R₄ and R₅ or R₅ and R₆ or R₆ and R₇ or R₇ and R₈ or R₈ and R₉; optionally R₁₃ along with either R₁₆ or R₁₇ and the two nitrogen atoms may form a 5-, 6- or 7- membered heterocyclic ring, which may be further substituted with R₁₄ and R₁₅, and may have either one, two or three double bonds; optionally R₁₂ and R₁₆ or R₁₄ and R₁₆ together with carbon atoms to which they are attached may contain either 4, 5 or 6 ring atoms, which optionally contains one or more heteroatoms, selected from the group containing oxygen, nitrogen or sulfur, and/or one or more double bonds and other possible combinations such as both double bond and hetero atoms. An example, of suitable structures thus formed at the 2-position of indole

nucleus includes, an optionally substituted piperazinyl, imidazolyl, pyrimidinyl, pyrazinyl, N,N,N',N'-tetraalkyldiaminoalkane, N,N,N',N'-tetraalkyldiaminoalkene, N-aryl,N,N',N'-trialkyldiaminoalkane, N-arylcarbonyl,N,N',N'-trialkyldiaminoalkane, N-arylthiocarbonyl,N,N',N'-trialkyldiaminoalkane and the like. Suitable substituents on these include hydroxy, halogen atom such as chlorine, bromine and iodine; nitro, cyano, amino, formyl, (C₁-C₃)alkyl, (C₁-C₃)alkoxy, thioalkyl, alkylthio, phenyl or benzyl groups.

Compounds of the present invention may be synthesized by synthetic routes that include processes analogous to those known in the chemical arts, particularly in light of the description contained herein. The starting materials are generally available from commercial sources such as Aldrich Chemicals (Milwaukee, WI) or are readily prepared using methods well known to those skilled in the art (e.g., prepared by methods generally described in Louis F. Fieser and Mary Fieser, Reagents for Organic Synthesis, v. 1-19, Wiley, New York (1967-1999 ed.), or Beilsteins Handbuch der organischen Chemie, 4, Aufl. ed. Springer-Verlag, Berlin, including supplements (also available via the Beilstein online database)).

For illustrative purposes, the reaction schemes depicted below provide potential routes for synthesizing the compounds of the present invention as well as key intermediates. For a more detailed description of the individual reaction steps, see the Examples section. Those skilled in the art will appreciate that other synthetic routes may be used to synthesize the inventive compounds. Although specific starting materials and reagents are depicted in the schemes and discussed below, other starting materials and reagents can be easily substituted to provide a variety of derivatives and/or reaction conditions. In addition, many of the compounds prepared by the methods described below can be further modified in light of this disclosure using conventional chemistry well known to those skilled in the art.

In certain circumstances there may also be a need to protect hydroxy groups and amino groups during the synthetic processes of the present invention. Those skilled in the art are familiar with such "hydroxy protecting groups" and such "amino protecting groups." For a general description of protecting groups and their use, see T. W. Greene, Protective Groups in Organic Synthesis, John Wiley & Sons, New York, 1991. One skilled in the art readily determines the need for such protection. The selection of protecting group employed is not critical so long as the derivatized group is stable to the condition of subsequent reaction(s) and can be removed at the appropriate point without disrupting the remainder of the molecule.

Suitable amino-protecting groups (NH-Pg) include acetyl, trifluoroacetyl, t-butoxycarbonyl (BOC), benzyloxycarbonyl (CBz) and Fluorenylmethylenecarbonyl

(Fmoc). Preferred indole -NH protecting groups are trimethylsilylethoxymethyl, benzyl, tosyl, carbamate, amide, alkyl or aryl sulfonamide, while maleimide protecting groups include alkoxy, benzyl, dialkoxybenzyl, benzyloxyalkyl or allyl. Preferred hydroxy protecting groups are ether or ester derivatives of the hydroxy group such as
 5 tert-butyldiphenylsilyloxy (TBDPS), tert-butyldimethylsilyloxy (TBDMS), triphenylmethyl (trityl), mono- or di- methoxytrityl, or an alkyl or aryl ester.

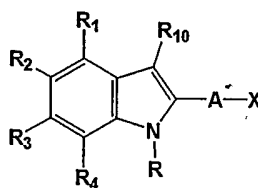
The present invention also provides processes for preparing compounds of general formula (I), as defined above their stereoisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates and
 10 novel intermediates involved therein, which are as described below.

In the following description and reaction schemes R_1 , R_2 , R_3 , R_4 , R_5 , R_6 , R_7 , R_8 , R_9 , R_{10} , R_{11} , R_{12} , R_{13} , R_{14} , R_{15} , R_{16} , R_{17} , Q, A and n are as defined previously for the compounds of general formula (I) and R is as defined elsewhere in the specification.

15 Compounds of general formula (I) can be prepared by any of the methods described below. Reference includes PCT application WO 99/09025, which has incorporated herein by reference.

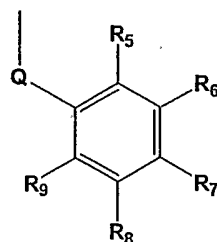
The present invention also provides processes for preparing compounds of general formula (I) as defined above, their derivatives, their analogs, their tautomeric
 20 forms, their stereoisomers, their geometric forms, their N-oxides, their polymorphs, their isotopically-labeled derivatives, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates and novel intermediates involved therein, which are as described below:

Scheme - 1 : Compounds of general formula (I), may be prepared by
 25 reacting a compound of formula (II) given below,

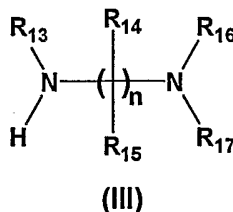


(II)

where R_1 , R_2 , R_3 , R_4 , R_{10} and A are as defined in relation to formula (I), X is halogeno, for example, a chloro, bromo or iodo; R represents either of a suitable N-
 30 protecting group such as acetyl, trifluoroacetyl, trityl, t-butyloxycarbonyl (t-BOC) or a group such as,



where R_5 , R_6 , R_7 , R_8 and R_9 are as defined earlier; with a compound of formula (III) or its acid addition salt,



where R_{13} , R_{14} , R_{15} , R_{16} and R_{17} are as defined in relation to compound of formula (I) or precursor thereof; and thereafter if necessary:

i) converting a compound of the formula (I) into another compound of the formula (I); and/or

10 ii) removing any protecting groups; and/or

iii) forming a pharmaceutically acceptable salt or prodrug thereof.

15 Preferably the substituents selected for the compounds of formulae (II) and (III) are either inert to the reaction conditions or the sensitive groups are protected using suitable protecting groups. Whenever R is a suitable protecting group, an additional step as described in Scheme 2 is required to prepare compounds of formula (I).

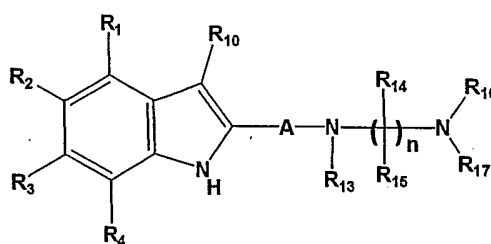
The above reaction is preferably carried out in a solvent such as THF, acetone, DMF, xylene, toluene, methanol, ethanol, propanol and the like and preferably using either acetone or DMF. The inert atmosphere may be maintained by using inert gases such as N_2 , Ar or He. The reaction mixture is generally heated to an elevated temperature or reflux temperature of the solvent, until the reaction is complete. A wide variety of acid-acceptor agents can be used in this condensation. However, preferred basic agents are sodium carbonate, sodium bicarbonate, potassium carbonate, sodium acetate, sodium alkoxides and the like, with a preferred basic agent being K_2CO_3 . Reaction times of about 30 minutes to 72 hours are common. At the end of reaction, the volatile components are removed under reduced pressure. The reaction mixture can be optionally acidified before work-up. The product can be isolated by precipitation, washed, dried and further purified by standard methods such as recrystallization, column chromatography etc.

30 Optional steps (i), (ii) and (iii) can be carried out using conventional methods.

These will depend upon the precise nature of the substituents on the indole in each case. Examples of suitable reactions are illustrated hereinafter.

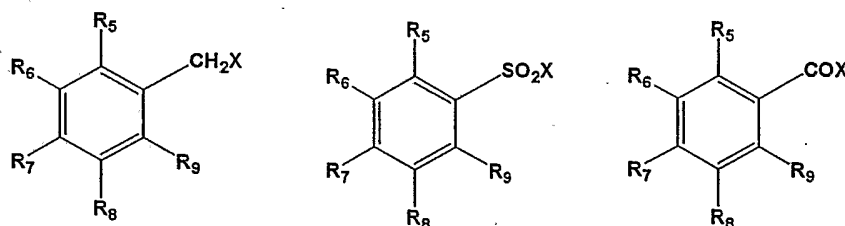
Compounds represented by the general formula (II) are prepared by the method described elsewhere in the specification. Compounds of formula (III) are commercially available, or they may be prepared by conventional methods or by modification, using known processes, of commercially available compounds of formula (III).

Scheme - 2 : Alternatively, compounds of formula (I) may be prepared by reacting a compound of formula (IV) given below,



(IV)

wherein A, R₁, R₂, R₃, R₄, R₁₀, R₁₃, R₁₄, R₁₅, R₁₆ and R₁₇ are as defined in relation to formula (I); with any one of the following compound represented by general formula (V),



(V)

where R₅, R₆, R₇, R₈ and R₉, are as defined in relation to formula (I) and X is a halogeno, preferably chloro or bromo; and thereafter if desired or necessary carrying out steps (i), (ii) and/or (iii) as described above.

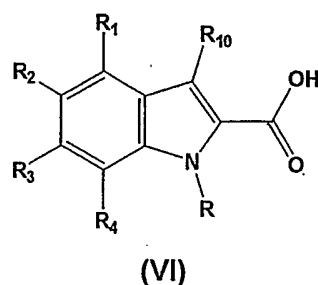
Preferably the substituents selected for the compounds of formula (IV) and (V) are either not affected by the reaction conditions or else the sensitive groups are protected using suitable groups.

Compounds of formula (IV) and (V) are suitably reacted together in an inert organic solvent which includes, aromatic hydrocarbons such as toluene, o-, m-, p-xylene; halogenated hydrocarbons such as methylene chloride, chloroform, and chlorobenzene; ethers such as diethylether, diisopropyl ether, tert-butyl methyl ether, dioxane, anisole, and tetrahydrofuran; nitriles such as acetonitrile and propionitrile; ketones such as acetone, methyl ethyl ketone, diethyl ketone and tert-butyl methyl ketone; alcohols such as methanol, ethanol, n-propanol, n-butanol, tert-butanol and

also DMF (N,N-dimethylformamide), DMSO (dimethyl sulfoxide) and water. The preferred list of solvents includes DMSO, DMF, acetonitrile and THF. Mixtures of these in varying ratios can also be used. Suitable bases are, generally, inorganic compounds such as alkali metal hydroxides and alkaline earth metal hydroxides, such as lithium hydroxide, sodium hydroxide, potassium hydroxide and calcium hydroxide; alkali metal oxides and alkaline earth metal oxides, lithium oxide, sodium oxide, magnesium oxide and calcium oxide; alkali metal hydrides and alkaline earth metal hydrides such as lithium hydride, sodium hydride, potassium hydride and calcium hydride; alkali metal amides and alkaline earth metal amides such as lithium amide, sodium amide, potassium amide and calcium amide; alkali metal carbonates and alkaline earth metal carbonates such as lithium carbonate and calcium carbonate; and also alkali metal hydrogen carbonates and alkaline earth metal hydrogen carbonates such as sodium hydrogen carbonate; organometallic compounds, particularly alkali-metal alkyls such as methyl lithium, butyl lithium, phenyl lithium; alkyl magnesium halides such as methyl magnesium chloride and alkali metal alkoxides and alkaline earth metal alkoxides such as sodium methoxide, sodium ethoxide, potassium ethoxide, potassium tert-butoxide and dimethoxymagnesium, further more organic bases e.g. triethylamine, triisopropylamine, and N-methylpiperidine, pyridine. Sodium hydroxide, Sodium methoxide, Sodium ethoxide, potassium hydroxide potassium carbonate and triethylamine are especially preferred. Suitably the reaction may be effected in the presence of phase transfer catalyst such as tetra-n-butylammonium hydrogen sulphate and the like. The inert atmosphere may be maintained by using inert gases such as N₂, Ar or He. Reaction times may vary from 1 to 24 hrs, preferably from 2 to 6 hours, whereafter, if desired, the resulting compound is continued into a salt thereof.

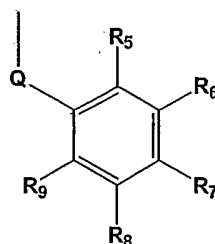
Compounds of formula (V) are commercially available, or they may be prepared by conventional methods or by modification, using known processes, of commercially available compounds of formula (V).

Scheme - 3 : Compounds of general formula (I) may be prepared by reacting a compound of formula (VI) given below,

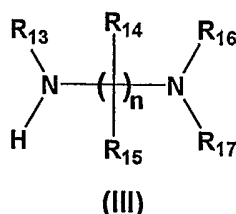


where R₁, R₂, R₃, R₄, and R₁₀ are as defined in relation to formula (I), R represents

either of a suitable N-protecting group such as acetyl, trifluoroacetyl, or a group such as,



where R_5 , R_6 , R_7 , R_8 and R_9 are as defined earlier; with a compound of formula (III) or its acid addition salt,



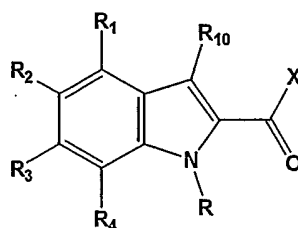
where R_{13} , R_{14} , R_{15} , R_{16} and R_{17} are as defined in relation to compound of formula (I) or precursor thereof; by standard peptide coupling for example using bis(2-oxo-3-oxazolidinyl) phosphoric chloride (BOP-Cl) and thereafter if desired or necessary carrying out steps (i), (ii) and/or (iii) as described above.

Scheme - 4 : In this method N,N'-thionyl-diimidazole is first prepared by reacting imidazole with thionyl chloride. The former is then reacted with the compound of formula (VI) N-(substituted indolyl)alkanoic acid and the resulting N-(substituted indolyl-alkanoyl)imidazole is reacted with N-substituted amine compound of formula (III). If desired the N,N'-thionyl-diimidazole and N-(substituted indolylalkanoyl)imidazole intermediates can be isolated prior to the next reaction in the succeeding step, but it is advantageous to carry out the entire sequence of steps upto formation of N-(substituted indolyl-alkanoyl)-4-substituted-amine in essentially one operation, that is by reacting each intermediate without isolation with the next succeeding reactant using the same solvent medium for the entire sequence of reactions. Suitable solvents are organic solvents inert under the conditions of the reactions, for example tetrahydrofuran, diethylether, dibutylether and the like. The reactions are preferably conducted at a temperature in the range from about -10°C to about 50°C .

Amide intermediates can be reduced to the desired compound of formula (I), wherein $A = -\text{CH}_2-$, by the use of reducing agents capable of converting the amido functionality to an amino moiety. Such agents are, for example, lithium aluminum hydride or other complex aluminum hydrides. The reducing reactions are, performed in diethyl ether or tetrahydrofuran, or in a stable diborane complex such as boran-

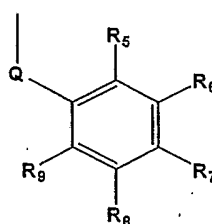
tetrahydrofuran or borane-dimethylsulphide or others (J. Org. Chem. 1982, 47, 1389) used in an appropriate solvent (e.g. tetrahydrofuran). Many other useful reducing agents are known to those skilled in the art (March J., Advanced Organic Chemistry, Wiley Interscience Ed., 1992, 1212).

- 5 **Scheme - 5 :** Compounds of general formula (I) may be prepared by reacting a compound of formula (VII) given below,

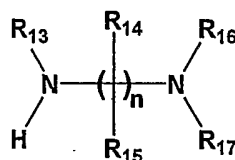


(VII)

- 10 wherein R₁, R₂, R₃, R₄ and R₁₀ are as defined in relation to formula (I), X is a halogeno, for example a chloro, bromo or iodo; while R represents either of a suitable N-protecting group such as acetyl, trifluoroacetyl, benzyl, trityl, t-butyloxycarbonyl (t-BOC) or a group such as,



- 15 where R₅, R₆, R₇, R₈ and R₉ are as defined earlier, with a compound of formula (III) or its acid addition salt,



(III)

- 20 where R₁₃, R₁₄, R₁₅, R₁₆ and R₁₇ are as defined in relation to compound of formula (I) or precursor thereof; in suitable anhydrous solvent; and thereafter if desired or necessary carrying out steps (i), (ii) and/or (iii) as described above.

- 25 The reaction is preferably carried out at a temperature in the range from about -5 °C to about 65 °C, in the presence of acid acceptor in an organic solvent inert under the conditions of the reactions, for example tetrahydrofuran, diethylether, ethylene chloride and the like. The purpose of acid acceptor is to take up the hydrogen halide which is split out during the course of the reaction and includes sodium carbonate, sodium bicarbonate, potassium carbonate, sodium acetate, sodium alkoxides and the like. The acid acceptor can also be in the form of an

excess quantity of substituted amine.

Scheme - 6 : Alternatively, the compounds of formula (I) where $A = -CH_2$, can be obtained by carrying out chemical, catalytic or enzymatic reduction of the compounds of formula (I) where $A = -C=O$ using the known procedures.

5 During any of the above synthetic sequences it may be necessary and/or desirable to protect sensitive or reactive groups on any of the molecules concerned. This may be achieved by means of conventional protecting groups, such as those described in Protective Groups in Organic Chemistry, Ed J. F. W. McOmie, Plenum Press, 1973; and T. W. Greene & P. G. M. Wuts, Protective Groups in Organic
10 Synthesis, John Wiley & Sons, 1991. For example, suitable protecting groups for the piperazine group include BOC, $-COCCl_3$, $-COCF_3$. The protecting groups may be removed according to the standard procedures. The protecting groups may be removed at a convenient subsequent stage using methods known from the art.

Certain amines, such as N-substituted piperazines, can be prepared by
15 acylation or alkylation of the appropriate NH-piperazine compound according to the standard procedures.

The compounds of the present invention may contain one or more asymmetric centers and therefore they also exist as stereoisomers. The stereoisomers of the compounds of the present invention may be prepared by one or
20 more ways presented below:

- i) One or more of the reagents may be used in their optically active form.
- ii) Optically pure catalyst or chiral ligands along with metal catalyst may be employed in the reduction process. The metal catalyst may be Rhodium, Ruthenium, Iridium and the like. The chiral ligands may preferably be chiral phosphines (Principles of
25 Asymmetric synthesis, J. E. Baldwin Ed., Tetrahedron series, 14, 311-316).
- iii) The mixture of stereoisomers may be resolved by conventional methods such as forming a diastereomeric salts with chiral acids or chiral amines, or chiral amino alcohols, chiral amino acids. The resulting mixture of diastereomers may then be separated by methods such as fractional crystallization, chromatography and the like,
30 which is followed by an additional step of isolating the optically active product by hydrolyzing the derivative (Jacques et. al., "Enantiomers, Racemates and Resolution", Wiley Interscience, 1981).
- iv) The mixture of stereoisomers may be resolved by conventional methods such as microbial resolution, resolving the diastereomeric salts formed with chiral acids or
35 chiral bases.

Chiral acids that can be employed may be tartaric acid, mandelic acid, lactic acid, camphorsulfonic acid, amino acids and the like. Chiral bases that can be

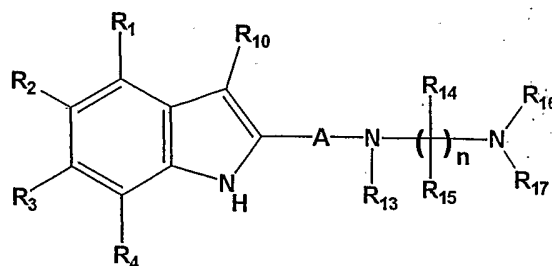
employed may be cinchona alkaloids, brucine or a basic amino acid such as lysine, arginine and the like.

The pharmaceutically acceptable salts forming a part of this invention may be prepared by treating the compound of formula (I) with 1-6 equivalents of a base such as Lithium, ammonia, substituted ammonia, sodium hydride, sodium methoxide, sodium ethoxide, sodium hydroxide, potassium t-butoxide, calcium hydroxide, calcium acetate, calcium chloride, magnesium hydroxide, magnesium chloride and the like. Solvents such as water, acetone, ether, THF, methanol, ethanol, t-butanol, dioxane, isopropanol, isopropyl ether or mixtures thereof may be used. Organic bases such lysine, arginine, methyl benzylamine, ethanolamine, diethanolamine, tromethamine, choline, guanidine and their derivatives may be used. Acid addition salts, wherever applicable may be prepared by treatment with acids such as tartaric acid, mandelic acid, fumaric acid, maleic acid, lactic acid, salicylic acid, citric acid, ascorbic acid, benzene sulfonic acid, p-toluene sulfonic acid, hydroxynaphthoic acid, methane sulfonic acid, malic acid, acetic acid, benzoic acid, succinic acid, palmitic acid, oxalic acid, hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid and the like in solvents such as water, alcohols, ethers, ethyl acetate, dioxane, DMF or a lower alkyl ketone such as acetone, or the mixtures thereof.

Different polymorphs may be prepared by crystallization of compounds of general formula (I) under different conditions such as different solvents or solvent mixtures in varying proportions for recrystallization, various ways of crystallization such as slow cooling, fast cooling or a very fast cooling or a gradual cooling during crystallization. Different polymorphs may also be obtained by heating the compound, melting the compound and solidification by gradual or fast cooling, heating or melting under vacuum or under inert atmosphere and cooling under either vacuum or inert atmosphere. The various polymorphs may be identified by either one or more of the following techniques such as differential scanning calorimeter, powder X-ray diffraction, IR spectroscopy, solid probe NMR spectroscopy and thermal microscopy.

The novel intermediates of formula represented by general formula (IV), which are useful in the preparation of compounds of formula (I), also form the part of this invention.

The novel intermediate of general formula (IV) is defined as below,



wherein A may be either a $-CR_{11}R_{12}-$, $-C=O$, $-SO_2-$, $-(CO)NH-$ or $-C=S$ group.

R_1 , R_2 , R_3 , R_4 , R_{10} , R_{11} , R_{12} , R_{14} and R_{15} may be same or different and each independently represent hydrogen, halogen, oxo, thio, perhaloalkyl, hydroxy, amino, nitro, cyano, formyl, amidino, guanidino, substituted or unsubstituted groups selected from linear or branched (C_1-C_{12}) alkyl, (C_2-C_{12}) alkenyl, (C_2-C_{12}) alkynyl, (C_3-C_7) cycloalkyl, (C_3-C_7) cycloalkenyl, bicycloalkyl, bicycloalkenyl, (C_1-C_{12}) alkoxy, cyclo (C_3-C_7) alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heterocyclylalkyl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, heterocyclylalkyloxy, acyl, acyloxy, acylamino, monoalkylamino, dialkylamino, arylamino, diarylamino, aralkylamino, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, heterocyclylalkoxycarbonyl, heteroaryloxycarbonyl, hydroxyalkyl, aminoalkyl, monoalkylaminoalkyl, dialkylaminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl, alkoxycarbonylamino, aryloxycarbonylamino, aralkyloxycarbonylamino, aminocarbonylamino, alkylaminocarbonylamino, dialkylaminocarbonylamino, alkylamidino, alkylguanidino, dialkylguanidino, hydrazino, hydroxylamino, carboxylic acid and its derivatives, sulfonic acids and its derivatives, phosphoric acid and its derivatives; or the adjacent groups like R_1 and R_2 or R_2 and R_3 or R_3 and R_4 together with carbon atoms to which they are attached may form a five or a six membered ring, optionally containing one or more double bonds and optionally containing one or more heteroatoms selected from "Oxygen", "Nitrogen", "Sulfur" or "Selenium" and combinations of double bond and heteroatoms; or R_{11} and R_{12} together with the carbon atoms to which they are attached may form a three to six membered ring, optionally containing one or more double bonds and optionally containing one or more heteroatoms selected from "Oxygen", "Nitrogen", "Sulfur" or "Selenium" and combinations of double bond and heteroatoms.

R_{13} , R_{16} and R_{17} may be same or different and each independently represents hydrogen, substituted or unsubstituted groups selected from linear or branched (C_1-C_{12}) alkyl, (C_2-C_{12}) alkenyl, (C_2-C_{12}) alkynyl, (C_3-C_7) cycloalkyl, (C_3-C_7) cycloalkenyl, bicycloalkyl, bicycloalkenyl, aryl, aralkyl, heteroaryl, heterocyclylalkyl; alternatively R_{13} along with either R_{16} or R_{17} and the two nitrogen atoms may form a 5-, 6- or 7-membered heterocyclic ring, which may be further substituted with R_{14} and R_{15} , and

may have either one, two or three double bonds, with the proviso that, When R_{13} along with R_{16} together with the intervening nitrogens form a piperazine or a substituted piperazine ring, then R_{17} is never aryl substituent.

5 "n" is an integer ranging from 1 to 4, wherein the carbon chains which "n" represents may be either linear or branched.

Another aspect of the present invention comprises of a pharmaceutical composition, containing at least one of the compounds of the general formula (I), their derivatives, their analogs, their derivatives, their tautomeric forms, their stereoisomers, their geometric forms, their N-oxides, their polymorphs, their
10 isotopically-labeled derivatives, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates thereof as an active ingredient, together with pharmaceutically employed carriers, auxiliaries and the like.

The pharmaceutical compositions of the present invention may be formulated in a conventional manner using one or more pharmaceutically acceptable carriers.
15 Thus, the active compounds of the invention may be formulated for oral, buccal, intranasal, parental (e.g., intravenous, intramuscular or subcutaneous) or rectal administration or a form suitable for administration by inhalation or insufflation.

The dose of the active compounds can vary depending on factors such as the route of administration, age and weight of patient, nature and severity of the disease
20 to be treated and similar factors. Therefore, any reference herein to a pharmacologically effective amount of the compounds of general formula (I) refers to the aforementioned factors.

For oral administration, the pharmaceutical compositions may take the form of, for example, tablets or capsules prepared by conventional means with
25 pharmaceutically acceptable excipients such as binding agents (e.g., pregelatinised maize starch, polyvinylpyrrolidone or hydroxypropyl methylcellulose); fillers (e.g., lactose, microcrystalline cellulose or calcium phosphate); lubricants (e.g., magnesium stearate, talc or silica); disintegrants (e.g., potato starch or sodium starch glycolate); or wetting agents (e.g., sodium lauryl sulphate). The tablets may be coated by
30 methods well known in the art. Liquid preparations for oral administration may take the form of, for example, solutions, syrups or suspensions, or they may be presented as a dry product for constitution with water or other suitable vehicle before use. Such liquid preparations may be prepared by conventional means with pharmaceutically acceptable additives such as suspending agents (e.g., sorbitol syrup, methyl
35 cellulose or hydrogenated edible fats); emulsifying agents (e.g., lecithin or acacia); non-aqueous vehicles (e.g., almond oil, oily esters or ethyl alcohol); and preservatives (e.g., methyl or propyl p-hydroxybenzoates or sorbic acid).

For buccal administration, the composition may take the form of tablets or lozenges formulated in conventional manner.

The active compounds of the invention may be formulated for parenteral administration by injection, including using conventional catheterization techniques or infusion. Formulations for injection may be presented in unit dosage form, e.g., in ampoules or in multi-dose containers, with an added preservative. The compositions may take such forms as suspensions, solutions or emulsions in oily or aqueous vehicles, and may contain formulating agents such as suspending, stabilizing and/or dispersing agents. Alternatively, the active ingredient may be in powder form for reconstitution with a suitable vehicle, e.g., sterile pyrogen-free water, before use.

The active compounds of the invention may also be formulated in rectal compositions such as suppositories or retention enemas, e.g., containing conventional suppository bases such as cocoa butter or other glycerides.

For intranasal administration or administration by inhalation, the active compounds of the invention are conveniently delivered in the form of an aerosol spray from a pressurized container or a nebulizer, or from a capsule using an inhaler or insufflator. In the case of a pressurized aerosol, a suitable propellant, e.g., dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane, carbon dioxide or other suitable gas and the dosage unit may be determined by providing a valve to deliver a metered amount. The medicament for pressurized container or nebulizer may contain a solution or suspension of the active compound while for a capsule it preferably should be in the form of powder. Capsules and cartridges (made, for example, from gelatin) for use in an inhaler or insufflator may be formulated containing a powder mix of a compound of the invention and a suitable powder base such as lactose or starch.

A proposed dose of the active compounds of this invention, for either oral, parenteral, nasal or buccal administration, to an average adult human, for the treatment of the conditions referred to above, is 0.1 to 200 mg of the active ingredient per unit dose which could be administered, for example, 1 to 4 times per day.

Aerosol formulations for treatment of the conditions referred to above (e.g., migraine) in the average adult human are preferably arranged so that each metered dose or "puff" of aerosol contains 20 μ g to 1000 μ g of the compound of the invention. The overall daily dose with an aerosol will be within the range 100 μ g to 10 mg. Administration may be several times daily, for example 2, 3, 4 or 8 times, giving for example, 1, 2 or 3 doses each time.

The affinities of the compound of this invention for the various serotonin receptors are evaluated using standard radioligand binding assays and are described here.

Radioligand binding assays for various 5-HT receptor sub-types :

- 5 International Patent Publication WO 04/000205, WO 04/000845, WO 04/000849, (Suven Lifesciences Limited) gives detailed list of methods used for Radioligand assays and related prior art, all of which is incorporated herein along with the references.

10 The following description illustrates the method of preparation of variously substituted compounds of general formula (I), according to the methods described herein. These are provided by the way of illustration only and therefore should not be construed to limit the scope of the invention.

Commercial reagents were utilized without further purification. Room temperature refers to 25 - 30 °C. Melting points are uncorrected. IR spectra were
15 taken using KBr and in solid state. Unless otherwise stated, all mass spectra were carried out using ESI conditions. ¹H NMR spectra were recorded at 200 or 400 MHz on a Bruker instrument. Deuterated chloroform (99.8 % D) was used as solvent. TMS was used as internal reference standard. Chemical shift values reported herein are expressed in parts per million (δ ppm) values. The following abbreviations are used
20 for the multiplicity for the NMR signals: s=singlet, bs=broad Singlet, d=doublet, t=triplet, q=quartet, qui=quintet, sep=septate, dd=doublet doublet, dt=doublet triplet, tt=triplet of triplets, m=multiple. NMR, mass were corrected for background peaks. Specific rotations were measured at room temperature using the sodium D (589 nm). Chromatography refers to column chromatography performed using 60 – 120 mesh
25 silica gel and executed under nitrogen pressure (flash chromatography) conditions.

Description 1 : (1H-Indol-2-yl)-(4-methylpiperazin-1-yl)methanone (D1)

1H-Indole-2-carboxylic acid (3 g, 15.7 mmoles) was stirred with oxalyl chloride (2.25 mL, 25.7 mmoles) in 20 mL dichloromethane at 25 °C. After completion of the reaction (TLC), volatile substances were distilled off under the reduced pressure. The
30 residue was taken in 20 mL dichloroethane, and to this stirred solution, was added N-methylpiperazine (1.1 g, 0.011 moles). The reaction mixture was further stirred for next 3 - 5 hours, till the reaction completes (TLC). Reaction mixture was diluted with dichloromethane (20 mL), washed with water, brine and saturated solution of sodium bicarbonate. The organic layer was dried over sodium sulfate and the organic
35 solvents were evaporated under vacuo. The product was isolated using column chromatography on silica gel G stationary phase and suitable combinations of ethyl

acetate and methanol in increasing gradient as the mobile phase. The structure of compound thus obtained was confirmed by IR, NMR and mass spectral analyses.

Description 2-18 (D2-D18)

Using essentially the same procedure described in description 1 hereinabove and employing appropriately substituted indole-2-carboxylic acid with substituted alkyl piperazine or N,N',N'-trimethylethylene-1,2-diamine, compounds given in the list 1 were prepared. The structure of compounds thus obtained were confirmed by IR, NMR and mass spectral analyses.

List - 1

Description	Mass ion (M+H) ⁺
D 1 (1H-Indol-2-yl)-(4-methylpiperazin-1-yl)methanone	244
D 2 (5-Methoxy-1H-indol-2-yl)-(4-methylpiperazin-1-yl)methanone	274
D 3 (5-Ethoxy-1H-indol-2-yl)-(4-methylpiperazin-1-yl)methanone	288
D 4 (5-Methylthio-1H-indol-2-yl)-(4-methylpiperazin-1-yl)methanone	290
D 5 (5-Methyl-1H-indol-2-yl)-(4-methylpiperazin-1-yl)methanone	258
D 6 (5-Isopropyl-1H-indol-2-yl)-(4-methylpiperazin-1-yl)methanone	286
D 7 (6,7-Dimethyl-1H-indol-2-yl)-(4-methylpiperazin-1-yl)methanone	272
D 8 (5,7-Dimethyl-1H-indol-2-yl)-(4-methylpiperazin-1-yl)methanone	272
D 9 5-Ethoxy-1H-indol-2-carboxylic acid, N-(N',N'-dimethylaminoethyl)-N-methylamide.	290
D 10 5-Methylthio-1H-indol-2-carboxylic acid, N-(N',N'-dimethylaminoethyl)-N-methylamide.	292
D 11 5-Methyl-1H-indol-2-carboxylic acid, N-(N',N'-dimethylaminoethyl)-N-methylamide.	260
D 12 5-Isopropyl-1H-indol-2-carboxylic acid, N-(N',N'-dimethylaminoethyl)-N-methylamide.	288
D 13 6,7-Dimethyl-1H-indol-2-carboxylic acid, N-(N',N'-dimethylaminoethyl)-N-methylamide.	274
D 14 5,7-Dimethyl-1H-indol-2-carboxylic acid, N-(N',N'-dimethylaminoethyl)-N-methylamide.	274
D 15 1H-Indole-2-carboxylic acid, N-(N',N'-dimethylaminoethyl)-N-methylamide	246
D 16 3-Chloro-(1H-indol-2-yl)-(4-methylpiperazin-1-yl)methanone	278
D 17 3-Chloro-(5-methoxy-1H-indol-2-yl)-(4-methylpiperazin-1-yl)methanone	308
D 18 (3-Bromo-(1H-indole-2-carboxylic acid)) N-(N',N'-	324

dimethylaminoethyl)-N-methylamide

Description 19 : 2-(4-Methylpiperazin-1-ylmethyl)-1H-indole (D19)

(1H-Indol-2-yl)-(4-methylpiperazin-1-yl)methanone (2.44 g, 0.01 moles) in THF was treated with cooled and stirred suspension of Lithium aluminum hydride (0.418 g, 5 0.011 moles) in 254 mL THF slowly over the period of 2 to 5 hours, the reaction mixture was heated to reflux for 2 - 4 hours, after the completion of reaction, the reaction mixture was poured on to the ice and the compound was extracted in ethyl acetate. The residue obtained was purified by flash chromatography (silica gel, EtOAc/hexanes, 2/8) to afford the compound, which was identified by IR, NMR and 10 mass spectral analyses as the title compound.

Description 20-35 (D20- D35)

Using essentially the same procedure described in description-19 the compounds obtained in description 1-18 (D1-D18), were reduced to the corresponding derivatives. The list of compounds thus obtained is given below. The structure of 15 compounds thus obtained were confirmed by IR, NMR and mass spectral analyses.

List - 2

	Description	Mass Ion (M+H) ⁺
D 19	2-(4-Methylpiperazin-1-ylmethyl)-1H-indole	230
D 20	2-(4-Methylpiperazin-1-ylmethyl)-5-methoxy-1H-indole	260
D 21	N-(1H-Indol-2-ylmethyl)-N,N',N'-trimethyl-ethane-1,2-diamine	232
D 22	3-Chloro-2-(4-methylpiperazin-1-ylmethyl)-1H-indole	264
D 23	3-Chloro-2-(4-methylpiperazin-1-yl-methyl)-5-methoxy-1H-indole	294
D 24	2-(4-Methylpiperazin-1-ylmethyl)-5-Ethoxy-1H-indole.	274
D 25	2-(4-Methylpiperazin-1-ylmethyl)-5-Methylthio-1H-indole.	276
D 26	2-(4-Methylpiperazin-1-ylmethyl)-5-Methyl-1H-indole.	244
D 27	2-(4-Methylpiperazin-1-ylmethyl)-5-Isopropyl-1H-indole.	272
D 28	2-(4-Methylpiperazin-1-ylmethyl)-6,7-Dimethyl-1H-indole.	258
D 29	2-(4-Methylpiperazin-1-ylmethyl)-5,7-Dimethyl-1H-indole.	258
D 30	N-(5-Ethoxy-1H-indol-2-ylmethyl)-N,N',N'-trimethyl-ethane-1,2-diamine.	276
D 31	N-(5-Methylthio-1H-indol-2-ylmethyl)-N,N',N'-trimethyl-ethane-1,2-diamine.	278
D 32	N-(5-Methyl-1H-indol-2-ylmethyl)-N,N',N'-trimethyl-ethane-1,2-diamine.	246

D 33	N-(5-Isopropyl-1H-indol-2-ylmethyl)-N,N',N'-trimethyl-ethane-1,2-diamine.	274
D 34	N-(6,7-Dimethyl-1H-indol-2-ylmethyl)-N,N',N'-trimethyl-ethane-1,2-diamine.	260
D 35	N-(5,7-Dimethyl-1H-indol-2-ylmethyl)-N,N',N'-trimethyl-ethane-1,2-diamine.	260

Example - 1 : 1-Benzenesulfonyl-2-(4-methylpiperazin-1-ylmethyl)-1H-indole ;
2-(4-Methylpiperazin-1-ylmethyl)-1H-indole (2.59 g, 0.01 moles) in DMF (30 mL) was
added slowly to a suspension of sodium hydride (0.26 g, 0.011 moles, (0.52 g of 50
5 % suspension in mineral oil)) in DMF (10 mL) maintaining the temperature below 10
°C. The mixture was stirred for 1 hr at 25 °C. and benzene sulfonyl chloride (1.76 g,
0.01 moles) was added at 10 °C drop-wise to the reaction mixture. The reaction
mixture was further stirred for 1 hr at 25 °C. After the completion of reaction (TLC),
the reaction mixture was poured onto an ice-water mixture and extracted with ethyl
10 acetate (20 mL x 2). The combined organic extracts were washed with water and
brine and dried over sodium sulfate. Volatile impurities were distilled off under
reduced pressure to obtain the crude residue. The residue obtained was purified by
flash chromatography (silica gel, EtOAc/TEA, 9.9/0.1) to afford the compound, which
was identified by IR, NMR and mass spectral analyses as the title compound.

15 Alternatively, (1-Benzenesulfonyl-1H-indol-2-yl)-(4-methylpiperazin-1-yl) methanone
(Example 20) (0.8 g, 0.002 moles) in THF (10 mL) was treated with cooled and
stirred suspension of LAH (0.04 g, 0.001 moles) in THF (10 mL) slowly over the
period of 2 to 5 hours, the reaction mixture was heated to reflux for 2 - 4 hours, after
the completion of reaction, the reaction mixture was poured on to the ice and the
20 compound was extracted in ethyl acetate. The residue obtained was purified by flash
chromatography (silica gel, EtOAc/hexanes, 2/8) to afford the compound, which was
found to be identical to the compound synthesized earlier. IR spectra (cm⁻¹) : 1176,
1242, 1364, 1454; Mass (m/z) : 370 (M+H)⁺ ; ¹H-NMR (□ ppm) : 2.25 (3H, s), 2.31 –
2.56 (8H, m), 3.87 (2H, s), 6.55 (1H, s), 7.20 – 7.53 (6H, m), 8.08 – 8.12 (3H, m).

25 Example - 2 : 1-(4-Fluorobenzenesulfonyl)-2-(4-methylpiperazin-1-ylmethyl)-1H-
indole ;

Using essentially the same procedure as described in example 1, above derivative
was prepared. IR spectra (cm⁻¹) : 1162, 1240, 1378, 1451; Mass (m/z) : 388 (M+H)⁺ ;
¹H-NMR (δ, ppm) : 2.31 (3H, s), 2.41 – 2.62 (8H, m), 3.87 (2H, s), 6.54 (1H, s), 7.04 –
30 7.32 (4H, m), 7.45 – 7.49 (1H, m), 8.03 – 8.19 (1H, dd), 8.20 – 8.23 (2H, m).

Example - 3 : 1-(4-Isopropylbenzenesulfonyl)-2-(4-methylpiperazin-1-ylmethyl)-

1H-indole

Using essentially the same procedure as described in example 1, above derivative was prepared. IR spectra (cm^{-1}) : 1178, 1240, 1368, 1454; Mass (m/z) : 412 ($M+H$)⁺; ¹H-NMR (δ , ppm) : 1.18 – 1.22 (6H, d), 2.26 (3H, s), 2.314 (4H, bs), 2.55 (4H, bs),
 5 2.90 (1H, sep), 3.87 (2H, s), 7.20 (1H, s), 7.21 – 7.28 (4H, m), 7.44 – 7.54 (1H, m), 7.96 – 7.99 (2H, dd), 8.00 – 8.13 (1H, dd).

Example - 4 : 1-(4-Methoxybenzenesulfonyl)-2-(4-methylpiperazin-1-ylmethyl)-
 1H-indole

Using essentially the same procedure as described in example 1, above derivative
 10 was prepared. IR spectra (cm^{-1}) : 1176, 1262, 1364, 1454; Mass (m/z) : 400 ($M+H$)⁺; ¹H-NMR (δ , ppm) : 2.28 (3H, s), 2.35 – 2.59 (8H, m), 3.80 (3H, s), 3.88 (2H, s), 6.53 (1H, s), 6.83 – 6.87 (2H, dd), 7.19 – 7.27 (2H, m), 7.43 – 7.47 (1H, m), 8.06 – 8.12 (3H, m).

Example - 5 : 1-(2-Bromo-4-methoxybenzenesulfonyl)-2-(4-methylpiperazin-1-
 15 ylmethyl)-1H-indole

Using essentially the same procedure as described in example 1, above derivative was prepared. IR spectra (cm^{-1}) : 1150, 1290, 1369, 1455; Mass (m/z) : 478, 480 ($M+H$)⁺; ¹H-NMR (δ , ppm) : 2.21 (3H, s), 2.31 – 2.50 (8H, m), 3.82 (5H, s), 6.62 (1H, s), 6.78 – 6.84 (1H, dd), 7.15 – 7.26 (3H, m), 7.48 – 7.56 (2H, m), 7.61 – 7.86 (1H, m).
 20 m).

Example - 6 : 1-(4-Methoxybenzenesulfonyl)-5-methoxy-2-(4-methylpiperazin-1-
 ylmethyl)-1H-indole

Using essentially the same procedure as described in example 1, above derivative was prepared. IR spectra (cm^{-1}) : 1163, 1263, 1366, 1474; Mass (m/z) : 430 ($M+H$)⁺; ¹H-NMR (δ , ppm) : 2.29 (3H, s), 2.41 – 2.59 (8H, m), 3.80 (3H, s), 3.81 (3H, s), 3.84 – 3.86 (2H, s), 6.46 (1H, s), 6.82 – 6.90 (4H, m), 7.96 – 8.03 (3H, m).
 25

Example - 7 : 1-(4-Methoxybenzenesulfonyl)-5-methoxy-2-(4-methylpiperazin-1-
 ylmethyl)-1H-indole Hydrochloride salt

Using essentially the same procedure as described in example 1, above derivative was prepared. IR spectra (cm^{-1}) : 1163, 1268, 1369, 1475; Mass (m/z) : 430 ($M+H$)⁺; ¹H-NMR (δ , ppm) : 3.03 (3H, s), 3.61 – 3.80 (8H, m), 3.82 (3H, s), 3.84 (3H, s), 4.80 (2H, s), 6.98 – 8.10 (8H, m).
 30

Example - 8 : 1-(4-Isopropylbenzenesulfonyl)-5-methoxy-2-(4-methylpiperazin-1-
 ylmethyl)-1H-indole

Using essentially the same procedure as described in example 1, above derivative was prepared. IR spectra (cm^{-1}) : 1168, 1207, 1366, 1474; Mass (m/z) : 442 ($M+H$)⁺; ¹H-NMR (δ , ppm) : 1.20 – 1.21 (6H, d), 2.27 (3H, s), 2.47 – 2.62 (8H, bm), 2.88 –
 35

2.92 (1H, sep.), 3.82 (3H, s), 3.84 (2H, s), 6.47 (1H, s), 6.88 – 6.92 (2H, m), 7.22 – 7.24 (2H, m), 7.88 – 7.91 (2H, m), 8.00 – 8.02 (1H, d).

Example - 9 : 3-Chloro-1-(4-isopropylbenzenesulfonyl-5-methoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole

5 Using essentially the same procedure as described in example 1, above derivative was prepared. Melting range (°C) : 118-120; IR spectra (cm⁻¹) : 1172, 1213, 1368, 1452; Mass (m/z) : 476, 478 (M+H)⁺; ¹H-NMR (δ, ppm) : 1.19 – 1.23 (6H, d), 2.22 – 2.60 (11, m), 2.88 – 2.95 (1H, sep.), 3.85 (3H, s), 3.95 (2H, s), 6.94 – 6.98 (2H, m), 7.00 – 7.22 (2H, m), 8.00 – 8.07 (3H, m).

10 Example - 10 : 1-(4-Isopropylbenzenesulfonyl-5-methoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole Hydrochloride salt

Using essentially the same procedure as described in example 1, above derivative was prepared. IR spectra (cm⁻¹) : 1166, 1210, 1373, 1595; Mass (m/z) : 442 (M+H)⁺; ¹H-NMR (δ, ppm) : 1.19 - 1.22 (6H, d), 2.82 - 2.89 (1H, sep), 3.01 (3H, s), 3.33 - 3.34 (8H, bs), 3.82 (3H, bs), 4.75 (2H, s), 7.04 - 8.10 (8H, m).

Example - 11 : 3-Chloro-1-(4-methoxybenzenesulfonyl)-5-methoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole

Using essentially the same procedure as described in example 1, above derivative was prepared. IR spectra (cm⁻¹) : 1166, 1215, 1370, 1480; Mass (m/z) : 464, 466 (M+H)⁺; ¹H-NMR (δ, ppm) : 2.29 (3H, s), 2.38 – 2.65 (8H, m), 3.81 (3H, s), 3.84 (3H, s), 3.96 (2H, s), 6.83 – 6.98 (4H, m), 7.97 – 8.01 (1H, dd), 8.16 – 8.20 (2H, dd).

Example - 12 : 3-Chloro-1-(4-methoxybenzenesulfonyl)-5-methoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole Hydrochloride salt

Using essentially the same procedure as described in example 1, above derivative was prepared. Mass (m/z) : 464 (M+H)⁺.

Example - 13 : 1-(2-Bromobenzenesulfonyl)-2-(4-methylpiperazin-1-ylmethyl)-1H-indole

Using essentially the same procedure as described in example 1, above derivative was prepared. IR spectra (cm⁻¹): 1112, 1213, 1368, 1573; Mass (m/z): 478, 480 (M+H)⁺.

Example - 14 : 1-(2-Bromobenzenesulfonyl)-3-chloro-2-(4-methylpiperazin-1-ylmethyl)-1H-indole

Using essentially the same procedure as described in example 1, above derivative was prepared. IR spectra (cm⁻¹) : 1112, 1169, 1368, 1578; Mass (m/z): 512, 514, 516 (M+H)⁺.

Example - 15 : N-(1-Benzenesulfonyl-1H-indol-2-yl)methyl-N,N',N'-trimethylethylene-1,2-diamine

Using essentially the same procedure as described in example 1, above derivative was prepared. Mass (m/z) : 372 (M+H)⁺.

Example - 16 : N-(1-Benzenesulfonyl)-3-bromo-1H-indol-2-yl)methyl-N,N',N'-trimethylethylene-1,2-diamine

- 5 Using essentially the same procedure as described in example 1, above derivative was prepared. IR spectra (cm⁻¹): 1175,1262,1380,1448. Mass (m/z): 450, 452 (M+H)⁺; ¹H-NMR (δ, ppm) : 3.01-3.18 (9H, bs), 3.88-3.91 (4H, m), 4.88 (2H, s), 7.43-8.28 (9H, m).

Example - 17 : N-(1-(4-Methylbenzenesulfonyl)-1H-indol-2-yl)methyl-N,N',N'-trimethylethylene-1,2-diamine

Using essentially the same procedure as described in example 1, above derivative was prepared. Mass (m/z): 386 (M+H)⁺.

Example - 18 : 1-(2-Bromo-4-methoxybenzenesulfonyl-1H-indol-2-yl)methyl-N,N',N'-trimethylethylene-1,2-diamine

- 15 Using essentially the same procedure as described in example 1, above derivative was prepared. Mass (m/z): 480 (M+H)⁺.

Example - 19 : 1-((2-Bromo-4-methoxybenzenesulfonyl)-3-chloro-1H-indol-2-yl)methyl-N,N',N'-trimethylethylene-1,2-diamine, hydrochloride.

- Using essentially the same procedure as described in example 1, above derivative was prepared. IR spectra (cm⁻¹): 1175, 1281, 1389, 1483. Mass (m/z): 514, 516 (M+H)⁺; ¹H-NMR (δ, ppm) : 3.06 - 3.31 (9H, bs), 3.90 (3H, s), 3.95 - 4.2 (4H, bs), 5.10 (2H, bs), 7.12 - 7.14 (1H, dd), 7.44 - 7.49 (1H, m), 7.58 - 7.68 (3H, m), 8.01 (1H, s), 8.12 - 8.25 (1H, d).

Example - 20 : [1-Benzenesulfonyl-1H-indol-2-yl]-(4-methylpiperazin-1-yl)methanone

- 25 1-Benzenesulfonyl-indole-2-carboxylic acid (3.01 g, 0.01 moles) was stirred with oxalyl chloride (1.39 g, 0.011 moles) in 20 mL dichloromethane at 0 to 25 °C for 3 - 4 hours. After completion of the reaction (TLC), volatile substances were distilled off under the reduced pressure. The residue was taken in 20 mL dichloroethane, and to this stirred solution, was added N-methylpiperazine (1.1 g, 0.011 moles). The reaction mixture was further stirred for next 3 - 5 hours till the reaction completes (TLC). Reaction mixture was diluted with dichloromethane 20 mL, washed with water, brine and saturated solution of sodium bicarbonate. The organic layer was dried over sodium sulfate and the organic solvents were evaporated under vacuo. The product was purified using column chromatography on silica gel G stationary phase and suitable combinations of ethyl acetate and methanol in increasing gradient as the
- 30
- 35

mobile phase. The residue obtained was identified by IR, NMR and mass spectral analyses as the title compound. Mass (m/z) : 384 (M+H)⁺.

Example - 21 : [1-(4-Fluorobenzenesulfonyl)-1H-indol-2-yl]-(4-methylpiperazin-1-yl)methanone

- 5 Using essentially the same procedure as described in example 20, above derivative was prepared. Mass (m/z) : 402 (M+H)⁺.

Example - 22 : [1-(4-Isopropylbenzenesulfonyl)-1H-indol-2-yl]-(4-methylpiperazin-1-yl)methanone

- 10 Using essentially the same procedure as described in example 20, above derivative was prepared. Mass (m/z) : 426 (M+H)⁺.

Example - 23 : [1-(4-Methoxybenzenesulfonyl)-1H-indol-2-yl]-(4-methylpiperazin-1-yl)methanone

Using essentially the same procedure as described in example 20, above derivative was prepared. Mass (m/z) : 414 (M+H)⁺.

- 15 Example - 24 : [1-(2-Bromo-4-methoxybenzenesulfonyl)-1H-indol-2-yl]-(4-methylpiperazin-1-yl)methanone

Using essentially the same procedure as described in example 20, above derivative was prepared. Mass (m/z) : 492, 494 (M+H)⁺.

- 20 Example - 25 : [1-(4-Methoxybenzenesulfonyl)-5-methoxy-1H-indol-2-yl]-(4-methylpiperazin-1-yl)methanone

- Using essentially the same procedure as described in example 20, above derivative was prepared. IR spectra (cm⁻¹) : 1164, 1264, 1371, 1641; Mass (m/z) : 444 (M+H)⁺; ¹H-NMR (δ, ppm) : 2.34 (3H, s), 2.51 – 2.55 (4H, m), 3.44 (2H, bs), 3.77 (3H, s), 3.80 (3H, s), 3.85 – 3.87 (2H, bs); 6.59 (1H, s), 6.85 – 6.96 (4H, m), 7.89 – 7.91 (1H, d), 7.99 – 8.02 (2H, dd).

Example - 26 : [1-(4-Isopropylbenzenesulfonyl)-5-methoxy-1H-indol-2-yl]-(4-methylpiperazin-1-yl)methanone

- Using essentially the same procedure as described in example 20, above derivative was prepared. Melting range (°C) : 77.4-87.5, IR spectra (cm⁻¹) : 1165, 1222, 1371, 1642. Mass (m/z) : 456 (M+H)⁺; ¹H-NMR (δ, ppm) : 1.16-1.85 (6H, d) 2.34 (3H, s), 2.55 (4H, m), 2.86-2.89 (1H, sept.) 3.45 (2H, bs), 3.80 (3H, s), 3.87 (2H, bs), 6.59 (1H, s), 6.93 – 6.97 (2H, m), 7.28 (2H, dd), 7.9– 7.93 (1H, d), 7.98-8.0 (2H, dd).

Example - 27 : [3-Chloro-1-(4-isopropylbenzenesulfonyl)-5-methoxy-1H-indol-2-yl]-(4-methylpiperazin-1-yl)methanone

- 35 Using essentially the same procedure as described in example 20, above derivative was prepared. Mass (m/z) : 490 (M+H)⁺.

Example - 28 : [3-Chloro-1-(4-Methoxybenzenesulfonyl)-5-methoxy-1H-indol-2-yl]-(4-methylpiperazin-1-yl)methanone

Using essentially the same procedure as described in example 20, above derivative was prepared. Mass (m/z) : 478, 480 (M+H)⁺.

5 Example - 29 : [1-(2-Bromobenzenesulfonyl)-1H-indol-2-yl]-(4-methylpiperazin-1-yl)methanone

Using essentially the same procedure as described in example 20, above derivative was prepared. Mass (m/z) : 462, 464 (M+H)⁺.

10 Example - 30 : [1-(2-Bromobenzenesulfonyl)-3-chloro-1H-indol-2-yl]-(4-methylpiperazin-1-yl)methanone

Using essentially the same procedure as described in example 20, above derivative was prepared. Mass (m/z) : 494, 496, 498 (M+H)⁺.

Example - 31 : 1-Benzenesulfonyl-1H-indole-2-carboxylic acid (2-dimethylaminoethyl)-N-methylamide

15 Using essentially the same procedure as described in example 20, above derivative was prepared. Mass (m/z) : 386 (M+H)⁺.

Example - 32 : 1-Benzenesulfonyl-3-bromo-1H-indole-2-carboxylic acid (2-dimethylaminoethyl)-N-methylamide

20 Using essentially the same procedure as described in example 20, above derivative was prepared. Mass (m/z) : 464, 466 (M+H)⁺.

Example - 33 : N-(1-(4-Methylbenzenesulfonyl)-3-bromo-1H-indole-2-carboxylic acid (2-dimethylaminoethyl)-N-methylamide

Using essentially the same procedure as described in example 20, above derivative was prepared. Mass (m/z) : 478 (M+H)⁺.

25 Example - 34 : 1-(2-Bromo-4-methoxybenzenesulfonyl)-1H-indole-2-carboxylic acid (2-dimethylaminoethyl)-N-methylamide

Using essentially the same procedure as described in example 20, above derivative was prepared. Mass (m/z) : 494, 496 (M+H)⁺.

30 Example - 35 : 1-(2-Bromo-4-methoxybenzenesulfonyl)-3-bromo-1H-indole-2-carboxylic acid (2-dimethylaminoethyl)-N-methylamide

Using essentially the same procedure as described in example 20, above derivative was prepared. Mass (m/z) : 572, 574, 576 (M+H)⁺.

Example - 36 : (1-Benzenesulfonyl-5-methoxy-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone

35 Using essentially the same procedure as described in example 1, above derivative was prepared, using corresponding 1-unsubstituted indole. IR spectra (cm⁻¹) : 1177, 1372, 1444, 1634; Mass (m/z) : 414 (M+H)⁺; ¹H-NMR (δ, □ppm) : 2.36 (3H, s), 2.49 -

2.57 (4H, m), 3.47 (2H, bs), 3.79 (3H, s), 3.84 (2H, bs), 6.61 (1H, s), 6.93 - 9.96 (2H, m), 7.41 - 7.45 (2H, m), 7.50 - 7.54 (1H, m), 7.88 - 7.91 (1H, d), 8.07 - 8.09 (2H, d).

Example - 37 : (1-(4'-Fluorobenzenesulfonyl-5-methyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone

- 5 Using essentially the same procedure as described in example 1, above derivative was prepared, using corresponding 1-unsubstituted indole. IR spectra (cm^{-1}) : 1182, 1376, 1440, 1641; Mass (m/z) : 416 ($M+H$)⁺ ; ¹H-NMR (δ , ppm) : 2.35 (3H, s), 2.39 (3H, s), 2.44 - 2.55 (4H, m), 3.45 (2H, bs), 3.86 (2H, bs), 6.61 (1H, s), 7.07 - 7.29 (4H, m), 7.85 - 7.87 (1H, d), 8.13 - 8.16 (2H, m).

- 10 Example - 38 : (1-(4'-trifluoromethyl)benzenesulfonyl-5-methoxy-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone

Using essentially the same procedure as described in example 1, above derivative was prepared, using corresponding 1-unsubstituted indole. IR spectra (cm^{-1}) : 1142, 1378, 1450, 1628; Mass (m/z) : 482 ($M+H$)⁺ ; ¹H-NMR (δ , ppm) : 2.36 (3H, s), 2.48 - 2.58 (4H, m), 3.47 (2H, bs), 3.8 (3H, s), 3.87 (2H, bs), 6.63 (1H, s), 6.94 - 6.99 (2H, m), 7.58 - 7.62 (1H, t), 7.76-7.78 (1H, d), 7.88-7.90 (1H, d), 8.33-8.35 (1H, d), 8.39 (1H, s).

- 15 Example - 39 : (1-(3'-trifluoromethyl)benzenesulfonyl-5-methyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone.

- 20 Using essentially the same procedure as described in example 1, above derivative was prepared, using corresponding 1-unsubstituted indole. IR spectra (cm^{-1}) : 1180, 1380, 1438, 1640; Mass (m/z) : 466 ($M+H$)⁺ ; ¹H-NMR (δ , ppm) : 2.35 (3H, s), 2.39 (3H, s), 2.40 - 2.57 (4H, m), 3.47 (2H, bs), 3.87 (2H, bs), 6.62 (1H, s), 7.17 - 7.20 (1H, dd), 7.30 (1H, s), 7.58 - 7.62 (1H, t), 7.76 - 7.78 (1H, d), 7.85-7.87 (1 H, d), 8.36 - 8.38 (1 H, d), 8.41 (1H, s).

25 Example - 40 : (1-(Benzenesulfonyl-5-ethoxy-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone.

- Using essentially the same procedure as described in example 1, above derivative was prepared, using corresponding 1-unsubstituted indole. IR spectra (cm^{-1}) : 1090, 1223, 1364, 1453, 1630; Mass (m/z) : 428 ($M+H$)⁺ ; ¹H-NMR (δ , ppm) : 1.38 - 1.41 (3H, t), 2.17 (3H, s), 2.47 - 2.55 (4H, m), 3.46 (2H, bs), 3.87 (2H, bs), 3.57 - 4.05 (2H, q), 6.60 (1H, s), 6.91 - 6.95 (2H, m), 7.41 - 7.45 (2H, m), 7.49 - 7.51 (2H, m), 7.88 - 7.90 (1H, d), 8.07 - 8.09 (2H, m).

- 30 Example - 41 : (1-(4'-Isopropylbenzenesulfonyl-5-ethoxy-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone.

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Using essentially the same procedure as described in example 1, above derivative was prepared, using corresponding 1-unsubstituted indole. IR spectra (cm^{-1}) : 1181, 1382, 1438, 1640; Mass (m/z) : 470 ($M+H$)⁺.

Example - 42 : (1-Benzenesulfonyl-5-thiomethyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone.

Using essentially the same procedure as described in example 1, above derivative was prepared, using corresponding 1-unsubstituted indole. IR spectra (cm^{-1}) : 794, 1261, 1374, 1437, 1641; Mass (m/z) : 430 ($M+H$)⁺; ¹H-NMR (δ , ppm) : 2.17 (3H, s), 2.35 (3H, s), 2.48 - 2.56 (4H, bm), 3.29 - 3.46 (2H, bs), 3.49 - 3.50 (2H, bs), 6.60 (1H, s), 7.26 - 7.28 (1H, dd), 7.38 - 7.54 (4H, m), 7.90 - 7.93 (1H, d), 8.10 - 8.12 (2H, m).

Example - 43 : (1-(4'-Fluorobenzenesulfonyl-5-thiomethyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone.

Using essentially the same procedure as described in example 1, above derivative was prepared, using corresponding 1-unsubstituted indole. IR spectra (cm^{-1}) : 793, 1261, 1377, 1436, 1641; Mass (m/z) : 448 ($M+H$)⁺; ¹H-NMR (δ , ppm) : 2.17 (3H, s), 2.35 (3H, s), 2.49 - 2.55 (4H, bm), 3.27 - 3.45 (2H, bs), 3.49 - 3.50 (2H, bs), 6.61 (1H, s), 7.10 - 7.14 (2H, m), 7.27 - 7.29 (1H, dd), 7.39 - 7.39 (1H, d), 7.89 - 7.91 (1H, d), 8.14 - 8.17 (2H, m).

Example - 44 : (1-(4'-Isopropylbenzenesulfonyl-5-thiomethyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone.

Using essentially the same procedure as described in example 1, above derivative was prepared, using corresponding 1-unsubstituted indole. IR spectra (cm^{-1}) : 802, 1174, 1378, 1466, 1633; Mass (m/z) : 472 ($M+H$)⁺.

Example - 45 : (1-(3'-trifluoromethyl)benzenesulfonyl-5-thiomethyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone

Using essentially the same procedure as described in example 1, above derivative was prepared, using corresponding 1-unsubstituted indole. IR spectra (cm^{-1}) : 801, 1173, 1378, 1467, 1632; Mass (m/z) : 498 ($M+H$)⁺; ¹H-NMR (δ , ppm) : 2.35 (3H, s), 2.49 (3H, s), 2.52 - 2.57 (4H, bm), 3.47 (2H, bs), 3.87 (2H, bs), 6.62 (1H, s), 7.26 - 7.31 (2H, m), 7.60 - 7.64 (1H, t), 7.79 - 7.81 (1H, d), 7.89 - 7.91 (1H, d), 8.36 - 8.38 (1H, d), 8.42 (1H, s).

Example - 46 : 5-methoxy -1-(Benzenesulfonyl) -2- (4-Methylpiperazine-1-yl)-methyl-1H-indole.

Using essentially the same procedure as described in example 1, above derivative was prepared, using corresponding 1-unsubstituted indole. IR spectra (cm^{-1}) : 1168, 1284, 1367, 1448; Mass (m/z) : 400 ($M+H$)⁺; ¹H-NMR (δ , ppm) : 2.26 (3H, s), 2.31 -

2.55 (8H, m), 3.81 (3H, s), 3.83 (2H, s), 6.48 (1H, s), 6.87 - 6.91 (2H, m), 7.38-7.42 (2H, m), 7.49 - 7.51 (1H, m), 7.98 - 8.47 (3H, m).

Example - 47 : 5-methoxy -1-(4'-Bromobenzenesulfonyl)-2-(4-Methylpiperazine-1-yl)-methyl)-1H-indole.

- 5 Using essentially the same procedure as described in example 1, above derivative was prepared, using corresponding 1-unsubstituted indole. IR spectra (cm^{-1}): 1169, 1209, 1370, 1476; Mass (m/z): 478, 480 ($M+H$)⁺; ¹H-NMR (δ , ppm) : 2.30 (3H, s), 2.35-2.59 (8H, m), 3.81 (3H, s), 3.82 (2H, s), 6.48 (1H, s), 6.88-6.91 (2H, m), 7.51 - 7.55 (2H, m), 7.93-7.96 (3H, m).

- 10 Example - 48 : 5-methoxy -1-(3'-Trifluoro methyl-benzenesulfonyl)-2-(4-methylpiperazine-1-yl)-methyl)-1H-indole.

Using essentially the same procedure as described in example 1, above derivative was prepared, using corresponding 1-unsubstituted indole. Melting range ($^{\circ}\text{C}$) : 99.5-101.5; IR spectra (cm^{-1}) : 1172, 1210, 1375, 1476; Mass (m/z) : 468 ($M+H$)⁺; ¹H-NMR

- 15 (δ , ppm) : 2.23 (3H, s), 2.29-2.54 (8H, m), 3.82 (5H, s), 3.84 (3H, s), 6.50 (1H, s), 6.90-6.93 (2H, m), 7.53-7.57 (1H, t), 7.77-7.79 (1H, d), 7.95-7.97 (1H, d), 8.21-8.25 (2H, m).

Example - 49 : (1-(4'-Bromobenzenesulfonyl-5-methyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone.

- 20 Using essentially the same procedure as described in example 1, above derivative was prepared, using corresponding 1-unsubstituted indole. Melting range ($^{\circ}\text{C}$) : 76.8-79.7; IR spectra (cm^{-1}) : 1182, 1263, 1375, 1640; Mass (m/z) : 476, 478 ($M+H$)⁺; ¹H-NMR (δ , ppm) : 2.35 (3H, s), 2.39 (3H, s), 2.44-2.55 (4H, m), 3.44 (2H, bs), 3.86 (2H, bs), 6.61 (1H, s), 7.15-7.18 (1H, dd), 7.29 (1H, s), 7.55-7.58 (2H, dd), 7.84-7.87 (1H, d), 7.95-7.98 (2H, dd).

Example - 50 : (1-(4'-Bromobenzenesulfonyl-5-methoxy-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone.

Using essentially the same procedure as described in example 1, above derivative was prepared, using corresponding 1-unsubstituted indole. IR spectra (cm^{-1}) : 1164,

- 30 1221, 1376, 1639; Mass (m/z) : 492, 494, ($M+H$)⁺; ¹H-NMR (δ , ppm) : 2.34 (3H, s), 2.45-2.54 (4H, m), 3.44 (2H, bs), 3.80 (3H, s), 3.85 (2H, bs), 6.62 (1H, s), 6.93-6.97 (2H, m), 7.54-7.57 (2H, dd), 7.86-7.89 (1H, d), 7.93-7.96 (2H, dd).

Example - 51 : (1-(4'-Fluorobenzenesulfonyl-5-methoxy-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone.

- 35 Using essentially the same procedure as described in example 1, above derivative was prepared. Melting range ($^{\circ}\text{C}$): 77-87.4, IR spectra (cm^{-1}) : 1163, 1223, 1375, 1639. Mass (m/z) : 432, 434, ($M+H$)⁺; ¹H-NMR (δ , ppm) : 2.35 (3H, s), 2.46-2.55

(4H, m), 3.45 (2H, bs), 3.80 (3H, s), 3.86 (2H, bs), 6.62 (1H, s), 6.93-6.97 (2H, m), 7.07-7.12 (2H, dd), 7.87-7.89 (1H, d), 8.11-8.14 (2H, m).

Example - 52 : 3-Chloro-5-methoxy-1-(2'-bromobenzenesulfonyl)-2-yl-(4-methylpiperazine-1-yl-methyl)-1H-indole

5 Using essentially the same procedure as described in example 1, above derivative was prepared. IR spectra (cm^{-1}) : 1169, 1213, 1368, 1453; Mass (m/z) : 512, 514, 516 ($M+H$)⁺; ¹H-NMR (δ , ppm) : 2.04 (3H, s), 2.02-2.45 (8H, m), 3.85 (3H, s), 3.88 (2H, s), 6.92-7.19 (2H, m), 7.20-7.39 (3H, m), 7.71-7.72 (1H, dd), 7.75-7.98 (1H, d).

Example - 53 : (1-(4'-Methoxy)benzenesulfonyl-5-methyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone.

10 Using essentially the same procedure as described in example 1, above derivative was prepared, using corresponding 1-unsubstituted indole. IR spectra (cm^{-1}) : 1169, 1267, 1366, 1634; Mass (m/z) : 428 ($M+H$)⁺; ¹H-NMR (δ , ppm) : 2.34 (3H, s), 2.39 (3H, s), 2.51-2.54 (4H, bm), 3.42-3.49 (2H, bs), 3.77 (3H, s), 3.84-3.86 (2H, bs), 6.58 (1H, s), 6.85-6.89 (2H, m), 7.14-7.16 (1H, dd), 7.26-7.28 (1H, d), 7.87-7.89 (1H, d), 8.02-8.06 (2H, m).

Example - 54 : (1-(3'-Trifluoromethyl)benzenesulfonyl-5-isopropyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone.

20 Using essentially the same procedure as described in example 1, above derivative was prepared, using corresponding 1-unsubstituted indole. IR spectra (cm^{-1}) : 1172, 1326, 1380, 1644; Mass (m/z) : 494 ($M+H$)⁺; ¹H-NMR (δ , ppm) : 1.24-1.26 (6H, d), 2.35 (3H, s), 2.45-2.56 (4H, bm), 2.93-3.00 (1H, sep.), 3.48 (2H, bs), 3.87 (2H, bs), 6.64 (1H, s), 7.24-7.26 (1H, dd), 7.35-7.358 (1H, d), 7.59-7.63 (1H, t), 7.77-7.79 (1H, d), 7.88-7.90 (1H, d), 8.39-8.41 (1H, d), 8.44 (1H, s).

25 Example - 55 : (1-(4'-Isopropyl)benzenesulfonyl-5-isopropyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone.

Using essentially the same procedure as described in example 1, above derivative was prepared, using corresponding 1-unsubstituted indole. IR spectra (cm^{-1}) : 1172, 1262, 1373, 1644; Mass (m/z) : 468 ($M+H$)⁺.

30 Example - 56 : (1-Benzenesulfonyl-5-isopropyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone.

Using essentially the same procedure as described in example 1, above derivative was prepared, using corresponding 1-unsubstituted indole. IR spectra (cm^{-1}) : 1173, 1218, 1374, 1644; Mass (m/z) : 426 ($M+H$)⁺; ¹H-NMR (δ , ppm) : 1.23-1.26 (6H, d), 2.34 (3H, s), 2.45-2.55 (4H, bm), 2.92-2.99 (1H, sep.), 3.46-3.48 (2H, bs), 3.87 (2H, bs), 6.62 (1H, s), 7.20-7.26 (2H, m), 7.340-7.343 (1H, d), 7.43-7.52 (3H, m), 7.89-7.91 (1H, d), 8.13-8.15 (2H, m).

Example - 57 : (1-(4'-Fluoro)benzenesulfonyl-5-isopropyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone.

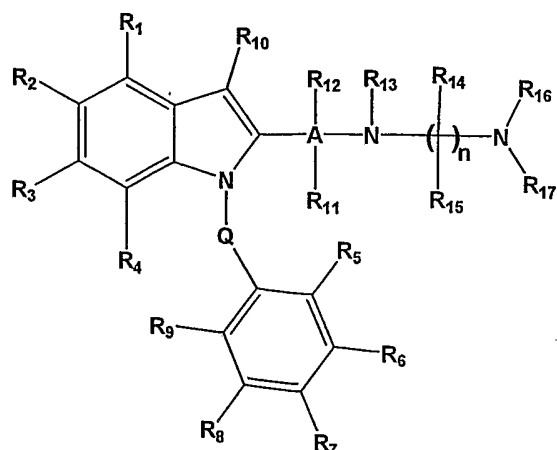
Using essentially the same procedure as described in example 1, above derivative was prepared, using corresponding 1-unsubstituted indole. IR spectra (cm^{-1}) : 1174, 1218, 1377, 1642; Mass (m/z) : 444 ($M+H$)⁺ ; ¹H-NMR (δ , ppm) : 1.24-1.26 (6H, d), 2.34 (3H, s), 2.44-2.55 (4H, bm), 2.92-2.99 (1H, sep.), 3.46-3.49 (2H, bs), 3.86 (2H, bs), 6.62 (1H, s), 7.09-7.13 (2H, m), 7.21-7.26 (1H, m), 7.34-7.35 (1H, d), 7.87-7.90 (1H, d), 8.16-8.20 (2H, m).

Example - 58 : (1-Benzenesulfonyl-6,7-dimethyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone.

Using essentially the same procedure as described in example 1, above derivative was prepared, using corresponding 1-unsubstituted indole. IR spectra (cm^{-1}) : 1175, 1218, 1377, 1640; Mass (m/z) : 412 ($M+H$)⁺ .

We Claim,

1. A compound of the general formula (I),

**General Formula (I)**

- 5 wherein A may be either a $-\text{CR}_{11}\text{R}_{12}-$, $-\text{C}=\text{O}$, $-\text{SO}_2-$, $-(\text{CO})\text{NH}-$ or $-\text{C}=\text{S}$ group;
Q may be either a $-\text{CR}_{11}\text{R}_{12}-$, $-\text{C}=\text{O}$, $-\text{SO}_2-$, $-(\text{CO})\text{NH}-$ or $-\text{C}=\text{S}$ group;
R₁, R₂, R₃, R₄, R₅, R₆, R₇, R₈, R₉, R₁₀, R₁₁, R₁₂, R₁₄ and R₁₅ may be same or
different and each independently represent hydrogen, halogen, oxo, thio,
perhaloalkyl, hydroxy, amino, nitro, cyano, formyl, amidino, guanidino, substituted
10 or unsubstituted groups selected from linear or branched (C₁-C₁₂)alkyl, (C₂-
C₁₂)alkenyl, (C₂-C₁₂)alkynyl, (C₃-C₇)cycloalkyl, (C₃-C₇)cycloalkenyl, bicycloalkyl,
bicycloalkenyl, (C₁-C₁₂)alkoxy, cyclo(C₃-C₇)alkoxy, aryl, aryloxy, aralkyl, aralkoxy,
heterocyclyl, heteroaryl, heterocyclylalkyl, heteroaralkyl, heteroaryloxy,
heteroaralkoxy, heterocyclylalkyloxy, acyl, acyloxy, acylamino, monoalkylamino,
15 dialkylamino, arylamino, diarylamino, aralkylamino, alkoxycarbonyl,
aryloxycarbonyl, aralkoxycarbonyl, heterocyclylalkoxycarbonyl,
heteroaryloxycarbonyl, hydroxyalkyl, aminoalkyl, monoalkylaminoalkyl,
dialkylaminoalkyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl,
alkoxycarbonylamino, aryloxycarbonylamino, aralkyloxycarbonylamino,
20 aminocarbonylamino, alkylaminocarbonylamino, dialkylaminocarbonylamino,
alkylamidino, alkylguanidino, dialkylguanidino, hydrazino, hydroxylamino,
carboxylic acid and its derivatives, sulfonic acids and its derivatives, phosphoric
acid and its derivatives; or the adjacent groups like R₁ and R₂ or R₂ and R₃ or R₃
and R₄ or R₅ and R₆ or R₆ and R₇ or R₇ and R₈ or R₈ and R₉ together with carbon
25 atoms to which they are attached may form a five or a six membered ring,
optionally containing one or more double bonds and optionally containing one or
more heteroatoms selected from "Oxygen", "Nitrogen", "Sulfur" or "Selenium" and
combinations of double bond and heteroatoms; or R₁₁ and R₁₂ together with the
carbon atoms to which they are attached may form a three to six membered ring,

optionally containing one or more double bonds and optionally containing one or more heteroatoms selected from "Oxygen", "Nitrogen", "Sulfur" or "Selenium" and combinations of double bond and heteroatoms;

5 R₁₃, R₁₆ and R₁₇ may be same or different and each independently represents hydrogen, substituted or unsubstituted groups selected from linear or branched (C₁-C₁₂)alkyl, (C₂-C₁₂)alkenyl, (C₂-C₁₂)alkynyl, (C₃-C₇)cycloalkyl, (C₃-C₇)cycloalkenyl, bicycloalkyl, bicycloalkenyl, aryl, aralkyl, heteroaryl, heterocyclalkyl; optionally R₁₃ along with either R₁₆ or R₁₇ and the two nitrogen atoms may form a 5 to 7-membered heterocyclic ring, which may be further
10 substituted with R₁₄ and R₁₅, and may have either one, two or three double bonds; and

"n" is an integer ranging from 1 to 4, wherein the carbon chains which "n" represents may be either linear or branched.

2. A compound according to Claim -1 which is selected from :
 - 15 1-Benzenesulfonyl-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
 - 1-(4-Fluorobenzenesulfonyl)-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
 - 1-(4-Isopropylbenzenesulfonyl)-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
 - 1-(4-Methoxybenzenesulfonyl)-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
 - 1-(2-Bromo-4-methoxybenzenesulfonyl)-2-(4-methylpiperazin-1-ylmethyl)-1H-
20 indole;
 - 1-(4-Methoxybenzenesulfonyl)-5-methoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
 - 1-(4-Methoxybenzenesulfonyl)-5-methoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole Hydrochloride salt;
 - 25 1-(4-Isopropylbenzenesulfonyl)-5-methoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
 - 3-Chloro-1-(4-isopropylbenzenesulfonyl)-5-methoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
 - 1-(4-Isopropylbenzenesulfonyl)-5-methoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-
30 indole Hydrochloride salt;
 - 3-Chloro-1-(4-methoxybenzenesulfonyl)-5-methoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
 - 3-Chloro-1-(4-methoxybenzenesulfonyl)-5-methoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole Hydrochloride salt;
 - 35 1-(2-Bromobenzenesulfonyl)-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
 - 1-(2-Bromobenzenesulfonyl)-3-chloro-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;

- N-(1-Benzenesulfonyl-1H-indol-2-yl)methyl-N,N',N'-trimethylethylene-1,2-diamine;
N-(1-Benzenesulfonyl)-3-bromo-1H-indol-2-yl)methyl-N,N',N'-trimethylethylene-
1,2-diamine;
N-(1-(4-Methylbenzenesulfonyl)-1H-indol-2-yl)methyl-N,N',N'-trimethylethylene-
1,2-diamine;
1-(2-Bromo-4-methoxybenzenesulfonyl-1H-indol-2-yl)methyl-N,N',N'-
trimethylethylene-1,2-diamine;
1-(2-Bromo-4-methoxybenzenesulfonyl-3-chloro-1H-indol-2-yl)methyl-N,N',N'-
trimethylethylene-1,2-diamine, hydrochloride;
[1-Benzenesulfonyl-1H-indol-2-yl]-(4-methylpiperazin-1-yl)methanone;
[1-(4-Fluorobenzenesulfonyl)-1H-indol-2-yl]-(4-methylpiperazin-1-yl)methanone;
[1-(4-Isopropylbenzenesulfonyl)-1H-indol-2-yl]-(4-methylpiperazin-1-
yl)methanone;
[1-(4-Methoxybenzenesulfonyl)-1H-indol-2-yl]-(4-methylpiperazin-1-
yl)methanone;
[1-(2-Bromo-4-methoxybenzenesulfonyl)-1H-indol-2-yl]-(4-methylpiperazin-1-
yl)methanone;
[1-(4-Methoxybenzenesulfonyl)-5-methoxy-1H-indol-2-yl]-(4-methylpiperazin-1-
yl)methanone;
[1-(4-Isopropylbenzenesulfonyl)-5-methoxy-1H-indol-2-yl]-(4-methylpiperazin-1-
yl)methanone;
[3-Chloro-1-(4-isopropylbenzenesulfonyl)-5-methoxy-1H-indol-2-yl]-(4-
methylpiperazin-1-yl)methanone;
[3-Chloro-1-(4-Methoxybenzenesulfonyl)-5-methoxy-1H-indol-2-yl]-(4-
methylpiperazin-1-yl)methanone;
[1-(2-Bromobenzenesulfonyl)-1H-indol-2-yl]-(4-methylpiperazin-1-yl)methanone;
[1-(2-Bromobenzenesulfonyl)-3-chloro-1H-indol-2-yl]-(4-methylpiperazin-1-
yl)methanone;
1-Benzenesulfonyl-1H-indole-2-carboxylic acid (2-dimethylaminoethyl)-N-
methylamide;
1-Benzenesulfonyl-3-bromo-1H-indole-2-carboxylic acid (2-dimethylaminoethyl)-
N-methylamide;
N-(1-(4-Methylbenzenesulfonyl)-3-bromo-1H-indole-2-carboxylic acid (2-
dimethylaminoethyl)-N-methylamide;
1-(2-Bromo-4-methoxybenzenesulfonyl-1H-indole-2-carboxylic acid (2-
dimethylaminoethyl)-N-methylamide;
1-(2-Bromo-4-methoxybenzenesulfonyl-3-bromo-1H-indole-2-carboxylic acid (2-

- dimethylaminoethyl)-N-methylamide;
 (1-Benzenesulfonyl-5-methoxy-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-
 methanone;
 (1-(4'-Fluoro - benzenesulfonyl-5-methyl-1H-indole-2-yl)-(4-Methylpiperazine-1-
 5 yl)-methanone;
 (1-(4'-trifluoromethyl)benzenesulfonyl-5-methoxy-1H-indole-2-yl)-(4-
 Methylpiperazine-1-yl)-methanone;
 (1-(3'-trifluoromethyl)benzenesulfonyl-5-methyl-1H-indole-2-yl)-(4-
 Methylpiperazine-1-yl)-methanone;
 10 (1-(Benzenesulfonyl-5-ethoxy-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-
 methanone;
 (1-(4'-Isopropylbenzenesulfonyl-5-ethoxy-1H-indole-2-yl)-(4-Methylpiperazine-1-
 yl)-methanone;
 (1-Benzenesulfonyl-5-thiomethyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-
 15 methanone;
 (1-(4'-Fluorobenzenesulfonyl-5-thiomethyl-1H-indole-2-yl)-(4-Methylpiperazine-1-
 yl)-methanone;
 (1-(4'-Isopropylbenzenesulfonyl-5-thiomethyl-1H-indole-2-yl)-(4-Methylpiperazine-
 1-yl)-methanone;
 20 (1-(3'-trifluoromethyl)benzenesulfonyl-5-thiomethyl-1H-indole-2-yl)-(4-
 Methylpiperazine-1-yl)-methanone;
 5-methoxy -1-(Benzenesulfonyl) -2- (4-Methylpiperazine-1-yl)-methyl)-1H-indole;
 5-methoxy -1-(4'-Bromobenzenesulfonyl) -2- (4-Methylpiperazine-1-yl)-methyl)-
 1H-indole;
 25 5-methoxy -1-(3'-Trifluoro methylbenzenesulfonyl)-2-(4-methylpiperazine-1-yl)-
 methyl)-1H-indole;
 (1-(4'-Bromo-benzenesulfonyl-5-methyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-
 methanone;
 (1-(4'-Bromobenzenesulfonyl-5-methoxyl-1H-indole-2-yl)-(4-Methylpiperazine-1-
 30 yl)-methanone;
 (1-(4'-Fluoro-benzenesulfonyl-5-methoxyl-1H-indole-2-yl)-(4-Methylpiperazine-1-
 yl)-methanone;
 3-Chloro-5-methoxy-1-(2'-bromobenzenesulfonyl)-2-yl-(4-methylpiperazine-1-yl
 methyl)-1H-indole;
 35 (1-(4'-Methoxy)benzenesulfonyl-5-methyl-1H-indole-2-yl)-(4-Methylpiperazine-1-
 yl)-methanone;

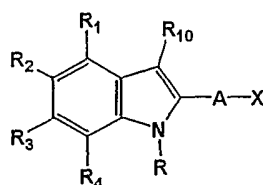
- (1-(3'-Trifluoromethyl)benzenesulfonyl-5-isopropyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;
- (1-(4'-Isopropyl)benzenesulfonyl-5-isopropyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;
- 5 (1-Benzenesulfonyl-5-isopropyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;
- (1-(4'-Fluoro)benzenesulfonyl-5-isopropyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;
- (1-Benzenesulfonyl-6,7-dimethyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;
- 10 1-Benzenesulfonyl-5-ethyl-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(4-Fluorobenzenesulfonyl)-5-ethyl-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(4-Isopropylbenzenesulfonyl)-5-ethyl-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 15 1-(4-Methoxybenzenesulfonyl)-5-ethyl-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(2-Bromo-4-methoxybenzenesulfonyl)-5-ethyl-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-Benzenesulfonyl-5-isopropoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 20 1-(4-Fluorobenzenesulfonyl)-5-isopropoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(4-Isopropylbenzenesulfonyl)-5-isopropoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(4-Methoxybenzenesulfonyl)-5-isopropoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 25 1-(2-Bromo-4-methoxybenzenesulfonyl)-5-isopropoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-Benzenesulfonyl-5-ethylthio-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(4-Fluorobenzenesulfonyl)-5-ethylthio-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 30 1-(4-Isopropylbenzenesulfonyl)-5-ethylthio-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(4-Methoxybenzenesulfonyl)-5-ethylthio-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 35 1-(2-Bromo-4-methoxybenzenesulfonyl)-5-ethylthio-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-Benzenesulfonyl-5-benzyloxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;

- 1-(4-Fluorobenzenesulfonyl)-5-benzyloxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(4-Isopropylbenzenesulfonyl)-5-benzyloxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 5 1-(4-Methoxybenzenesulfonyl)-5-benzyloxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(2-Bromo-4-methoxybenzenesulfonyl)-5-benzyloxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-Benzenesulfonyl-5-cyclopentyloxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 10 1-(4-Fluorobenzenesulfonyl)-5-cyclopentyloxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(4-Isopropylbenzenesulfonyl)-5-cyclopentyloxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(4-Methoxybenzenesulfonyl)-5-cyclopentyloxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 15 1-(2-Bromobenzenesulfonyl)-5-cyclopentyloxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-Benzenesulfonyl-3-bromo-5-ethoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(4-Fluorobenzenesulfonyl)-3-bromo-5-ethoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 20 1-(4-Isopropylbenzenesulfonyl)-3-bromo-5-ethoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(4-Methoxybenzenesulfonyl)-3-bromo-5-ethoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 25 1-(2-Bromobenzenesulfonyl)-3-bromo-5-ethoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-Benzenesulfonyl-3-chloro-5-ethoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(4-Fluorobenzenesulfonyl)-3-chloro-5-ethoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 30 1-(4-Isopropylbenzenesulfonyl)-3-chloro-5-ethoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(4-Methoxybenzenesulfonyl)-3-chloro-5-ethoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 1-(2-Bromobenzenesulfonyl)-3-chloro-5-ethoxy-2-(4-methylpiperazin-1-ylmethyl)-1H-indole;
- 35 1-(4'-Bromo-benzenesulfonyl-5-ethyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;

- (1-(2'-Bromo-benzenesulfonyl-5-ethyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;
- (1-(4'-trifluoromethylbenzenesulfonyl-5-ethyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;
- 5 (1-(4'-trifluoromethylbenzenesulfonyl-5-ethoxyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone; and
- (1-(4'-fluorobenzenesulfonyl-5-ethoxyl-1H-indole-2-yl)-(4-Methylpiperazine-1-yl)-methanone;
- and their pharmaceutically acceptable salts, polymorphs and solvates.
- 10 3. A pharmaceutical composition comprising either of a pharmaceutically acceptable carrier, diluent, excipients or solvate along with a therapeutically effective amount of a compound according to Claim-1, its derivatives, its analogs, its tautomeric forms, its stereoisomers, its geometric forms, its N-oxides, its polymorphs, its pharmaceutically acceptable salts, or its pharmaceutically acceptable solvates.
- 15 4. A pharmaceutical composition according to Claim-3, in the form of a tablet, capsule, powder, syrup, injectible, solution or suspension.
5. Use of compound of general formula (I), as defined in Claim-1 or a pharmaceutical composition as defined in Claim-3 for preparing medicaments.
6. Use of compound of general formula (I), as defined in Claim-1 or a pharmaceutical composition as defined in Claim-3 for the treatment where a modulation of 5-HT activity is desired.
- 20 7. Use of a compound as claimed in Claim-1 for the manufacture of a medicament for the treatment and/or prevention of clinical conditions for which a selective action on 5-HT receptors is indicated.
- 25 8. Use of a compound as claimed in Claim-1 for the treatment and/or prevention of clinical conditions such as anxiety, depression, convulsive disorders, obsessive-compulsive disorders, migraine headache, cognitive memory disorders, ADHD (Attention Deficient Disorder/ Hyperactivity Syndrome), personality disorders, psychosis, paraphrenia, psychotic depression, mania, schizophrenia, schizophreniform disorders, withdrawal from drug abuse, panic attacks, sleep disorders and also disorders associated with spinal trauma and /or head injury.
- 30 9. Use of a compound as claimed in Claim-1 for the treatment of mild cognitive impairment and other neurodegenerative disorders like Alzheimer's disease, Parkinsonism and Huntington's chorea.
- 35 10. Use of a compound as claimed in Claim-1 for the treatment of certain GI (Gastrointestinal) disorders such as IBS (Irritable bowel syndrome) or chemotherapy induced emesis.

11. Use of a compound as claimed in Claim-1 to reduce morbidity and mortality associated with the excess weight.
12. Use of a radiolabelled compound as claimed in Claim-1, as a diagnostic tool for modulating 5-HT receptor function.
- 5 13. Use of a compound as claimed in Claims 1 in combination with a 5-HT re-uptake inhibitor, and / or a pharmaceutically acceptable salt thereof.
14. A compound of the general formula (1), its derivatives, its analogs, its tautomeric forms, its stereoisomers, its polymorphs, its pharmaceutically acceptable salts and its pharmaceutically acceptable solvates for preparing a medicament.
- 10 15. A method for the treatment and/or prophylaxis of clinical conditions such as anxiety, convulsive disorders, obsessive-compulsive disorders, migraine headache, cognitive memory disorders, ADHD (Attention Deficient Disorder/ Hyperactivity Syndrome), personality disorders, psychosis, paraphrenia, psychotic depression, mania, schizophrenia, schizophreniform disorders,
- 15 withdrawal from drug abuse, panic attacks, sleep disorders and also disorders associated with spinal trauma and /or head injury, which comprises administering to a patient in need thereof, an effective amount of a compound of general formula (I) as claimed in Claim-1.
16. A method for the treatment and/or prophylaxis of mild cognitive impairment and other neurodegenerative disorders like Alzheimer's disease, Parkinsonism and
- 20 Huntington's chorea which comprises administering to a patient in need thereof, an effective amount of a compound of general formula (I) as claimed in Claim-1.
17. A method for the treatment of certain GI (Gastrointestinal) disorders such as IBS (Irritable bowel syndrome) or chemotherapy induced emesis using a compound
- 25 of general formula (I) as claimed in Claim-1.
18. A method to reduce morbidity and mortality associated with the excess weight using a compound of general formula (I) as claimed in Claim-1.
19. A process for the preparation of compound of formula (I), which comprises of anyone of the following schemes:

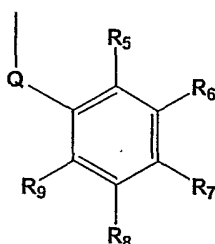
30 **Scheme - 1** : reacting a compound of formula (II) given below,



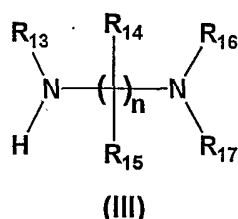
(II)

where R₁, R₂, R₃, R₄, R₁₀ and A are as defined in relation to formula (I), X is halogeno, for example, a chloro, bromo or iodo; R represents either of a suitable

N-protecting group such as acetyl, trifluoroacetyl, trityl, t-butyloxycarbonyl (t-BOC) or a group such as,



5 where R₅, R₆, R₇, R₈ and R₉ are as defined earlier; with a compound of formula (III) or its acid addition salt,

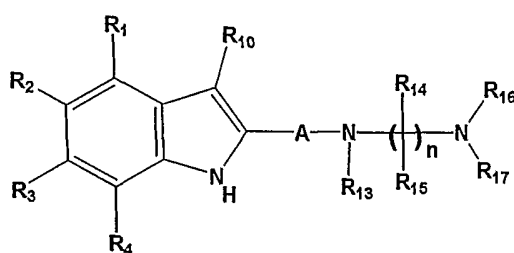


where R₁₃, R₁₄, R₁₅, R₁₆ and R₁₇ are as defined in relation to compound of formula (I) or precursor thereof; and thereafter if necessary:

- 10 i) converting a compound of the formula (I) into another compound of the formula (I); and/or,
 ii) removing any protecting groups; and/or,
 iii) forming a pharmaceutically acceptable salt or prodrug thereof;

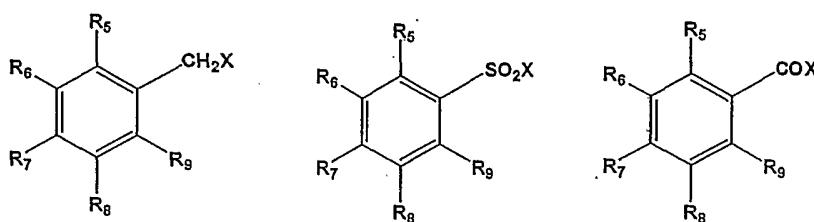
Scheme - 2 : reacting a compound of formula (IV) given below,

15 **Scheme - 3 :**



(IV)

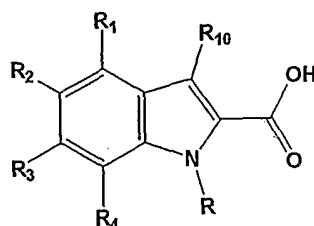
wherein A, R₁, R₂, R₃, R₄, R₁₀, R₁₃, R₁₄, R₁₅, R₁₆ and R₁₇ are as defined in relation to formula (I); with anyone of the following compound represented by a general formula (V),



(V)

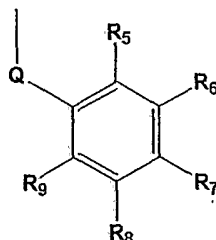
where R_5 , R_6 , R_7 , R_8 and R_9 , are as defined in relation to formula (I) and X is a halogeno, preferably chloro or bromo;

Scheme - 4 : reacting a compound of formula (VI) given below,

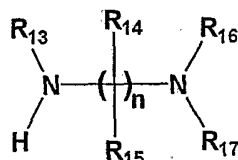


(VI)

where R_1 , R_2 , R_3 , R_4 , and R_{10} are as defined in relation to formula (I), R represents either of a suitable N-protecting group such as acetyl, trifluoroacetyl, or a group such as,



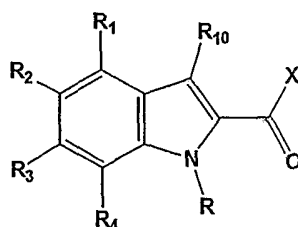
where R_5 , R_6 , R_7 , R_8 and R_9 are as defined earlier; with a compound of formula (III) or its acid addition salt,



(III)

where R_{13} , R_{14} , R_{15} , R_{16} and R_{17} are as defined in relation to compound of formula (I) or precursor thereof; by standard peptide coupling for example using bis(2-oxo-3-oxazolidinyl) phosphoric chloride (BOP-Cl);

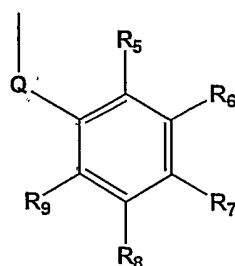
Scheme - 5 : reacting a compound of formula (VII) given below,



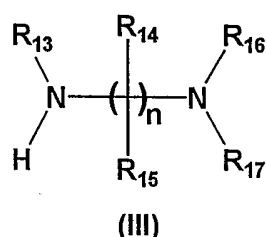
(VII)

wherein R_1 , R_2 , R_3 , R_4 and R_{10} are as defined in relation to formula (I), X is a halogeno group, such as chloro, bromo or iodo; while R represents either of a suitable N-protecting group such as acetyl, trifluoroacetyl, benzyl, trityl, t-

butyloxycarbonyl (t-BOC) or a group such as,



where R_5 , R_6 , R_7 , R_8 and R_9 are as defined earlier, with a compound of formula (III) or its acid addition salt,

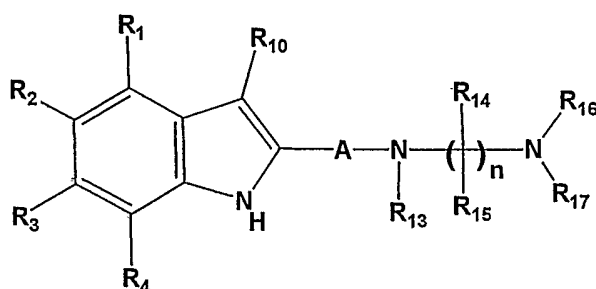


wherein R_{13} , R_{14} , R_{15} , R_{16} and R_{17} are as defined in relation to compound of formula (I) or precursor thereof; in suitable anhydrous solvent.

Scheme - 6 : few compounds of formula (I) where $A = -CH_2-$, can be obtained by carrying out chemical, catalytic or enzymatic reduction of the compounds of formula (I) where $A = -C=O$ using the known procedures.

20. A process according to Claim-19, comprising of carrying out one or more of the following optional steps: i) removing any protecting group; ii) resolving the racemic mixture into pure enantiomers by the known methods and iii) preparing a pharmaceutically acceptable salt of a compound of formula (I) and/or iv) preparing a pharmaceutically acceptable prodrug thereof.

21. The novel intermediate of general formula (IV) is defined as below,



wherein A may be either a $-CR_{11}R_{12}-$, $-C=O$, $-SO_2-$, $-(CO)NH-$ or $-C=S$ group, R_1 , R_2 , R_3 , R_4 , R_{10} , R_{11} , R_{12} , R_{14} and R_{15} may be same or different and each independently represent hydrogen, halogen, oxo, thio, perhaloalkyl, hydroxy, amino, nitro, cyano, formyl, amidino, guanidino, substituted or unsubstituted groups selected from linear or branched (C_1-C_{12}) alkyl, (C_2-C_{12}) alkenyl, $(C_2-$

C₁₂)alkynyl, (C₃-C₇)cycloalkyl, (C₃-C₇)cycloalkenyl, bicycloalkyl, bicycloalkenyl,
 (C₁-C₁₂)alkoxy, cyclo(C₃-C₇)alkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl,
 heteroaryl, heterocyclalkyl, heteroaralkyl, heteroaryloxy, heteroaralkoxy,
 heterocyclalkyloxy, acyl, acyloxy, acylamino, monoalkylamino, dialkylamino,
 5 arylamino, diarylamino, aralkylamino, alkoxycarbonyl, aryloxycarbonyl,
 aralkoxycarbonyl, heterocyclalkoxycarbonyl, heteroaryloxycarbonyl,
 hydroxyalkyl, aminoalkyl, monoalkylaminoalkyl, dialkylaminoalkyl, alkoxyalkyl,
 aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl, alkoxycarbonylamino,
 aryloxycarbonylamino, aralkyloxycarbonylamino, aminocarbonylamino,
 10 alkylaminocarbonylamino, dialkylaminocarbonylamino, alkylamidino,
 alkylguanidino, dialkylguanidino, hydrazino, hydroxylamino, carboxylic acid and
 its derivatives, sulfonic acids and its derivatives, phosphoric acid and its
 derivatives; or the adjacent groups like R₁ and R₂ or R₂ and R₃ or R₃ and R₄
 together with carbon atoms to which they are attached may form a five or a six
 15 membered ring, optionally containing one or more double bonds and optionally
 containing one or more heteroatoms selected from "Oxygen", "Nitrogen", "Sulfur"
 or "Selenium" and combinations of double bond and heteroatoms; or R₁₁ and R₁₂
 together with the carbon atoms to which they are attached may form a three to
 six membered ring, optionally containing one or more double bonds and
 20 optionally containing one or more heteroatoms selected from "Oxygen",
 "Nitrogen", "Sulfur" or "Selenium" and combinations of double bond and
 heteroatoms;
 R₁₃, R₁₆ and R₁₇ may be same or different and each independently represents
 hydrogen, substituted or unsubstituted groups selected from linear or branched
 25 (C₁-C₁₂)alkyl, (C₂-C₁₂)alkenyl, (C₂-C₁₂)alkynyl, (C₃-C₇)cycloalkyl, (C₃-
 C₇)cycloalkenyl, bicycloalkyl, bicycloalkenyl, aryl, aralkyl, heteroaryl,
 heterocyclalkyl; alternatively R₁₃ along with either R₁₆ or R₁₇ and the two
 nitrogen atoms may form a 5-, 6- or 7- membered heterocyclic ring, which may
 be further substituted with R₁₄ and R₁₅, and may have either one, two or three
 30 double bonds, with the proviso that, When R₁₃ along with R₁₆ together with the
 intervening nitrogens form a piperazine or a substituted piperazine ring, then R₁₇
 is never aryl substituent; and "n" is an integer ranging from 1 to 4, wherein the
 carbon chains which "n" represents may be either linear or branched.

35

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IN2004/000154

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D209/14 C07D209/30 C07D209/42 A61K31/405 A61K31/4045
A61P25/00

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, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 1 314 733 A1 (AVENTIS PHARMA DEUTSCHLAND GMBH, GERMANY) 28 May 2003 (2003-05-28) see e.g. compounds 57 and 141	1,3-5, 14,19,20
X	WO 02/44150 A1 (SANOFI-SYNTHELABO, FR.) 6 June 2002 (2002-06-06) see e.g. preparations 7, 8, 10 and 23	1,3-5,14
X	WO 02/24685 A (LE BAUT GUILLAUME ; ABDALA HIAM (FR); LE BORGNE MARC (FR); LE PAPE PAT) 28 March 2002 (2002-03-28) see compound on p. 6, l. 11 and/ in connection with process on p. 22	1,3-5, 14,19-21
X	US 6 184 244 B1 (KARANEWSKY, DONALD S. ET AL) 6 February 2001 (2001-02-06) see e.g. examples 22, 23 and 24	1,3-5, 14,19,20
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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.

& document member of the same patent family

Date of the actual completion of the international search

4 October 2004

Date of mailing of the international search report

11/10/2004

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Traegler-Goeldel, M

INTERNATIONAL SEARCH REPORT

In ternational Application No
PCT/IN2004/000154

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99/57113 A1 (ZENECA LIMITED, UK AVENTIS PHARMA DEUTSCHLAND G.M.B.H., GERMANY) 11 November 1999 (1999-11-11) see examples 7 and 10 and its intermediates -----	1,14, 19-21
X	WO 99/07351 A2 (ZENECA LIMITED, UK) 18 February 1999 (1999-02-18) see e.g. example 7 -----	1,3-5, 14,19-21
X	WO 99/33800 A1 (HOECHST MARION ROUSSEL DEUTSCHLAND GMBH, GERMANY) 8 July 1999 (1999-07-08) see example 81 -----	1,3-5, 14,19,20
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X	US 2003/100757 A1 (FLIRI, ANTON FRANZ JOSEF ET AL) 29 May 2003 (2003-05-29) e.g. examples 1-21 -----	21
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X	WO 96/39384 A1 (PFIZER, INC., USA; HULIN, BERNARD; HOOVER, DENNIS J.; TREADWAY, JUDITH) 12 December 1996 (1996-12-12) see many examples, i.a. 13, 16-18, 22, 23, 25, 29, 32, 68 -----	21
X	WO 91/09849 A1 (UPJOHN CO., USA) 11 July 1991 (1991-07-11) many examples, see i.e. preparations 10, 17, 22, 39, 44-46, 74, 129 and inter alia examples 10, 11, 16, 17, 19, 20, 21-25, 28, 31-39, 101, 102 -----	21
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X	GB 1 400 934 A (HOFFMANN-LA ROCHE, F., UND CO., A.-G.) 23 July 1975 (1975-07-23) see e.g. the starting materials of examples 16, 25-27, 29, 30, 32-35 -----	21
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INTERNATIONAL SEARCH REPORT

International Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 02/32863 A (BIOVITRUM AB ; JOHANSSON GARY (SE); CALDIROLA PATRIZIA (SE); NILSSON B) 25 April 2002 (2002-04-25) see formula (I) and activity -----	2
A	WO 01/14330 A (TULP MARTINUS T M ; VLIET BERNARD J VAN (NL); HES ROELOF VAN (NL); TIP) 1 March 2001 (2001-03-01) see formula (I) and activity -----	2
A	WO 01/96328 A (BANG ANDERSEN BENNY ; FELDING JAKOB (DK); ANDERSEN KIM (DK); KEHLER JA) 20 December 2001 (2001-12-20) see formula (I) and activity -----	2

INTERNATIONAL SEARCH REPORT

national application No.
PCT/IN2004/000154

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 6, 8-13 and 15-18 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
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PCT/IN2004/000154

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