

ABSTRACT

Pyridine derivatives display a broad range of biological activities such as antimicrobial, antioxidant, anti-inflammation, anticancer, analgesic, agonistic, hypotensive, hallucinogenic and anti-metastatic. In particular it has been fused as a core skeleton in drug candidates involved in enzyme inhibitions. Pyridine bearing hydrazide moieties such as isonicotinic acid hydrazide (INH, isoniazid) and pyridine-2,6-dicarbohydrazide are pharmacologically useful targets as anticonvulsants, antidepressants, anti-inflammatory, antimalarials, antimycobacterials, anticancer and antimicrobials.

Since their discovery they have gained tremendous attention of the researchers working around the world in the field of medicinal chemistry because of the valuable biological activities. The current work presented in this thesis was intended to synthesize some new pyridine based heterocyclic compounds including pyridine 2,4,6-trisubstituted carbohydrazide **247** and its derivatives to unveil their effective enzyme inhibitory potential against urease, cholinesterase, lipoxygenase and α -glucosidase enzymes. Their anti-bacterial potential against various gram-positive and gram-negative bacteria was also ascertained in search of new therapeutic agents. The synthesis of novel pyridine 2,4,6-tricarbohydrazide moiety was further used for four major reaction schemes. The synthetic **Scheme 3.2** depicted herein involved initially the synthesis of novel biological active Schiff bases treating 2,4,6-tricarbohydrazide with selected aldehydes in methanol using few drops of glacial acetic acid. In **Scheme 3.3** synthesized parent novel pyridine 2,4,6-tricarbohydrazide was treated with various aliphatic/aromatic sulfonyl chlorides in aqueous medium at room temperature and pH from 9-10, maintained by occasional addition of sodium carbonate to get novel series of potent sulfonamides. **Scheme 3.4** comprises the synthesis of a novel 5,5',5''-(pyridine-2,4,6-triyl)tris(1,3,4-oxadiazole-2-thiol) moiety **252** which was further subjected to the alkylation to produce a series of novel alkylated compounds following multistep and one pot synthesis. The **Scheme 3.5 & 3.6** were initiated following acylation reaction of pyridine 2,4,6-tricarbohydrazide with acetic and trifluoroacetic anhydrides at 0 °C to room temperature under stirring in mild alkaline media. The next **Scheme 3.7** included the condensation of various anhydrides with the same novel parent hydrazide under basic conditions. In my next schemes **3.9 to 3.12** quaternary pyridinium compounds were synthesized by stirring selected pyridine moieties with alkyl halides in methanol. The predictable structures have been established on

the basis of modern spectroscopic techniques i.e. FTIR, $^1\text{H-NMR}$, $^{13}\text{C-NMR}$, EIMS and single XRD analysis. The synthesized compounds were screened against urease, acetylcholinesterase (AChE), butyrylcholinesterase (BChE), lipoxygenase (LOX) and α -glucosidase enzymes, most of them were found to be active against α -glucosidase and cholinesterases and were less active against lipoxygenase and urease enzymes. The structure activity relationship was studied and was ascertained that particularly Schiff bases showed excellent entrant even to the reference for inhibiting Alpha-glucosidase enzyme. Some of them were found to be moderately to reasonably good active against cholinesterases. Moreover anti-bacterial studies were performed with some of the synthesized compounds and compounds pertaining to **Scheme 3.5, 3.6 & 3.7** portrayed admirable antibacterial activity as evident from their zone of inhibition against various gram-positive and gram-negative bacterial strains. Furthermore, to find out binding modes of the synthesized compounds, all the compounds were computationally docked with acetylcholinesterase and α -glucosidase enzymes. The results obtained were in high agreement with the observed good potency of substituted pyridine derivatives. So, my results revealed that by using simple and more efficient environmentally suitable conditions novel synthesized molecules can serve as potent therapeutic agents.