SYNTHESIS CHARACTERIZATION AND BIOLOGICAL EVOLUTION OF SOME NOVEL ANTIDEPRESSANT TRICYCLIC HETROCYCLE OXAZEPINE

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ABSTRACT

The majority of pharmaceuticals and biologically active agrochemicals are heterocyclic compounds; it represents their immense importance in serving mankind. The purpose of this thesis was to investigate feasibility of making potential biological active noval heterocyclic compounds designed based on lead molecules. The work accomplished in this thesis includes five different chapters to explain importance, achieve simple and fused-ring heteropolicyclic systems having potential pharmacological properties.

KEYWORD: hetrocycle, biological evolution

INTRODUCTION

Heterocycles constitute one of the largest areas of research in organic chemistry. Heterocycles occur in a variety of organic compounds with their significant applications in electronics, biology, optics, pharmacology, material sciences and so on. A large number of heterocyclic compounds having natural as well as synthetic origin, which have been found to be pharmacologically active and have paramount importance in clinical use. Synthetic heterocycles have widespread therapeutic uses such as antibacterial, antifungal, antimycobacterial, trypanocidal, anti-HIV activity, antitubercular, antimalarial, analgesic, anti-inflammatory, antileishmanial, muscle relaxants, anticonvulsant, anticancer and lipid peroxidation inhibitor, hypnotics, antidepressant, antitumor, antihelmintic and insecticidal agents. Several heterocyclic compounds have applications in

agriculture as insecticides, fungicides, herbicides and pesticides. The fundamental unit of life, such as purine and pyrimidine bases, structural units of RNA and DNA, haem derivatives in blood, the chlorophylls essential for photosynthesis and enzymes like serotonin, a neurotransmitter found in our body, being is responsible for various bodily functions, are all heterocycles. Heterocycles bearing nitrogen atoms constitute the core structure of a number of important physiologically active molecules and play an important role in the metabolism of living cells. Their useful applications vary from in depth clinical use to fields as numerous as agriculture, photography, and biocide formulation, polymer science with the range of these glorious compounds being limitless, encompassing stantial spectrum of physical, chemical and biological properties. Nitrogen containing heterocyclic compounds has maintained the interest of researchers through decades of historical development of organic synthesis. The nitrogen heterocycles whether natural or synthetic one owing to their interesting biological properties is very often involved as key component in biological processes. Many synthetic nitrogen heterocycles have wide spread uses as antiviral, antibacterial, antifungal, anti-inflammatory, antioxidant and anticancer agents. In nature too, especially in plant kingdom, the nitrogen containing heterocyclic compounds have made indelible mark as insecticides, pesticides and weed killers. The multifaceted properties and captivating structure of N-heterocyclic compounds encourage chemists to keep on synthesizing novel nitrogen heterocycles with versatile pharmacological activities. Azoles belong to a category of five membered heterocyclic compounds containing nitrogen with one or more than one non-carbon atoms of either nitrogen, or sulfur. Several natural products, medication and biologically active molecules have azole moiety.

REVIEW OF LITERATURE

Liegeios (2002) et al reported a progression of pyridobenzodiazepine derivatives (23, 24) and the influence of the replacement of one of the benzene ring of clozapine by pyridine (pyridobenzodiazepine). The pyridobenzodiazepine derivatives indicated modified selectivity towards D2, D4 and 5HT2A receptors contrasted with clozapine and haloperidol. HE have reported aromatic substitution of the distal nitrogen (phenyl, 3-chlorophenyl or 3-trifluoromethylphenyl (27) absolutely stifle the proclivity at D2, D4 and 5HT2A

receptors while substitution of cyclohexyl ring retained some fondness. On account of phenyl piperazine analogs the basicity of distal N4 nitrogen is exceedingly decreased by electron pulling back potential of a phenyl ring.

Hussenether (2004) et al reported arrangement of 2, 3-dihydro-1H-1,4 and 1,5-benzodiazepines derivatives (25, 26) with D1, D2, D3 and D4 restricting affinities. There is almost no improvement as far as liking on D2 and also D4 receptor in contrast with clozapine, yet a portion of the compounds demonstrated a momentous increment in selectivity for D4 over D2 and D3.

Ben capauno (2003) et al, reported a synthesis of 4'- arylmethyl analogs of clozapine (28) in view of its structural adjustment and assessed their affinities for dopamine (D2, D4) and serotonin (5-HT2A) receptors. The inductively electron with illustration substituent at either the meta or para position of the benzene ring demonstrated a sensational decrease in D4 receptor proclivity while presentation of the feebly ring actuating methyl/methoxy bunch at either the meta or para position of benzyl moiety delivered moderate partiality for both dopamine and serotonin receptors.

Chandra Sekhar (2008) et al. have reported that substitution of acetamide on distal nitrogen (N4) of piperazine builds partiality towards 5HT2A receptors. A progression of N-2-(4-(4-(2-substitutedthiazol-4-yl) piperazin-1-yl)- 2-oxoethyl) acetamides (32) were synthesized and assessed for their antipsychotic action. The compounds with 5-HT2A/D2 proportion of 1.1286 and a normal cataleptic score of zero (risperidone's 5-HT2A/D2 proportion is 1.0989). Consequently fulfills every one of the criteria required for a particle to be atypical antipsychotic as indicated by Meltzer's classification.

Upadhayaya R S, Sinha N (2004) et al Piperazine is an intriguing heterocyclic moiety as constituent of a few biologically active particles. The polar nitrogen particles in the piperazine ring give bioactivity to atoms and upgrade positive interaction with macromolecules. Piperazinyl-connected ciprofloxacin dimers are powerful antibacterial agents against resistant strains, antimalarial agents and potential antipsychotic agents. Piperazine derivatives containing tetrazole core have been reported as antifungal agents.

Chavez, D.E.; Parrish, D.A. J. (2009) et al The synthesis of high nitrogen containing heterocyclic frameworks has been drawing in expanding enthusiasm over the previous decade in light of their utility in different applications, for example, charges, explosives, fireworks and particularly chemotherapy. In the restorative science, azoles are broadly utilized and examined class of antimicrobial agents because of their wellbeing profile and high helpful file. Among these, Conazoles are a major class of azole-based drugs, for example, Itraconazole, Fluconazole, Voriconazole, Ravuconazole and so on. Some of other major applications of conazoles are on product insurance.

Sbardella, G.; Mai, An.; Artico, M.; Loddo, R.; Setzuc, M.G.; La Collac, P. Bioorg (2004) et al According to the World Health Organization (WHO), around 30 million individuals will be contaminated inside next 20 years. Accordingly, the treatment of contaminations has turned into an essential and challenging issue as a result of the expanding number of multi-drug resistant microbial pathogens.

Wilmes R (1981) et al The Thazole moiety is a vital and regular insecticidal, agrochemical structural component of numerous biologically active compounds, for example, cytochrome P450 chemical inhibitors and peptide simple inhibitors. As of late, much consideration has been focused on 1H-1,2,4-triazole derivatives for their wide range exercises, for example, fungicidal, herbicidal, anticonvulsant and plant development administrative exercises.

DISCOVERING DRUG TARGETS

Before, the existence of a drug target must be built up if a drug or a toxic substance delivered a biological impact, demonstrating the existence of a sub-atomic target. Subsequently, the disclosure of drug targets relied upon finding the drug first. Numerous early drugs were natural products from plants. Be that as it may, natural products from is plant are not synthesized to cooperate with a receptor or chemical in the human body is such associations are because of fortuitous event as opposed to design. Along these lines, identifying drug targets thusly was particularly a hit and miss issue.

the job of a fairly more methodical Indiana jones that brings in 'the substantial squad 'to clear the wilderness from the sanctuary, therefore uncovering all the conceivable entryways. Once uncovered, he is looked with

countless unsuspected entryways. Be that as it may, he has no keys to fit them. To tackle the issue, he can complete at least one of the accompanying:

DRUG DISCOVERY AND DEVELOPMENT

These natural products started off a major manufactured exertion in which scientific experts made actually a great many analogs trying to improve on what nature had given. Quite a bit of this work was done on a trial and error premise, yet the outcomes got uncovered a few general standards behind drug design. A general example for drug disclosure and drug development additionally advanced yet there was as yet an expansive component of trial and error engaged with the procedure. The mechanism by which a drug worked at the atomic level was once in a while comprehended and drug research particularly focused on what is known as the lead compound-the active guideline isolated from the plant.

ORGANIC SYNTHESIS

The area of drug discovery and natural products Benzoxazepines are for the most part synthesized by condensation of 2-aryloxyethylamines with 2-formylbenzoic corrosive. Others have additionally been synthesized from amides and amino acids. Be that as it may, the majority of these methodologies are related with several drawbacks, for example, low synthetic effectiveness and sensitivity. In this manner, an astounding hole remains in the pursuit of economical amalgamation techniques. Couple transformation is a standout amongst the best approaches to achieve this objective. Considering the above focuses, Scheme 1 The critical benzo-1,4-oxazepine subsidiaries.

The challenge in natural union is building up an efficient and eco-accommodating protocol, particularly in the area of drug discovery and natural products. Benzoxazepines are for the most part synthesized by condensation of 2-aryloxyethylamines with 2-formylbenzoic corrosive.

BIOLOGICAL EVOLUTION

Biological evolution is the process through which the characteristics of organisms change over successive generations, by means of genetic variation and natural selection. It is most commonly defined as "changes in gene frequencies in populations."[1] The result of the process may be minimal or substantial; it embraces

everything from slight changes within a species, to the successive alterations that lead to the diversification of an organism into countless unique species.

Creation scientists accept the observable quantity of change taking place within living organisms - often called microevolution, but contest the assertion by Darwinists that this process has led to the existence of all life on Earth. Biological evolution should not be confused with the general theory of evolution, which also includes cosmological evolution. In addition, changes such as metamorphosis or embryonic development are not considered evolutionary. Biological evolution transcends the lifetime of a single individual and is best summarized as the changes that are inherited through genetic information from one generation to the next.

A frequent point of confusion is generated because many evolutionists use the term biological evolution to refer to either the process of change, or the theory of common descent of living organisms (see: Equivocation). Note the following definition from Talk. Origins

> Biological evolution is a change in the genetic characteristics of a population over time. That this happens is a fact. Biological evolution also refers to the common descent of living organisms from shared ancestors

CONCLUSION

heterocyclic systems containing isoxazole, pyrazole, diazepine, and thiazepine nuclei have attracted the attention of chemists, on account of the significant medicinal properties associated with them. In view of the prodigious range of activities of these compounds, it has been considered worthwhile in the present work to undertake investigation on the synthesis of condensed nitrogen sulfur heterocyclic systems containing above nuclei fused to 3,5 dimethyl pyrazole framework. It is hoped that synthesis of these condensed heterocyclic system and evaluation of their biological properties would provide a rational approach to the study of the structure activity relationship of these molecules.

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