Salts in the solid form may exist in more than one crystal structure, and may also be in the form of hydrates. Salts derived from pharmaceutically acceptable organic non-toxic bases include salts of primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines, and basic ion exchange resins, such as arginine, betaine, caffeine, choline, *N,N'*-dibenzylethylene-diamine, diethylamine, 2-diethylaminoethanol, 2-dimethylaminoethanol, ethanolamine, ethylenediamine, *N*-ethylmorpholine, *N*-ethylpiperidine, glucamine, glucosamine, histidine, hydrabamine, isopropylamine, lysine, methylglucamine, morpholine, piperazine, piperidine, polyamine resins, procaine, purines, theobromine, triethylamine, trimethylamine, tripropylamine or tromethamine.

When the compound of the present invention is basic, salts may be prepared from pharmaceutically acceptable non-toxic acids, including inorganic and organic acids. Such acids include acetic, trifluoroacetic, benzenesulfonic, benzoic, camphorsulfonic, citric, ethanesulfonic, fumaric, gluconic, glutamic, hydrobromic, hydrochloric, isethionic, lactic, maleic, malic, mandelic, methanesulfonic, mucic, nitric, pamoic, pantothenic, phosphoric, succinic, sulfuric, tartaric or *para*-toluenesulfonic acid.

The present invention is directed to the use of the compounds of formulae (I) to (III) disclosed herein as M1 allosteric modulators in a patient or subject such as a mammal in need of such activity, comprising the administration of an effective amount of the compound. ~~In addition to humans, a variety of other mammals can be treated according to the method of the present invention.~~

The compounds of the present invention have utility in treating or ameliorating Alzheimer's disease. The compounds may also be useful in treating or ameliorating other diseases mediated by the muscarinic M1 receptor, such as schizophrenia, sleep disorders, pain disorders (including acute pain, inflammatory pain and neuropathic pain) and cognitive disorders (including mild cognitive impairment). Other conditions that may be treated by the compounds of the invention include Parkinson's Disease, pulmonary hypertension, chronic obstructive pulmonary disease (COPD), asthma, urinary incontinence, glaucoma, schizophrenia, Trisomy 21 (Down Syndrome), cerebral amyloid angiopathy, degenerative dementia, Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch-Type (HCHWA-D), Creutzfeld-Jakob disease, prion disorders, amyotrophic lateral sclerosis, progressive supranuclear palsy, head trauma, stroke, pancreatitis, inclusion body myositis, other peripheral amyloidoses, diabetes, autism and atherosclerosis.

In preferred embodiments, the compounds of the invention are useful in treating Alzheimer's Disease, cognitive disorders, schizophrenia, pain disorders and sleep disorders. For example, the compounds may be useful for the prevention of dementia of the Alzheimer's type, as well as for the treatment of early stage, intermediate stage or late stage dementia of the Alzheimer's type.

illness associated with psychosis (such as major depression, manic depressive (bipolar) disorder, Alzheimer's disease and post-traumatic stress syndrome), including both the positive and the negative symptoms of schizophrenia and other psychoses; cognitive disorders including dementia (associated with Alzheimer's disease, ischemia, multi-infarct dementia, trauma, vascular problems or stroke, HIV disease, Parkinson's disease, Huntington's disease, Pick's disease, Creutzfeldt-Jacob disease, perinatal hypoxia, other general medical conditions or substance abuse); delirium, amnestic disorders or age related cognitive decline.

~~In another specific embodiment, the present invention provides a method for treating schizophrenia or psychosis comprising administering to a patient in need thereof an effective amount of a compound of the present invention.~~ Particular schizophrenia or psychosis pathologies are paranoid, disorganized, catatonic or undifferentiated schizophrenia and substance-induced psychotic disorder. At present, the text revision of the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) (2000, American Psychiatric Association, Washington DC) provides a diagnostic tool that includes paranoid, disorganized, catatonic or undifferentiated schizophrenia and substance-induced psychotic disorder. As used herein, the term "schizophrenia or psychosis" includes treatment of those mental disorders as described in DSM-IV-TR. The skilled artisan will recognize that there are alternative nomenclatures, nosologies and classification systems for mental disorders, and that these systems evolve with medical and scientific progress. Thus the term "schizophrenia or psychosis" is intended to include like disorders that are described in other diagnostic sources.

Examples of combinations of the compounds include combinations with agents for the treatment of schizophrenia, for example in combination with sedatives, hypnotics, anxiolytics, antipsychotics, antianxiety agents, cyclopyrrolones, imidazopyridines, pyrazolopyrimidines, minor tranquilizers, melatonin agonists and antagonists, melatonergic agents, benzodiazepines, barbiturates or 5HT-2 antagonists, such as: adinazolam, allobarbital, alonimid, aiprazolam, amisulpride, amitriptyline, amobarbital, amoxapine, aripiprazole, bentazepam, benzoctamine, brotizolam, bupropion, busprione, butabarbital, butalbital, capuride, carbocloral, chloral betaine, chloral hydrate, clomipramine, clonazepam, cloperidone, clorazepate, chlordiazepoxide, clorethate, chlorpromazine, clozapine, cyprazepam, desipramine, dexclamol, diazepam, dichloralphenazone, divalproex, diphenhydramine, doxepin, estazolam, ethchlorvynol, etomidate, fenobam, flunitrazepam, flupentixol, fluphenazine, flurazepam, fluvoxamine, fluoxetine, fosazepam, glutethimide, halazepam, haloperidol, hydroxyzine, imipramine, lithium, lorazepam, lormetazepam, maprotiline, mecloqualone, melatonin, mephobarbital, meprobamate, methaqualone, midaflur, midazolam, nefazodone, nisobamate, nitrazepam, nortriptyline,

(8) –CN,

(9) a heteroaryl group, which is an aromatic cyclic group, having from five to twelve ring atoms, said ring atoms selected from C, O, N, N→O or S, at least one of which is O, N, N→O or S,

~~(10) O-heterocyclyl,~~

(~~11~~10) -NR^AR^B,

wherein R^A and R^B are selected from the group consisting of

(a) hydrogen, or

(b) –C_{1-6} alkyl,

or R^A and R^B are linked together with the nitrogen to which they are attached to form a 4-6 membered carbocyclic ring, wherein one or two of the ring carbon atoms is optionally replaced by a nitrogen, oxygen or sulfur, and the ring is optionally substituted with one or more

(a) halogen,

(b) hydroxyl,

(c) C_{1-6} alkyl,

(d) –O-C_{1-6} alkyl,

(e) –C(=O)-$(O)_n$ -C_{1-6} alkyl;

wherein n is 0-1; and the alkyl, cycloalkyl, aryl or heteroaryl R^4 group is optionally substituted with one or more

(a) halogen,

(b) hydroxy,

(c) –O-C_{1-6} alkyl,

(d) –C_{1-6} alkyl,

(e) –S-C_{1-6} alkyl, or

(f) a heteroaryl group, which is an aromatic cyclic group, having from five to twelve ring atoms, said ring atoms selected from C, O, N, N→O or S, at least one of which is O, N, N→O or S,

wherein the alkyl, aryl or heteroaryl moiety is optionally substituted with one or more

(i) halogen,

(ii) hydroxy,

(iii) –O-C_{1-6} alkyl, or

(iv) –C_{1-6} alkyl;

or two R^4 groups are linked together to form a three or four atom fused ring heteroaryl group, said ring atoms selected from C, O, N, N→O or S, at least one of which is O, N, N→O or S,

N-[(3R,4S)-3-hydroxytetrahydro-2H-pyran-4-yl]-4-{[6-(methylsulfanyl)pyridin-3-yl]methyl}quinoline-2-carboxamide;
4-[(2-ethoxypyridin-4-yl)methyl]-8-fluoro-N-[(3R,4S)-3-hydroxytetrahydro-2H-pyran-4-yl]quinoline-2-carboxamide;
4-[(6-ethoxypyridin-3-yl)methyl]-8-fluoro-N-[(3R,4S)-3-hydroxytetrahydro-2H-pyran-4-yl]quinoline-2-carboxamide;
N-[(3R,4S)-3-hydroxytetrahydro-2H-pyran-4-yl]-4-{[2-(methylsulfanyl)pyridin-4-yl]methyl}quinoline-2-carboxamide;
or a pharmaceutically acceptable salts thereof.

19. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claims 1 or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

20. A pharmaceutical composition for the treatment of a disease or disorder mediated by the muscarinic M1 receptor, wherein said disease or disorder is selected from the group consisting of Alzheimer's disease, schizophrenia, pain or sleep disorders, comprising a therapeutically effective amount of a compound of claim 1 or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

21. Use of a compound of claim 1 or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, for the manufacture of a medicament for the treatment of a disease or disorder mediated by the muscarinic M1 receptor, wherein said disease or disorder is selected from the group consisting of Alzheimer's disease, schizophrenia, pain or sleep disorders.

22. A compound of claim 1 which is *N*-[(3*R*,4*S*)-3-Hydroxytetrahydro-2H-pyran-4-yl]-4-[(6-methoxypyridin-3-yl)methyl]-quinoline-2-carboxamide, or a pharmaceutically acceptable salt thereof.

23. A compound of claim 1 which is 4-[(6-Ethoxypyridin-3-yl)methyl]-*N*-[(3*R*,4*S*)-3-hydroxytetrahydro-2*H*-pyran-4-yl]quinoline-2-carboxamide, or a pharmaceutically acceptable salt thereof.

24. A compound of claim 1 which is *N*-[(3*R*,4*S*)-3-Hydroxytetrahydro-2*H*-pyran-4-yl]-4-[(2-methoxypyridin-4-yl)methyl]quinoline-2-carboxamide, or a pharmaceutically acceptable salt thereof.

25. A compound of claim 1 which is 4-[(6-Chloropyridin-3-yl)methyl]-8-fluoro-*N*-[(3*R*,4*S*)-3-hydroxytetrahydro-2*H*-pyran-4-yl]quinoline-2-carboxamide, or a pharmaceutically acceptable salt thereof.

26. A compound of claim 1 which is 4-{[6-(Difluoromethyl)pyridin-3-yl]methyl}-8-fluoro-*N*-[(3*R*,4*S*)-3-hydroxytetrahydro-2*H*-pyran-4-yl]quinoline-2-carboxamide, or a pharmaceutically acceptable salt thereof.

27. A compound of claim 1 which is 8-Fluoro-*N*-[(3*R*,4*S*)-3-hydroxytetrahydro-2*H*-pyran-4-yl]-4-[(6-methoxypyridin-3-yl)methyl]quinoline-2-carboxamide, or a pharmaceutically acceptable salt thereof.

28. A compound of claim 1 which is 8-Fluoro-4-[(6-hydroxypyridin-3-yl)methyl]-*N*-[(3*R*,4*S*)-3-hydroxytetrahydro-2*H*-pyran-4-yl]quinoline-2-carboxamide, or a pharmaceutically acceptable salt thereof.