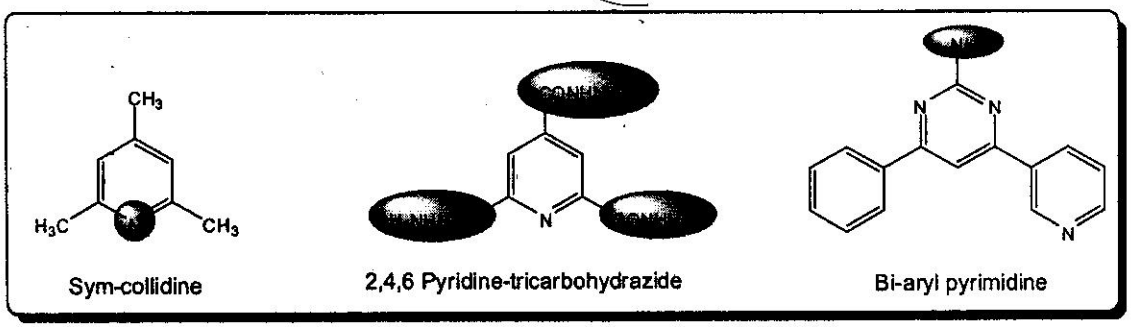
ABSTRACT

Heterocyclic chemistry is the most diverse and biologically significant branch of chemistry that has gained much attention in almost all fields, especially in medicinal chemistry. Heterocyclic compounds have an enormous importance in drugs synthesis due to their reactivity and ability to undergo a wide range of chemical reactions by controlling reaction conditions. The importance of heterocyclic compounds, especially in medicinal chemistry, prompted us to synthesize biologically potent heterocyclic candidates. We selected here, exceedingly significant motifs, i.e., 2,4,6 trimethyl pyridine (Sym-collidine), 2,4,6 pyridine-tricarbohydrazide and bi-aryl pyrimidines that are well-known pharmacophores in drugs discovery.



Sym-collidine | 2,4,6 Pyridine-tricarbohydrazide | Bi-aryl pyrimidine

Pyridine pyrimidines are the most significant class of the heterocycles in medicinal chemistry. Recently, these compounds have attracted much attention and especially amino substituted pyrimidine derivatives that delivered a wide range of pharmacological activities like antibacterial, antifungal, antidepressant, antitumor and antiviral. Among the amino pyrimidine heterocycles, 2-aminopyrimidine motif has been most commonly explored, which is also present in the chemical structure of DNA.

The current research work presented in this thesis was divided into five schemes. The synthetic **Scheme 1** depicted herein involved initially the synthesis of novel pyrimidine based sulfonamides **175a-s** in short periods of time under conventional and microwave conditions in good to excellent yields. The chemical structures of these heterocycles constitute central pyrimidine ring having phenyl group and pyrimidine group with sulfonamides motifs. The enzyme inhibitory potential of these compounds was investigated against acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) because these enzymes play crucial role to treat Alzheimer's disease.

In **Scheme 2,** synthesized novel 4-(5-bromopyridin-3-yl)-6-phenylpyrimidin-2-amine **178** was treated with substituted phenyl thiourea motifs and synthesized **180a-r** derivatives.

Their enzyme inhibitory potential was investigated against α-glucosidase as this enzyme plays an active role in treating type II diabetes mellitus. The quantitative structure–activity relationship (QSAR) of the synthesized compounds was also studied.

In **Scheme 3** a wide range of novel substitute benzylidene-4-(5-bromopyridin-3-yl)-6-phenylpyrimidin 2-amine derivatives **1822a-l** were synthesized by conventional and microwave methodology and their biological inhibitions towards α- and β-glucosidases were studied. Most of the compounds to be most active against α-glucosidase and quite inactive against β-glucosidase. A number of compounds were found to be more active against α-glucosidase than the reference compound acarbose. Molecular modeling studies showed the interactions of most active compound with the active site of target α-glucosidase.

In **Scheme 4** compound **186** was treated with substituted phenyl isothiocyanates to synthesize pyridine-2,4,6-tricarbohydrazide thiourea compounds **188a-r**.

In **Schemes 5** quaternary pyridinium compounds were synthesized by stirring 2,4,6 trimethyl pyridine with substituted aromatic ketones in methanol. The predictable structures have been established on the basis of modern spectroscopic techniques i.e. FTIR, ^{1}H-NMR, ^{13}C-NMR and EIMS. Furthermore, to find out binding modes of the synthesized compounds, all the compounds were computationally docked with different enzymes like acetylcholinesterase, butylcholinesterase, lipoxygenase, and α-glucosidase enzymes. *In silico* drug likeness properties and metabolic stability of synthesized compounds were also calculated. The results obtained were in high agreement with the observed good potency of substituted pyridine pyrimidine derivatives. So, my results revealed that by using simple and more efficient environmentally suitable conditions novel synthesized molecules can serve as potent therapeutic agents.