

Thus, PDE1 is a therapeutic target for regulation of intracellular signalling pathways, preferably in the nervous system and PDE1 inhibitors can enhance the levels of the second messengers cAMP/cGMP leading to modulation of neuronal processes and to the expression of neuronal plasticity-related genes, neurotrophic factors, and neuroprotective molecules. These neuronal plasticity enhancement properties together with the modulation of synaptic transmission make PDE1 inhibitors good candidates as therapeutic agents in many neurological and psychiatric conditions. The evaluation of PDE1 inhibitors in animal models (for reviews see e.g. Blokland et al. Expert Opinion on Therapeutic Patents (2012), 22(4), 349-354; and Medina, A. E. Frontiers in Neuropharmacology (2011), 5(Feb.), 21) have suggested the potential for the therapeutic use of PDE1 inhibitors in neurological disorders, like e.g. Alzheimer's, Parkinson's and Huntington's Diseases and in psychiatric disorders like e.g. Attention Deficit hyperactivity Disorder (ADHD), restless leg syndrome, depression, narcolepsy, cognitive impairment and cognitive impairment associated with schizophrenia (CIAS). There have also been patent applications claiming that PDE1 inhibitors are useful in diseases that may be alleviated by the enhancement of progesterone-signalling such as female sexual dysfunction.

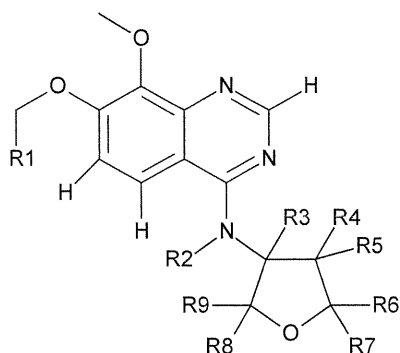
The compounds of the invention may offer alternatives to current marketed treatments for neurodegenerative and/or psychiatric disorders, which are not efficacious in all patients. Hence, there remains a need for alternative methods of treatment.

SUMMARY OF THE INVENTION

PDE1 enzymes are expressed in the Central Nervous System (CNS), making this gene family an attractive source of new targets for the treatment of psychiatric and neurodegenerative disorders.

The objective of the present ~~invention~~ disclosure is to provide compounds that are PDE1 inhibitors, and as such are useful to treat neurodegenerative disorders and psychiatric disorders. In a preferred embodiment the compounds are selective PDE1 inhibitors.

Accordingly, ~~the present invention~~ one aspect relates to compounds of formula (I)



(I)

wherein

5 R_1 is selected from the group consisting of H and C_1 to C_3 alkyl;

R_2 is selected from the group consisting of H and C_1 - C_3 alkyl, wherein the C_1 - C_3 alkyl optionally is substituted one or more times with one or more substituents selected from the group consisting of phenyl and C_3 - C_6 cycloalkyl,

R_3 is selected from the group consisting of H, methyl and ethyl,

10 R_4 is selected from the group consisting of H, hydroxy, methoxy and ethoxy,

R_5 , R_6 and R_7 are H,

R_8 is selected from the group consisting of H, methyl, ethyl and cyclopropyl

R_9 is selected from the group consisting of H, methyl and ethyl

and pharmaceutically acceptable acid addition salts of Compound I, racemic

15 mixtures of Compound I, or the corresponding enantiomer and/or optical isomer of Compound I, and polymorphic forms of Compound I as well as tautomeric forms of Compound I. Another aspect relates to the compound as disclosed herein for use as a medicament.

20 In another aspect, there is provided the use of the compound as disclosed herein in the manufacture of a medicament for the treatment of ADHD, schizophrenia or cognitive impairment associated with schizophrenia.

N-(2,3-Dimethyltetrahydrofuran-3-yl)-7,8-dimethoxy-N-methylquinazolin-4-amine

N-(2,2-dimethyltetrahydrofuran-3-yl)-7,8-dimethoxyquinazolin-4-amine

7,8-dimethoxy-N-methyl-N-(2-methyltetrahydrofuran-3-yl)quinazolin-4-amine

5 7,8-dimethoxy-N-methyl-N-(3-methyltetrahydrofuran-3-yl)quinazolin-4-amine

N-(3-Ethyltetrahydrofuran-3-yl)-7,8-dimethoxyquinazolin-4-amine

N-(2-Cyclopropyltetrahydrofuran-3-yl)-7,8-dimethoxyquinazolin-4-amine

6. The compound of any of claims 1 to 5, ~~wherein the compound is for use as a~~
medicament.

10 ~~7. The compound of any of claims 1 to 5, wherein the compound is for use in
treating ADHD, schizophrenia or cognitive impairment associated with
schizophrenia~~

8.7. Use of ~~The~~ compound of any of claim 1 to 5 ~~for~~ in the manufacture of a
medicament for the treatment of ADHD, schizophrenia or cognitive
15 impairment associated with schizophrenia.