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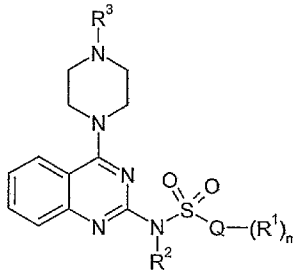
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(54) **Title:** NOVEL QUINAZOLINES AS 5-HT6 MODULATORS



I

(57) **Abstract:** The present invention relates to new compounds of formula I, [Chemical formula should be inserted here. Please see paper copy] I or salts, solvates or solvated salts thereof, wherein Q, R^1, R^2, R^3 and n are defined as in claim 1, processes for their preparation and to new intermediates used in the preparation thereof, pharmaceutical formulations containing said compounds and to the use of said compounds in therapy.

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NOVEL QUINAZOLINES AS 5-HT6 MODULATORS

TECHNICAL FIELD OF INVENTION

The present invention relates to new compounds, to pharmaceutical formulations containing said compounds and to the use of said compounds in therapy. The present invention further relates to processes for the preparation of said compounds and to new intermediates useful in the preparation thereof.

BACKGROUND OF THE INVENTION

Serotonin (5-hydroxy-tryptamine) (5-HT) receptors play an important role in many physiological and pathological functions like anxiety, sleep regulation, aggression, feeding and depression. The 5-HT receptors are distributed throughout the body and can be divided into seven different 5-HT receptor subtypes, i.e. 5-HT1, 5-HT2, 5-HT3, 5-HT4, 5-HT5, 5-HT6, and 5-HT7, with different properties.

The 5-HT6 receptor is mostly found in the central nervous system (CNS). From *in situ* hybridization studies it is known that the 5-HT6 receptor in rat brain is localized in areas like striatum, nucleus accumbens, olfactory tubercle and hippocampal formation (Ward et al., Neuroscience, 64, p 1105-1111, 1995).

Scientific research has revealed a potential therapeutic use for modulators of the 5-HT6 receptor, especially with regard to various CNS disorders. Blocking 5-HT6 receptor function has been shown to enhance cholinergic transmission (Bentley et al, Br J Pharmacol 126: 1537-1542).

Studies have shown that 5-HT6 antagonists increase levels of glutamate and aspartate in the frontal cortex and dorsal hippocampus as well as acetylcholine in the frontal cortex. These neurochemicals are known to be involved in memory and cognition (Dawson et al., Neuropsychopharmacology, 25(5), p 662-668, 2001) (Gerard et al., Brain Res., 746, p 207-219, 1997) (Riemer et al J Med Chem 46(7), p 1273-1276, 2003).

Acetylcholinesterase inhibitors increase the levels of acetylcholine in the CNS and are used in the treatment of cognitive disorders such as Alzheimer's disease. 5-HT6 antagonists may therefore be used in the treatment of cognitive disorders.

Studies have also shown that 5-HT6 antagonist increases the level of dopamine and noradrenaline in the medial prefrontal cortex suggesting a role for 5-HT6 ligands in cognitive aspects of schizophrenia. Several antidepressants and atypical antipsychotics bind to the 5-HT6 receptor and this may be a factor in their profile of activities (Roth et al., J. Pharm. Exp. Therapeut., 268, 1402-1420, 1994; Sleight et al., Exp. Opin. Ther. Patents, 8, 1217-1224, 1998; Kohen et al., J. Neurochem., 66(1), p 47-56, 1996; Sleight et al. Brit. J. Pharmacol., 124, p 556-562, 1998; Bourson et al., Brit. J. Pharmacol., 125, p 1562-1566, 1998).

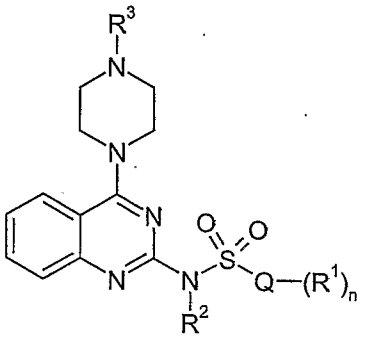
Stean et al., (Brit. J. Pharmacol. 127 Proc. Supplement 131P, 1999) have described the potential use of 5-HT6 modulators in the treatment of epilepsy. 5-HT6 receptors have also been linked to generalized stress and anxiety states (Yoshioka et al., Life Sciences, 17/18, p 1473-1477, 1998). The use of modulators for this receptor is therefore expected for a wide range of CNS disorders.

Moreover, a reduction in food intake in rats has been reported using 5-HT6 receptor modulators (Bentley et al., Br. J. Pharmacol. Suppl. 126, P66, 1999; Bentley et al. J. Psychopharmacol. Supl. A64, 255, 1997). 5-HT6 receptor modulators may therefore also be useful in the treatment of feeding disorders like anorexia, obesity, bulimia and similar disorders and also type 2 diabetes.

DETAILED DESCRIPTION OF THE INVENTION

The object of the present invention is to provide compounds exhibiting a modulating activity at the 5-hydroxy-tryptamine 6 receptor.

The present invention therefore relates to a compound having the formula I



I

wherein

Q is C_{6-10}arylC_{0-6}alkyl or C_{5-11}heteroarylC_{0-6}alkyl;

R^1 is hydroxy, halogen, C_{1-6}alkyl, C_{1-6}alkoxy, C_{6-10}arylC_{0-3}alkyl, C_{5-6}heteroarylC_{0-3}alkyl, C_{1-6}haloalkyl, R^4OC_{0-6}alkyl, cyano, $R^5SO_2C_{0-6}$alkyl, SOR^5, $R^4CON(R^4)C_{0-6}$alkyl, COR^5, $R^5CO_2C_{0-6}$alkyl, $R^5OC(O)C_{0-6}$alkyl, $(R^5)_2NCOC_{0-6}$alkyl, NO_2, C_{3-7}heterocycloalkyl or oxo;

n is 0, 1, 2 or 3;

R^2 is hydrogen, C_{1-10}alkyl, C_{1-6}haloalkyl, cyanoC_{1-6}alkyl, $(R^6)_2NCOC_{1-6}$alkyl, R^6OC_{2-6}alkyl or $R^6C(O)N(R^6)C_{1-6}$alkyl; or

R^1 and R^2 are connected to give a 5 or 6 membered heterocyclic ring;

R^3 is hydrogen, C_{1-10}alkyl, C_{1-6}haloalkyl, cyanoC_{1-6}alkyl, $(R^6)_2NCOC_{1-6}$alkyl, R^6OC_{2-6}alkyl or $R^6C(O)N(R^6)C_{1-6}$alkyl;

R^4 is hydrogen, C_{1-6}alkyl, C_{6-10}arylC_{0-3}alkyl, C_{5-6}heteroarylC_{0-3}alkyl or C_{1-3}haloalkyl;

R^5 is C_{1-6}alkyl, C_{1-6}haloalkyl, C_{6-10}arylC_{0-6}alkyl or C_{5-6}heteroarylC_{0-6}alkyl;

wherein any aryl, cycloalkyl, heterocycloalkyl or heteroaryl as defined for R^1, R^4 and R^5 may be substituted by one or more groups independently selected from hydrogen, halogen, hydroxy, C_{1-6}haloalkyl, cyano, OR^6, C_{1-6}alkyl, oxo, SR^6, $CON(R^6)_2$, $N(R^6)COR^{12}$, SO_2R^{12}, SOR^{12}, $N(R^6)_2$ and COR^6; and

R^6 is hydrogen, C_{1-6}alkyl or C_{1-6}haloalkyl;

or pharmaceutically acceptable salts, solvates or solvated salts thereof.

One embodiment of the present invention relates to a compound of formula (I) wherein
Q is $C_{6-10}arylC_{0-6}alkyl$;
R^1 is halogen, $C_{1-6}alkyl$, $C_{6-10}arylC_{0-3}alkyl$, $C_{1-6}haloalkyl$, $R^5CO_2C_{0-6}alkyl$, $R^5OC(O)C_{0-6}alkyl$ or $C_{3-7}heterocycloalkyl$;
n is 0, 1 or 2;
R^2 is hydrogen, $C_{1-10}alkyl$ or $C_{1-6}haloalkyl$; or
R^1 and R^2 are connected to give a 5 or 6 membered heterocyclic ring; and
R^3 is hydrogen or $C_{1-10}alkyl$ thereof.

According to one embodiment of the present invention, R^3 is $C_{1-10}alkyl$.

According to another embodiment of the present invention, R^3 is methyl.

According to yet another embodiment of the present invention, Q is C_6aryl.

According to a further embodiment of the present invention, Q is phenyl.

According to yet a further embodiment of the present invention, Q is $C_{10}aryl$

According to yet another embodiment of the present invention, Q is $C_2alkylC_6aryl$.

According to one embodiment of the present invention, R^1 is $C_{1-10}alkyl$.

According to another embodiment of the present invention, R^1 is $C_{6-10}aryl$.

According to yet one embodiment of the present invention, R^1 is methyl.

According to a further embodiment of the present invention, R^1 is $C_{6-10}aryl$.

According to another embodiment of the present invention, R^1 is C_6aryl

According to yet another embodiment of the present invention, R^1 is $C_{1-6}haloalkyl$.

According a further embodiment of the present invention, R^1 is halogen.

According to yet another embodiment of the present invention, R^2 is methyl

The present invention also relates to compounds according to formula I, said compounds being:
N-Methyl-*N*-[4-(4-methylpiperazin-1-yl)quinazolin-2-yl]-3-(trifluoromethyl)benzenesulfonamide;
4-chloro-*N*-methyl-*N*-[4-(4-methylpiperazin-1-yl)quinazolin-2-yl]benzenesulfonamide;
N,4-dimethyl-*N*-[4-(4-methylpiperazin-1-yl)quinazolin-2-yl]benzenesulfonamide;
N-Methyl-*N*-(4-piperazin-1-ylquinazolin-2-yl)-3-(trifluoromethyl)benzenesulfonamide;
N-methyl-*N*-(4-piperazin-1-ylquinazolin-2-yl)biphenyl-4-sulfonamide;
N-methyl-*N*-(4-piperazin-1-ylquinazolin-2-yl)naphthalene-2-sulfonamide;
3-bromo-*N*-methyl-*N*-(4-piperazin-1-ylquinazolin-2-yl)benzenesulfonamide;
3,4-dichloro-*N*-methyl-*N*-(4-piperazin-1-ylquinazolin-2-yl)benzenesulfonamide;
N,4-dimethyl-*N*-(4-piperazin-1-ylquinazolin-2-yl)benzenesulfonamide;
N-(2-Fluoroethyl)-2-(1-naphthyl)-*N*-(4-piperazin-1-ylquinazolin-2-yl)ethanesulfonamide;
2-(4-Chlorophenyl)-*N*-methyl-*N*-(4-piperazin-1-ylquinazolin-2-yl)ethanesulfonamide; and
2-(1,1-Dioxido-1,2-benzisothiazol-2(3*H*)-yl)-4-piperazin-1-ylquinazoline,
or pharmaceutically salts, solvates or solvated salts thereof.

Listed below are definition of various terms used in the specification and claims to describe the present invention.

For the avoidance of doubt it is to be understood that where in this specification a group is qualified by 'hereinbefore defined', 'defined hereinbefore' or 'defined above' the said group encompasses the first occurring and broadest definition as well as each and all of the other definitions for that group.

The term "C_{m-n}" or "C_{m-n} group" used alone or as a prefix, refers to any group having m to n carbon atoms.

The term "alkyl" used alone or as a suffix or prefix, refers to a saturated monovalent straight or branched chain hydrocarbon radical comprising from 1 to about(?) 10 carbon atoms. Illustrative examples of alkyls include, but are not limited to, C_{1-6}alkyl groups, such as methyl, ethyl, propyl, isopropyl, 2-methyl-1-propyl, 2-methyl-2-propyl, 2-methyl-1-butyl, 3-methyl-1-butyl, 2-methyl-3-butyl, 2,2-dimethyl-1-propyl, 2-methyl-1-pentyl, 3-methyl-1-pentyl, 4-methyl-1-pentyl, 2-methyl-2-pentyl, 3-methyl-2-pentyl, 4-methyl-2-pentyl, 2,2-dimethyl-1-butyl, 3,3-dimethyl-1-butyl, 2-ethyl-1-butyl, butyl, isobutyl, t-butyl, pentyl, isopentyl, neopentyl, and hexyl, and longer alkyl groups, such as heptyl, and octyl.

The term 'C_0' means a bond or does not exist. For example "arylC_0alkyl" is equivalent with "aryl", and "C_2alkylOC_0alkyl" is equivalent with "C_2alkylO".

As used herein, "alkenyl" refers to an unsaturated carbon chain having one or more double carbon-carbon bonds and includes both straight and branched chain alkenyl groups. Example on alkenyl groups includes, but is not limited to, vinyl, allyl, propenyl, butenyl, , pentenyl, or hexenyl, and a butenyl group may for example be buten-2-yl, buten-3-yl or buten-4-yl.

As used herein, "alkynyl" refers to an unsaturated carbon chain one or more triple carbon-carbon bonds and includes both straight and branched chain alkynyl groups. Example on alkynyl groups includes, but is not limited to, etynyl, propargyl, pentynyl or hexynyl and a butynyl group may for example be butyn-3-yl or butyn-4-yl.

In this specification, unless stated otherwise, the term "cycloalkyl" refers to an optionally substituted, partially or completely saturated cyclic hydrocarbon ring system. The term "C_{3-7}cycloalkyl" may be, but is not limited to cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl or cyclopentenyl.

As used herein, the term, "alkoxy", unless stated otherwise, refers to radicals of the general formula –O-R, wherein R is selected from a hydrocarbon radical. The term "alkoxy" may

include, but is not limited to methoxy, ethoxy, propoxy, isopropoxy, butoxy, t-butoxy, isobutoxy, cyclopropylmethoxy, allyloxy or propargyloxy.

In this specification, unless stated otherwise, the term "amine" or "amino" refers to radicals of the general formula –NRR', wherein R and R' are selected independently from hydrogen or a hydrocarbon radical.

The term "heterocycloalkyl" denotes a non-aromatic, partially or completely saturated hydrocarbon group, which contains one ring and at least one heteroatom. Examples of said heterocycle include, but are not limited to pyrrolidinyl, pyrrolidonyl, piperidinyl, piperazinyl, morpholinyl, oxazolyl, 2-oxazolidonyl or tetrahydrofuranyl.

In this specification, unless stated otherwise, the term "aryl" refers to an optionally substituted monocyclic or bicyclic hydrocarbon ring system with at least one unsaturated aromatic ring. Examples of "aryl" may be, but are not limited to phenyl, naphthyl or tetralinyl.

In this specification, unless stated otherwise, the term "heteroaryl" refers to an optionally substituted monocyclic or bicyclic hydrocarbon ring system with at least one unsaturated ring and containing at least one heteroatom selected independently from N, O or S. Examples of "heteroaryl" may be, but are not limited to pyridyl, pyrrolyl, furyl, thienyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, pyrazolyl, benzofuryl, indolyl, isoindolyl, benzimidazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, tetrazolyl, triazolyl, quinazolinyl or isotiazolyl. For the avoidance of doubt, a C_5heteroaryl refers to a 5 membered aromatic ring system containing at least one heteroatom.

In this specification, unless stated otherwise, the terms "arylalkyl" and "heteroarylalkyl" refer to a substituent that is attached via the alkyl group to an aryl or heteroaryl group.

In this specification, unless stated otherwise, the terms "halo" and "halogen" may be fluoro, iodo, chloro or bromo.

In this specification, unless stated otherwise, the term "haloalkyl" means an alkyl group as defined above, which is substituted with halo as defined above. The term "C_{1-6}haloalkyl" may include, but is not limited to fluoromethyl, difluoromethyl, trifluoromethyl, fluoroethyl, difluoroethyl or bromopropyl. The term "C_{1-6}haloalkylO" may include, but is not limited to fluoromethoxy, difluoromethoxy, trifluoromethoxy, fluoroethoxy or difluoroethoxy.

The present invention relates to the compounds of formula I as hereinbefore defined as well as to the salts, solvates or solvated salts thereof. Salts for use in pharmaceutical formulations will be pharmaceutically acceptable salts, but other salts may be useful in the production of the compounds of formula I.

A suitable pharmaceutically acceptable salt of the compounds of the invention is, for example, an acid-addition salt, for example a salt with an inorganic or organic acid. In addition, a suitable pharmaceutically acceptable salt of the compounds of the invention is an alkali metal salt, an alkaline earth metal salt or a salt with an organic base.
Other pharmaceutically acceptable salts and methods of preparing these salts may be found in, for example, Remington's Pharmaceutical Sciences (18^{th} Edition, Mack Publishing Co.).

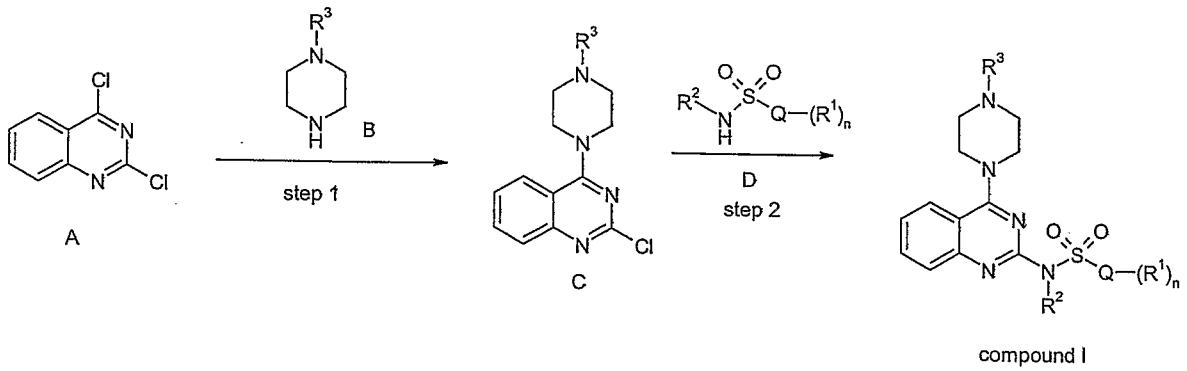
Some compounds of formula I may have chiral centres and/or geometric isomeric centres (E- and Z-isomers), and it is to be understood that the invention encompasses all such optical, diastereoisomeric and geometric isomers.

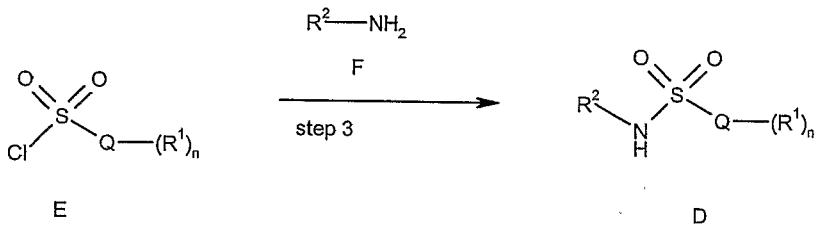
The invention also relates to any and all tautomeric forms of the compounds of formula I.

Methods of Preparation

Throughout the following description of such processes it is understood that, where appropriate, suitable protecting groups will be added to, and subsequently removed from, the various reactants and intermediates in a manner that will be readily understood by one skilled in the art of organic synthesis. The specific sequences of reactions depicted under 'General procedure' are not critical. For many of the compounds described the order of the

reaction steps may be varied. The reactions are run until judged complete by LC-UV, LC-MS, TLC or NMR.





Step 1

A compound A may be reacted with a compound B, wherein R^3 is as defined above, in a solvent such as DMF, DMSO, ethanol, pentanol or *i*-propanol or mixtures thereof, optionally in the presence of a base such as potassium carbonate, DIPEA or triethylamine to form a compound C, wherein R^3 is as defined above. The reaction may be performed at temperatures between RT and the reflux temperature of the solvent for 1-10 h. Compound C, wherein R^3 is as defined above, may be isolated by extraction, chromatography or precipitation or combinations thereof.

Step 2

A compound C, wherein R^3 is as defined above, may be reacted with a compound D, wherein R^1, R^2, Q and n are as defined above, to form a compound I in a solvent such as DMSO, DMF, dioxane, *i*-propanol or THF, or mixtures thereof, in the presence of a base such as potassium carbonate, sodium carbonate or sodium hydride. The reaction may be performed at temperatures between RT and the reflux temperature of the solvent, for

reaction times between 10 minutes and 24 h. Compound I, wherein R^1, R^2, R^3, Q and n are as defined above may be isolated by evaporation of the solvent, extraction, precipitation or chromatography.

Step 3

A compound D, wherein R^1, R^2, Q and n are as defined above, may be prepared from a compound E, wherein R^1, Q and n are as defined above , by reaction with a compound F, wherein R^2 is as defined above in a solvent such as methanol, ethanol, dioxane, dichloromethane or mixtures thereof in the presence of a base such as triethylamine, pyridine, DIPEA or an excess of compound F. The reaction may be performed at temperatures between –10° and the reflux temperature of the solvent, preferably at 0°C and RT for reaction times between 1 minute to 2 h. If an acid salt, such as the hydrochloride, of compound F is used a base such as triethylamine or DIPEA can be added to the reaction mixture to liberate the free base of compound F. The product may be isolated by extraction, precipitation or chromatography.

Intermediates

A further embodiment of the invention relates to compounds selected from the group consisting of:

2-chloro-4-(4-Boc-piperazin-1-yl)quinazoline;

N-methyl-3-(trifluoromethyl)benzenesulfonamide;

4-chloro-*N*-methylbenzenesulfonamide;

3,4-dichloro-*N*-methylbenzenesulfonamide;

N-methylbiphenyl-4-sulfonamide;

N-methylnaphthalene-2-sulfonamide; and

2-(4-chlorophenyl)-*N*-methylethanesulfonamide; and

N-(2-fluoroethyl)-2-(1-naphthyl)ethanesulfonamide,

which may be used as intermediates in the preparation of compounds suited for the treatment of 5-HT6 mediated disorders, especially for use as intermediates for the preparation of compounds of formula I.

Pharmaceutical composition

According to one embodiment of the present invention there is provided a pharmaceutical composition comprising as active ingredient a therapeutically effective amount of the compound of formula I, or salts, solvates or solvated salts thereof, in association with one or more pharmaceutically acceptable diluents, excipients and/or inert carriers.

The composition may be in a form suitable for oral administration, for example as a tablet, pill, syrup, powder, granule or capsule, for parenteral injection (including intravenous, subcutaneous, intramuscular, intravascular or infusion) as a sterile solution, suspension or emulsion, for topical administration e.g. as an ointment, patch or cream, for rectal administration, e.g. as a suppository, or for inhalation.

In general, the above compositions may be prepared in a conventional manner using one or more conventional excipients, pharmaceutical acceptable diluents and/or inert carriers. Suitable daily doses of the compounds of formula I in the treatment of a mammal, including man, are approximately 0.01 to 250 mg/kg bodyweight at peroral administration and about 0.001 to 250 mg/kg bodyweight at parenteral administration.

The typical daily dose of the active ingredient varies within a wide range and will depend on various factors such as the relevant indication, severity of the illness being treated, the route of administration, the age, weight and sex of the patient and the particular compound being used, and may be determined by a physician.

Medical use

Interestingly, it has been found that the compounds according to the present invention are useful in therapy. The compounds of formula I, or salts, solvates or solvated salts thereof, as well as their corresponding active metabolites, exhibit a high degree of potency and selectivity for 5-hydroxy-tryptamine 6 (5-HT6) receptors. Accordingly, the compounds of the present invention are expected to be useful in the treatment of conditions associated with excessive activation of 5-HT6 receptors.

The compounds may be used to produce an inhibitory effect of 5-HT6 receptors in mammals, including man.

The compounds of the present invention are expected to be suitable for the treatment of disorders relating to or affected by the 5-HT6 receptor including cognitive, personality, behaviour, psychiatric and neurodegenerative disorders.

Examples of such disorder may be selected from the group comprising of Alzheimer's disease anxiety, depression, convulsive disorders such as epilepsy, personality disorders, obsessive compulsive disorders, migraine, cognitive disorders such as memory dysfunction, sleep disorders, feeding disorders such as anorexia, obesity, bulimia, panic attacks, withdrawal from drug abuse, schizophrenia, attention deficit hyperactive disorder (ADHD), attention deficit disorder (ADD), dementia, memory loss, disorders associated with spinal trauma and/or head injury, stroke, diabetes type 2, binge disorders, bipolar disorders, psychoses, Parkinson's disease, Huntington's disease, neurodegenerative disorders characterized by impaired neuronal growth, and pain.

Further relevant disorders may be selected from the group comprising gastro-intestinal disorders such as gastro-esophageal reflux disease (GERD) and irritable bowel syndrome (IBS).

The compounds may also be used for treatment of tolerance to 5-HT6 activators.

One embodiment of the invention relates to a compounds of the present invention as hereinbefore defined, for use in therapy.

Another embodiment of the invention relates to a compound of the present invention as hereinbefore defined, for use in treatment of 5-HT6 mediated disorders.

A further embodiment of the invention relates to a compound of the present invention as hereinbefore defined, for use in treatment of Alzheimer's disease.

Another embodiment of the invention relates to a compound of the present invention as hereinbefore defined, for use in treatment of cognitive impairment associated with schizophrenia.

Yet a further embodiment of the invention relates to a compound of the present invention as hereinbefore defined, for use in treatment of obesity.

One embodiment of the invention relates to a compound of the present invention as hereinbefore defined, for use in Parkinson's disease.

Another embodiment of the invention relates to the use of a compound of the present invention as hereinbefore defined, in the manufacture of a medicament for treatment of 5-HT6 mediated disorders, Alzheimer's disease, cognitive impairment associated with schizophrenia, obesity and/or Parkinson's disease, and any other disorder mentioned above.

A further embodiment of the invention relates to a method of treatment of 5-HT6 mediated disorders, Alzheimer's disease, cognitive impairment associated with schizophrenia, obesity and/or Parkinson's disease, and any other disorder mentioned above, comprising administering to a mammal, including man in need of such treatment, a therapeutically effective amount of a compound of the present invention, as hereinbefore defined.

Yet another embodiment of the invention relates to a pharmaceutical composition comprising a compound of the present invention as hereinbefore defined, for use in treatment of 5-HT6 mediated disorders, Alzheimer's disease, cognitive impairment associated with schizophrenia, obesity and/or Parkinson's disease, and any other disorder mentioned above.

One embodiment of the invention relates to an agent for the prevention or treatment of 5-HT6 mediated disorders, Alzheimer's disease, cognitive impairment associated with schizophrenia, obesity and/or Parkinson's disease, and any other disorder mentioned

above, which comprises as active ingredient a compound of the present invention as hereinbefore defined.

In the context of the present specification, the term "therapy" and "treatment" includes prevention and prophylaxis, unless there are specific indications to the contrary. The terms "treat"," therapeutic" and "therapeutically" should be construed accordingly.

In this specification, unless stated otherwise, the terms "inhibitor" and "antagonist" mean a compound that by any means, partly or completely, blocks the transduction pathway leading to the production of a response by the agonist.

The compounds according to the present invention are modulators of the 5-HT6 receptors, and may be inhibitors, as well as agonists, inverse-agonists or partial-agonist.

The term "disorder", unless stated otherwise, means any condition and disease associated with 5-HT6 receptor activity.

Non- Medical use

In addition to their use in therapeutic medicine, the compounds of formula I, or salts, solvates or solvated salts thereof, are also useful as pharmacological tools in the development and standardisation of *in vitro* and *in vivo* test systems for the evaluation of the effects of modulators of 5-HT6 related activity in laboratory animals such as cats, dogs, rabbits, monkeys, rats and mice, as part of the search for new therapeutics agents.

Examples

General methods

The invention will now be illustrated by the following Examples in which, generally:

(i) operations were carried out at ambient or room temperature, *i.e.* in the range 17 to 25°C and under an atmosphere of an inert gas such as argon unless otherwise stated;

(ii) evaporations were carried out by rotary evaporation *in vacuo* and work-up procedures were carried out after removal of residual solids by filtration;

(iii) HPLC analyses were performed on an Agilent HP1100 system consisting of G1379A Micro Vacuum Degasser, G1312A Binary Pump, G1367A Well plate auto-sampler, G1316A Thermostatted Column Compartment and G1315B Diode Array Detector. Column: X-Terra MS, Waters, 3.0 x 100 mm, 3.5 μm. The column temperature was set to 40 °C and the flow rate to 1.0 ml/min. The Diode Array Detector was scanned from 210-300 nm, step and peak width were set to 2 nm and 0.05 min, respectively. A linear gradient was applied, starting at 100 % A (A: 10 mM NH_4OAc in 5 % MeCN) and ending at 100% B (B: MeCN), in 6 min;

(iv) Thin layer chromatography (TLC) was performed on Merck TLC-plates (Silica gel 60 F_{254}) and UV visualized the spots. Flash chromatography was preformed on a Combi Flash® Companion™ using RediSep™ normal-phase flash columns or on Merck Silica gel 60 (0.040-0.063 mm). Typical solvents used for flash chromatography were mixtures of chloroform/methanol, toluene/ethyl acetate and ethyl acetate/hexanes;

(v) ^1H spectra were recorded at 400 MHz either on a Varian Unity+ 400 NMR Spectrometer equipped with a 5mm BBO probehead with Z-gradients, or Bruker av400 NMR spectrometer operating at 400 MHz for proton, equipped with a 3mm flow injection SEI $^1H/D$-^{13}C probehead with Z-gradients, using a BEST 215 liquid handler for sample injection, or a Bruker DPX400 NMR spectrometer equipped with a 4-nucleus probe equipped with Z-gradients. Alternatively ^1H spectra were recorded at 600 MHz on a Bruker av600 NMR spectrometer, equipped with a 5mm BBI probehead with Z-gradients. The following reference signals were used: the middle line of DMSO-d_6 δ 2.49; the middle line of CD_3OD δ 3.30; acetone-d_6 2.04 and $CDCl_3$ δ 7.25 (unless otherwise indicated); Resonance multiplicities are denoted s, d, t, q, m, br and app for singlet, doublet, triplet, quartet, multiplet, broad and apparent, respectively;

(vi) Mass spectra were recorded on a Waters LCMS consisting of an Alliance 2795 (LC), Waters PDA 2996, ELS detector (Sedex 75) and a ZQ single quadrupole mass spectrometer. The mass spectrometer was equipped with an electrospray ion source (ESI) operated in a positive or negative ion mode. The capillary voltage was 3 kV and cone voltage was 30 V. The mass spectrometer was scanned between *m/z* 100-700 with a scan time of 0.3s. The Diode Array Detector was scanned from 200-400 nm. The temperature of the ELS detector was adjusted to 40 °C and the pressure was set to 1.9 bar. Separation was performed on a Waters X-Terra MS C8 3.0 x 50, 3.5 µm at 1 ml/min. The column temperature was set to 40 °C. A linear gradient was applied using a neutral starting at 100% A (A: 10mM NH_4OAc in 5% MeCN, or 8 mM HCOOH in 5% MeCN) ending at 100% B (MeCN),

alternatively

(vii) mass spectra were recorded on a Waters LCMS system (Sample Manager 2777C, 1525µ binary pump, 1500 Column Oven, ZQ, PDA2996 and ELS detector, Sedex 85). Separation was performed using a Gemini column, C18, 3.0 x 50 mm, 3 µm, (Phenomenex). A four minute linear gradient was used starting at 100 % A (A: 10 mM NH4OAc in 5% MeOH) and ending at 100% B (MeOH). The ZQ was equipped with a combined APPI/APCI ion source and scanned in the positive mode between *m/z* 120-800 using a scan time of 0.3 s. The APPI repeller and the APCI corona were set to 0.86 kV and 0.80 µA, respectively. In addition, the desolvation temperature (300°C), desolvation gas (400 L/Hr) and cone gas (5 L/Hr) were constant for both APCI and APPI mode;

(viii) Preparative chromatography was run on a Waters auto purification HPLC with a diode array detector. Column: XTerra MS C8, 19 x 300 mm, 10 µm. Gradients with MeCN/0.1M NH_4OAc in 5 % MeCN in MilliQ Water, were used. Flow rate: 20 ml/min. Alternatively, purification was achieved on a semi preparative Shimadzu LC-8A HPLC with a Shimadzu SPD-10A UV-vis.-detector equipped with a Waters Symmetry® column (C18, 5 µm, 100 mm x 19 mm). Gradients with MeCN/0.1% trifluoroacetic acid in MilliQ Water, were

used. Flow rate: 10 ml/min. Alternatively, another column was used; Atlantis C18 19 x 100 mm, 5 µm column. Gradients with MeCN/0.1M NH_4OAc in 5% MeCN in MilliQ Water, were used. Flow rate: 15 ml/min.

(ix) All solvents used were analytical grade and commercially available anhydrous solvents for reactions;

(x) yields, where present, are not necessarily the maximum attainable;

(xi) intermediates were not necessarily fully purified but their structures and purity were assessed by thin layer chromatographic, HPLC, infra-red (IR) and/or NMR analysis;

(xii) melting points are uncorrected and were determined using a Mettler SP62 automatic melting point apparatus or an oil-bath apparatus; melting points for the end-products of the Formula I were determined after crystallisation from an appropriate organic solvent or solvent mixture;

(xiii) the following abbreviations have been used

Boc	*tert*-butoxycarbonyl
HPLC	high performance liquid chromatography
LC	liquid chromatography
ESI-MS	electrospray ionization-mass spectometry
NMR	nuclear magnetic resonance
TFA	trifluroacetic acid
THF	tetrahydrofurane
DMF	dimethyformamide
DIPEA	*N,N*-diisopropylethylamine
DMSO	dimethylsulfoxide
NMP	1-methyl-2-pyrrolidinone
THF	tetrahydrofuran
MeOH	methanol
RT	room temperature

Throughout the following description of such processes it is understood that, where appropriate, suitable groups will be added to, and subsequently removed from, the various reactants and intermediates in a manner that will be readily understood by one skilled in

the art of organic synthesis. The specific sequence of reactions depicted is not critical. For many of the compounds the order of the reaction steps may be varied.

Starting materials

Starting material 2-chloro-4-(4-methylpiperazin-1-yl)quinazoline was prepared according to Bioorg. Med. Chem. Lett. 2000, 10, 1317-1320; 2,3-dihydro-1,2-benzisothiazole 1,1-dioxide according to DE 19836406 A1.

Other starting materials used were either available from commercial sources or prepared according to literature procedures.

Example 1

***N*-Methyl-*N*-[4-(4-methylpiperazin-1-yl)quinazolin-2-yl]-3-(trifluoromethyl)benzene-sulfonamide**

2-Chloro-4-(4-methylpiperazin-1-yl)quinazoline (80 mg, 0.30 mmol), potassium carbonate (97 mg, 0.70 mmol) and *N*-methyl-3-(trifluoromethyl)benzenesulfonamide (79 mg, 0.39 mmol) were dissolved in DMSO (2.5 ml). The mixture was heated at 100°C for 3 days. The mixture was filtered and purified by preparative HPLC to give a white solid (16 mg, 12%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.34 (1 H, s) 8.29 (1 H, d) 8.06 (1 H, d) 7.83 - 7.88 (2 H, m) 7.70 - 7.75 (1 H, m) 7.58 (1 H, dd) 7.33 - 7.38 (1 H, m) 3.69 (3 H, s) 3.51 - 3.57 (4 H, m) 2.28 - 2.35 (4 H, m) 2.17 (3 H, s); ESI-MS m/z M+H$^+$ 466.

Examples 2 and 3 were prepared according to Example 1

Example No	Compound Name	^{1}H NMR (400 MHz, DMSO-d_6) δ ppm	ESI-MS m/z M+H$^+$	Yield
2	4-chloro-*N*-methyl-*N*-[4-(4-methylpiperazin-1-yl)quinazolin-2-yl]benzenesulfonamide	8.02 (2 H, d) 7.88 (1 H, d) 7.70 - 7.76 (1 H, m) 7.67 (2 H, d) 7.63 (1 H, d) 7.34 - 7.40 (1 H, m) 3.66 (3 H, s) 3.64 (4 H, br. s.) 2.58 (4 H, br. s.) 2.35 (3 H,	432, 434	10%

		br. s.)		
3	*N*,4-dimethyl-*N*-[4-(4-methylpiperazin-1-yl)quinazolin-2-yl]benzenesulfonamide	7.85 (3 H, app. d) 7.70 (1 H, t) 7.60 (1 H, d) 7.39 (2 H, d) 7.33 (1 H, t) 3.65 (3 H, s) 3.54 - 3.60 (4 H, m) 2.36 (3 H, s) 2.26 - 2.31 (4 H, m) 2.17 (3 H, s)	412	3%

Example 4

***N*-Methyl-*N*-(4-piperazin-1-ylquinazolin-2-yl)-3-(trifluoromethyl)benzenesulfonamide**

2-Chloro-4-(4-Boc-piperazin-1-yl)quinazoline (70 mg, 0.20 mmol), *N*-methyl-3-(trifluoromethyl)benzenesulfonamide (48 mg, 0.20 mmol) and potassium carbonate (55 mg, 0.40 mmol) in DMSO (2 ml) were heated at 90° for 16 h. The reaction mixture was diluted with brine and extracted with dichloromethane (×3). The combined organic phases were dried ($MgSO_4$) and evaporated to dryness. The residue was dissolved in dichloromethane (2 ml) and TFA (0.5 ml) was added. The reaction mixture was stirred at ambient temperature for 16 h. The solvent was evaporated and the residue was purified by preparative HPLC to give a solid (8 mg, 8%).

^{1}H NMR (400 MHz, MeOD-d_4) δ ppm 8.36 (1 H, s) 8.21 (1 H, d) 7.94 (1 H, d) 7.86 (1 H, d) 7.74 - 7.81 (1 H, m) 7.62 - 7.73 (2 H, m) 7.32 - 7.42 (1 H, m) 3.75 (3 H, s) 3.57 - 3.66 (4 H, m) 2.96 - 3.05 (4 H, m); ESI-MS m/z $M+H^+$ 452.

Examples 5-9 were prepared using the same method as in Example 4 unless otherwise indicated.

Example no	**Compound Name**	**^{1}H NMR**	**LC-MS $M+H^+$**	**Comments, state and yield.**
5	*N*-methyl-*N*-(4-piperazin-1-ylquinazolin-2-yl)biphenyl-4-sulfonamide	(400 MHz, MeOD-d_4) δ ppm 8.01 - 8.06 (2 H, m) 7.85 - 7.90 (1 H, m) 7.80 - 7.85 (2 H, m) 7.71 - 7.75	460	24%

		(2 H, m) 7.65 - 7.70 (2 H, m) 7.44 - 7.50 (2 H, m) 7.34 - 7.43 (2 H, m) 3.79 (3 H, s) 3.64 - 3.72 (4 H, m) 3.06 - 3.13 (4 H, m)		
6	*N*-methyl-*N*-(4-piperazin-1-ylquinazolin-2-yl)naphthalene-2-sulfonamide	(400 MHz, DMSO-d_6) δ ppm 8.72 (1 H, s) 8.22 - 8.27 (1 H, m) 8.10 (1 H, d) 8.01 - 8.06 (1 H, m) 7.93 - 7.98 (1 H, m) 7.84 (1 H, d) 7.61 - 7.74 (4 H, m) 7.29 - 7.35 (1 H, m) 3.75 (3 H, s) 3.48 - 3.55 (4 H, m) 2.78 - 2.87 (4 H, m)	434	17%

Example no	Compound Name	^{1}H NMR	LC-MS M+H$^+$	Comments, state and yield.
7	3-bromo-*N*-methyl-*N*-(4-piperazin-1-ylquinazolin-2-yl)benzene-sulfonamide	(400 MHz, MeOD-d_4) δ ppm 8.22 (1 H, t) 7.87 - 7.94 (2 H, m) 7.69 - 7.81 (3 H, m) 7.49 (1 H, t) 7.37 - 7.43 (1 H, m) 3.75 (3 H, s) 3.67 - 3.72 (4 H, m) 3.13 - 3.19 (4 H, m)	462, 464	Heated at 120°C in first reaction step. 39%
8	3,4-dichloro-*N*-methyl-*N*-(4-piperazin-1-ylquinazolin-2-yl)benzenesulfonamide	(400 MHz, $CDCl_3$) δ ppm 8.26 (1 H, d) 7.85 (1 H, dd) 7.74 (1 H, d) 7.63 - 7.70 (2 H, m) 7.57 (1 H, d) 7.28 - 7.32 (1 H, m) 3.76 (3 H, s) 3.65 - 3.70 (4 H, m) 3.02 - 3.07 (4 H, m)	452, 454	37%
9	*N*,4-dimethyl-*N*-(4-piperazin-1-ylquinazolin-2-yl)benzene-sulfonamide	(600 MHz, $CDCl_3$) δ ppm 7.89 - 7.92 (2 H, m) 7.72 (1 H, d) 7.66 - 7.69 (1 H, m) 7.59 - 7.63 (1 H, m) 7.22 - 7.28 (3 H, m) 3.78 (3 H, s) 3.60 (4 H, br. s.) 2.97 (4 H, br. s.) 2.40 (3 H, s)	398	42%

Example 10

***N*-(2-Fluoroethyl)-2-(1-naphthyl)-*N*-(4-piperazin-1-ylquinazolin-2-yl)ethanesulfonamide**

2-Chloro-4-(4-Boc-piperazin-1-yl)quinazoline (80 mg, 0.23 mmol), *N*-(2-fluoroethyl)-2-(1-naphthyl)ethanesulfonamide (65 mg, 0.23 mmol) and potassium carbonate (80 mg, 0.58 mmol) in DMSO (2.5 ml) was heated at 90° for 4 days. The reaction mixture was diluted with brine and extracted with dichloromethane (×3). Water (150 ml) was added and the precipitate was collected by filtration and dried under vacuum. The solid was dissolved in dichloromethane (2 ml) and TFA (0.15 ml) was added. The reaction mixture was stirred at ambient temperature for 2 h. Toluene (2 ml) was added and the mixture was concentrated by evaporation. Water was added and the pH was adjusted to 9-10 by the addition of 1M aqueous sodium hydroxide. The mixture was extracted with dichloromethane (×3). The combined organic phases were combined, dried (Na_2SO_4) and evaporated. The crude was purified by preparative HPLC to give a solid (4 mg, 4%).

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.00 (1 H, d) 7.64 - 7.87 (5 H, m) 7.30 - 7.49 (5 H, m) 4.81 - 4.86 (1 H, m) 4.69 - 4.74 (1 H, m) 4.59 - 4.65 (1 H, m) 4.54 - 4.59 (1 H, m) 4.28 - 4.35 (2 H, m) 3.64 - 3.77 (6 H, m) 2.99 - 3.06 (4 H, m); ESI-MS m/z $M+H^+$ 494.

Example 11

2-(4-Chlorophenyl)-*N*-methyl-*N*-(4-piperazin-1-ylquinazolin-2-yl)ethanesulfonamide

The title compound was prepared using the method in example 10 and isolated as a solid (22 mg, 11 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.81 (1 H, d) 7.64 - 7.75 (2 H, m) 7.29 - 7.35 (1 H, m) 7.22 (2 H, d) 7.10 (2 H, d) 4.11 - 4.18 (2 H, m) 3.72 - 3.79 (4 H, m) 3.57 (3 H, s) 3.12 - 3.19 (2 H, m) 3.04 - 3.10 (4 H, m); ESI-MS m/z $M+H^+$ 446, 448.

Example 12

2-(1,1-Dioxido-1,2-benzisothiazol-2(3*H*)-yl)-4-piperazin-1-ylquinazoline

2-Chloro-4-(4-Boc-piperazin-1-yl)quinazoline (140 mg, 0.40 mmol), 2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (85 mg, 0.50 mmol) and potassium carbonate (110 mg, 0.80 mmol) in DMSO (2 ml) were heated at 90° for 16 h and then at 110° for 5 h. The reaction mixture was diluted with brine and extracted with dichloromethane (×3). The combined organic phases were dried ($MgSO_4$) and evaporated to dryness. The residue was dissolved in dichloromethane (2 ml) and TFA (0.5 ml) was added. The reaction mixture was stirred

at ambient temperature for 16 h. The solvent was evaporated and the crude was purified by preparative HPLC to give the acetate of the title compound (71 mg, 40%).

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.90 - 8.02 (2 H, m) 7.61 - 7.84 (5 H, m) 7.33 - 7.41 (1 H, m) 5.19 (2 H, s) 3.79 - 3.88 (4 H, m) 2.87 - 2.95 (4 H, m); ESI-MS m/z M+H$^+$ 382.

Intermediates

Intermediate 1

2-Chloro-4-(4-Boc-piperazin-1-yl)quinazoline

2,4-Dichloroquinazoline (3.0 g, 15 mmol), *N*-Boc-piperazine (2.79 g, 15 mmol) and DIPEA (1.51 ml, 16.5 mmol) were dissolved in DMF (100 ml) and the mixture was heated at 80°C for 1 h. The mixture was cooled and dichloromethane (40 ml) was added. The mixture was washed with brine and the aqueous phase was extracted with dichloromethane (×3). The combined organic phases were dried (Na_2SO_4) and the solvent was evaporated. The residue was purified by chromatography on silica eluting with 5% methanol in dichloromethane. Fractions containing the product were pooled and evaporated. The resulting solid was recrystallized from dichloromethane and heptane to give a solid (4.0 g, 76%).

^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.85 - 7.90 (2 H, m) 7.77 (1 H, t) 7.47 (1 H, t) 3.83 - 3.90 (4 H, m) 3.64 - 3.69 (4 H, m) 1.51 (9 H, s); ESI-MS m/z M+H$^+$ 349, 351.

Intermediate 2

***N*-Methyl-3-(trifluoromethyl)benzenesulfonamide**

To 3-(trifluoromethyl)benzenesulfonyl chloride (245 mg, 1.0 mmol) in dioxane (1 ml) was added methylamine (8M in ethanol, 0.38 ml, 3.0 mmol). The slurry was stirred at ambient temperature for 30 min. The mixture was diluted with aqueous sulfuric acid (2%) and extracted with dichloromethane (×3). The organic phase was dried ($MgSO_4$), filtered and the solvent was evaporated to give a solid (297 mg, quant.).

1H NMR (400 MHz, MeOD-d_4) δ ppm 8.08 - 8.12 (2 H, m) 7.95 (1 H, d) 7.78 - 7.83 (1 H, m) 2.55 (3 H, s); MS ESI m/z M-H$^+$ 238.

Intermediates 3-7 were prepared according to the method in intermediate 2.

Intermediate no	Compound Name	^{1}H NMR (400 MHz, $CDCl_3$) δ ppm	MS ESI m/z
i3	4-chloro-*N*-methylbenzene-sulfonamide	7.82 (2 H, d) 7.52 (2 H, d) 4.38 (1 H, br. s.) 2.69 (3 H, d)	M-H$^+$ 204, 206
i4	3,4-dichloro-*N*-methylbenzene-sulfonamide		M-H$^+$ 238, 240, 242
i5	*N*-methylbiphenyl-4-sulfonamide	7.94 (2 H, d) 7.74 (2 H, d) 7.59 - 7.65 (2 H, m) 7.40 - 7.53 (3 H, m) 4.36 (1 H, br. s.) 2.73 (3 H, d)	M+H$^+$ 248
i6	*N*-methylnaphthalene-2-sulfonamide	8.45 (1 H, s) 7.97 - 8.01 (2 H, m) 7.93 (1 H, d) 7.85 (1 H, dd) 7.61 - 7.70 (2 H, m) 4.42 (1 H, br. s.) 2.71 (3 H, d)	M+H$^+$ 222
i7	2-(4-chlorophenyl)-*N*-methylethane-sulfonamide		M+H$^+$ 232, 234

Intermediate 8

***N*-(2-Fluoroethyl)-2-(1-naphthyl)ethanesulfonamide**

N-(2-Fluoroethyl)-2-(1-naphthyl)ethanesulfonyl chloride (254 mg, 1.0 mmol), 1-fluoroethylamine hydrochloride (150 mg, 1.5 mmol) and DIPEA (0.35 ml, 3.0 mmol) were mixed in dioxane (anhydrous, 2 ml). The mixture was stirred at ambient temperature for 1 h. The mixture was diluted with aqueous sulfuric acid (2%) and extracted with dichloromethane (×3). The organic phase was dried ($MgSO_4$), filtered and the solvent was evaporated to give a solid (289 mg, 92%). MS ESI m/z M+H$^+$ 282, M-H$^+$ 280.

Pharmacology

Method for [125I]SB258585 binding to rat striatal 5-HT6 receptors

Materials

[^{125}I]SB258585 (1) with specific radioactivity 2000 Ci/mmol was purchased from Amersham Biosciences Europe GmbH, Freiburg, Germany. Other chemicals were purchased from commercial sources and were of analytical grade.

Preparation of membranes

Striatal tissue from adult rats (Sprague-Dawley, 320-370 g, B & K Sweden) were dissected out, weighed and homogenized in buffer containing 50 mM Tris-HCl, 4 mM MgCl2, 1 mM EDTA, 10 μM pargyline and protease inhibitor (Complete, Roche Diagnostics) pH 7.4 using an Ultra-Turrax T8 (IKA Labortechnik, Germany). The tissue homogenate was centrifuged at 48 000xg for 10 min and the pellet was resuspended and recentrifuged as above. The final membranes were diluted in buffer to a concentration of 60 mg original wet weight (w.w.) per ml and stored in aliquots at -70°C.

Radioligand binding assays

Saturation binding studies were carried out in duplicate with 1-3 mg w.w. per tube in 0.5 ml buffer (50 mM Tris, 4 mM MgCl2, 100 mM NaCl, 1 mM EDTA, 5 mM ascorbate and 10 μM pargyline at pH 7.4), 0.2 nM [^{125}I]SB258585 and unlabelled SB258585 to give a final concentration range of 0.23- 20 nM (12 conc.). Non-specific binding was determined in the presence of 10 μM methiothepin. In the competition experiments 0.8-2 mg w.w. per tube and a radioligand concentration of 0.5-1 nM were used with 7 concentrations of the competing drug pre-dissolved in DMSO and diluted in buffer. The assays were incubated for 1-3 hours at room temperature, and terminated by rapid filtration through Whatman GF/B filters pretreated with 0.3% polyethyleneimine using a Brandel cell harvester. The radioactivity was determined in a Packard Tri-Carb 2900TR liquid scintillation counter. Data were analyzed by non-linear regression analyses using PRISM 4.00 (GraphPad Software Inc., San Diego, CA).

More informantion about the asay can be found in Hirst, W.D., Minton, J.A.L., Bromidge, S.M., Moss, S.F., Latter, A., Riley, G., Routledge, C., Middlemiss, D.N. & Price, G.W. (2000). Characterization of [^{125}I]-SB-258585 binding to human recombinant and native 5-HT6 receptors in rat, pig and human brain tissue is described in Br. J. Pharmacol., 130, 1597-1605.

Results

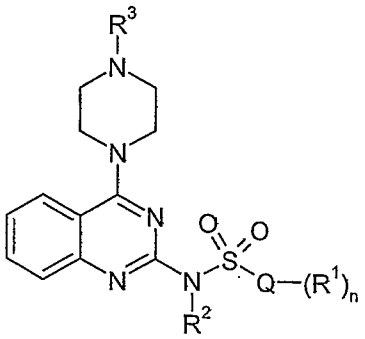
Typical IC_{50} values as measured in the assays described above are 1 μM or less. In one aspect of the invention the IC_{50} is below 500 nM. In another aspect of the invention the IC_{50} is below 50 nM. In a further aspect of the invention the IC_{50} is below 10 nM.

Table. Specimen results from assay.

Example no	**K_i (nM)**
2	200

CLAIMS

1. A compound having the formula I



I

wherein

Q is C_{6-10}arylC_{0-6}alkyl or C_{5-11}heteroarylC_{0-6}alkyl;

R^1 is hydroxy, halogen, C_{1-6}alkyl, C_{1-6}alkoxy, C_{6-10}arylC_{0-3}alkyl, C_{5-6}heteroarylC_{0-3}alkyl, C_{1-6}haloalkyl, R^4OC_{0-6}alkyl, cyano, $R^5SO_2C_{0-6}$alkyl, SOR^5, $R^4CON(R^4)C_{0-6}$alkyl, COR^5, $R^5CO_2C_{0-6}$alkyl, $R^5OC(O)C_{0-6}$alkyl, $(R^5)_2NCOC_{0-6}$alkyl, NO_2, C_{3-7}heterocycloalkyl or oxo;

n is 0, 1, 2 or 3;

R^2 is hydrogen, C_{1-10}alkyl, C_{1-6}haloalkyl, cyanoC_{1-6}alkyl, $(R^6)_2NCOC_{1-6}$alkyl, R^6OC_{2-6}alkyl or $R^6C(O)N(R^6)C_{1-6}$alkyl; or

R^1 and R^2 are connected to give a 5 or 6 membered heterocyclic ring;

R^3 is hydrogen, C_{1-10}alkyl, C_{1-6}haloalkyl, cyanoC_{1-6}alkyl, $(R^6)_2NCOC_{1-6}$alkyl, R^6OC_{2-6}alkyl or $R^6C(O)N(R^6)C_{1-6}$alkyl;

R^4 is hydrogen, C_{1-6}alkyl, C_{6-10}arylC_{0-3}alkyl, C_{5-6}heteroarylC_{0-3}alkyl or C_{1-3}haloalkyl;

R^5 is C_{1-6}alkyl, C_{1-6}haloalkyl, C_{6-10}arylC_{0-6}alkyl or C_{5-6}heteroarylC_{0-6}alkyl;

whereby any aryl, heterocycloalkyl and heteroaryl under R^1, R^4 and R^5 may be substituted by one or more groups selected independently from hydrogen, halogen, hydroxy, C_{1-6}haloalkyl, cyano, OR^6, C_{1-6}alkyl, oxo, SR^6, $CON(R^6)_2$, $N(R^6)COR^{12}$, SO_2R^{12}, SOR^{12}, $N(R^6)_2$ and COR^6; and

R^6 is hydrogen, C_{1-6}alkyl or C_{1-6}haloalkyl;

or pharmaceutically acceptable salts, solvates or solvated salts thereof.

2. A compound according to claim 1, wherein

Q is C_{6-10}arylC_{0-6}alkyl;

R^1 is halogen, C_{1-6}alkyl, C_{6-10}arylC_{0-3}alkyl, C_{1-6}haloalkyl, $R^5CO_2C_{0-6}$alkyl, $R^5OC(O)C_{0-6}$alkyl or C_{3-7}heterocycloalkyl;

n is 0, 1 or 2;

R^2 is hydrogen, C_{1-10}alkyl or C_{1-6}haloalkyl; or

R^1 and R^2 are connected to give a 5 or 6 membered heterocyclic ring; and

R^3 is hydrogen or C_{1-10}alkyl thereof.

3. A compound according to claim 1 or claim 2, wherein R^3 is C_{1-10}alkyl.

4. A compound according to claim 3, wherein R^3 is methyl.

5. A compound according to any one of claims 1 to 4, wherein Q is C_6aryl.

6. A compound according to claim 5, wherein Q is phenyl.

7. A compound according to any one of claims 1 to 4, wherein Q is C_{10}aryl

8. A compound according to any one of claims 1 to 4, wherein Q is C_2alkylC_6aryl.

9. A compound according to any one of claims 1 to 6, wherein R^1 is C_{1-10}alkyl.

10. A compound according to any one of claims 1 to 6, wherein R^1 is C_{6-10}aryl.

11. A compound according to claim 10, wherein R^1 is methyl.

12. A compound according to any one of claims 1 to 5, wherein R^1 is C_{6-10}aryl.

13. A compound according to claim 12, wherein R^1 is C_6aryl

14. A compound according to any one of claims 1 to 6, wherein R^1 is C_{1-6}haloalkyl.

15. A compound according to any one of claims 1 to 6, wherein R^1 is halogen.

16. A compound according to any one of claims 1 to 15, wherein R^2 is methyl.

17. Compounds according to claim 1, said compounds being:
N-Methyl-*N*-[4-(4-methylpiperazin-1-yl)quinazolin-2-yl]-3-(trifluoromethyl)benzenesulfonamide;
4-chloro-*N*-methyl-*N*-[4-(4-methylpiperazin-1-yl)quinazolin-2-yl]benzenesulfonamide;
N,4-dimethyl-*N*-[4-(4-methylpiperazin-1-yl)quinazolin-2-yl]benzenesulfonamide;
N-Methyl-*N*-(4-piperazin-1-ylquinazolin-2-yl)-3-(trifluoromethyl)benzenesulfonamide;
N-methyl-*N*-(4-piperazin-1-ylquinazolin-2-yl)biphenyl-4-sulfonamide;
N-methyl-*N*-(4-piperazin-1-ylquinazolin-2-yl)naphthalene-2-sulfonamide;
3-bromo-*N*-methyl-*N*-(4-piperazin-1-ylquinazolin-2-yl)benzenesulfonamide;
3,4-dichloro-*N*-methyl-*N*-(4-piperazin-1-ylquinazolin-2-yl)benzenesulfonamide;
N,4-dimethyl-*N*-(4-piperazin-1-ylquinazolin-2-yl)benzenesulfonamide;
N-(2-Fluoroethyl)-2-(1-naphthyl)-*N*-(4-piperazin-1-ylquinazolin-2-yl)ethanesulfonamide;
2-(4-Chlorophenyl)-*N*-methyl-*N*-(4-piperazin-1-ylquinazolin-2-yl)ethanesulfonamide; and
2-(1,1-Dioxido-1,2-benzisothiazol-2(3*H*)-yl)-4-piperazin-1-ylquinazoline,
or pharmaceutically acceptable salts, solvates or solvated salts thereof.

18. A compound according to any one of claims 1 to 17, for use in therapy.

19 Use of a compound according to any one of claims 1 to 17, in the manufacture of a medicament for treatment of 5-HT6 mediated disorders.

20. Use of a compound according to any one of claims 1 to 17, in the manufacture of a medicament for treatment of Alzheimer's disease, cognitive impairment associated with schizophrenia, obesity and/or Parkinson's disease.

21. A pharmaceutical composition comprising as active ingredient a therapeutically effective amount of a compound according to any one of claims 1 to 17, in association with one or more pharmaceutically acceptable diluents, excipients and/or inert carriers.

22. The pharmaceutical composition according to claim 21, for use in the treatment of Alzheimer's disease, cognitive impairment associated with schizophrenia, obesity or Parkinson's disease.

23. A method of treatment of Alzheimer's disease, cognitive impairment associated with schizophrenia, obesity or Parkinson's disease, comprising administrering to a mammal, including man in need of such treatment, a therapeutically effective amount of a compound according to any one of claims 1 to 17.

24. An agent for the prevention or treatment of Alzheimer's disease, cognitive impairment associated with schizophrenia, obesity or Parkinson's disease, which comprises as active ingredient a compound according to any one of claims 1 to 17.

25. 2-Chloro-4-(4-Boc-piperazin-1-yl)quinazoline.

26. *N*-(2-fluoroethyl)-2-(1-naphthyl)ethanesulfonamide.

27. Use of the compound according to claim 25 or claim 26, as intermediate in the preparation of compounds according to claim 1.