Part B

STUDIES ON FUSED HETEROCYCLIC DERIVATIVES
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Introduction

For more than a century, heterocycles have constituted one the largest areas of research in organic chemistry. They have contributed to the development of society from a biological and industrial point of view as well as to the understanding of life processes and to the efforts to improve the quality of life. Heterocycles play an important role in biochemical processes because the side groups of the most typical and essential constituents of living cells, DNA and RNA, are based on aromatic heterocycles. Among the approximately 20 million chemical compounds identified by the end of the second millennium, more than two-thirds are fully or partially aromatic, and approximately half are heterocyclic. The presence of heterocycles in all kinds of organic compounds of interest in biology, pharmacology, optics, electronics, material sciences, and so on is very well known. Between them, sulfur and nitrogen-containing heterocyclic compounds have maintained the interest of researchers through decades of historical development of organic synthesis. The grounds of this interest were their biological activities and unique structures that led to several applications in different areas of pharmaceutical and agrochemical research or, more recently, in material sciences. To overcome the problems regarding multi drug resistance, the development of new and safe antimicrobial agents with better effectiveness is urgently required.

The family of nitrogen and sulfur heterocycles includes highly stable aromatic compounds that display physicochemical properties with relevance in the design of new materials, especially those relating to molecular conductors and magnets. During the past few decades, interest has been rapidly growing in gaining insight into the properties and transformations of these heterocycles. The interesting characteristics found in many of them have led to the development of modern synthetic methods that are the subject of this special issue. Nitrogen and sulfur heterocycles are formally derived from aromatic carbon cycles with a heteroatom taking the place of a ring carbon atom or a complete CH=CH group. The presence of heteroatoms results in significant changes in the cyclic molecular structure due to the availability of unshared pairs of electrons and the difference in electronegativity between heteroatoms and carbon. Therefore, nitrogen and sulfur heterocyclic compounds display
physicochemical characteristics and reactivity quite different from the parent aromatic hydrocarbons.

To this end, one of the best ways to design new antimicrobial agents is to generate hybrid molecules by combining two bioactive heterocyclic moieties in a single molecular scaffold. Condensed heterocyclic systems are characterized to have a significant pharmacological activity. Heterocycles make up an exceedingly important class of compounds due to their expansive range of applications. They are predominant among all types of pharmaceuticals, agrochemicals and veterinary products. Heterocycles containing nitrogen, sulfur and oxygen have been under investigation for a long time because of their important medicinal properties. The recent literature is enriched with progressive findings about the synthesis and pharmacological action of fused heterocycles. There has been increasing interest in the role played by benzimidazoles, benzothiazole, oxazole, imidazole, pyrazole like five member and pyridine, pyrimidine, pyran like six member ring condensed with other heterocycles have shown their broad pharmacological activities. Today, there is an increased interest in the combination of two pharmacophore on the same scaffold leading to hybrid molecules or conjugates. These hybrid drugs combine two drugs in a single molecule with the goal of creating a chemical entity more medically effective than its individual components.\textsuperscript{3-10} Fused heterocycles have huge practically usefully, mainly due to extremely broad spectrum of genetic actions. The pyrimidine ring is fused to mixture of heterocycles such as quinazoline, pyrimidoazepines, pyralopyrimidines triazolo pyrimidines, pteridines, pyridopyrimidines, furopyrimidines and pyrazole pyrimidines\textsuperscript{11}.

Many active pharmaceutical ingredients containing fused heterocyclic ring systems in their core structure. They are showing wide range of therapeutic activities like antibiotic, antibacterial, calcium channel blocker, anti-inflammatory, anti-depressant, sedative etc.
Few examples of currently available marketed drugs which bearing fused and bridgehead heterocyclic ring system.

Owing to the importance of this heterocyclic system, the present work is an attempt to study the pharmacological activities, structural modifications and the structure-activity relationship (SAR) of bridgehead nitrogen heterocycles and fused heterocycles. The work is mainly based on the three important scaffold i.e. pyrido[2,1-b]benzothiazole, pyrimido[1,2-a]benzimidazole and pyrido[3,2-d]pyrimidine and evaluate their biological activities. The work is summarized into below three sections as under.
SECTION-1: SYNTHESIS AND BIOLOGICAL EVALUATION OF 1-AMINO-3-ARYL-3H-PYRIDO[2,1-b][1,3]BENZOTHIAZOLE-2,4-DICARBONITRILES

SECTION-2: SYNTHESIS AND BIOLOGICAL EVALUATION OF 4-(FURAN-2-YL)-2-ARYL-1,4-DIHYDRO PYRIMIDO[1,2-a]BENZIMIDAZOLES

SECTION-3: SYNTHESIS AND BIOLOGICAL EVALUATION OF 7-AMINO-2,4-DIOXO-5-ARYL-1,2,3,4-TETRAHYDRO PYRIDO[2,3-d]PYRIMIDINE-6-CARBONITRILES
REFERENCES