ABSTRACT

Organic chemists have effectively and extensively elaborated the chemistry of life. Scientists from every field of science are working for the betterment of humanity, and the struggle of chemists is astonishing in this regard. Pharmaceutical or organic chemists are working hard to improve the quality of health. Organic scientists have synthesized successfully a large number of compounds in order to discover new therapeutic agents. Currently available drugs are becoming inactive against various diseases as disease-causing agents are becoming resistant to existing drugs. So, it is necessary to design and synthesize novel compounds having the potential to act as new drug candidates to treat different diseases.

This was a source of motivation for us to design new compounds and screen them for their biological activities. Heterocyclic cores having good potential for biological and pharmaceutical activities (as mentioned in the introduction and survey of literature) encouraged us to synthesize compounds having two cores of heterocyclic moieties, that is, 1,3,4-oxadiazole and piperidine, in order to enhance their potential for bioactivities. Different functional groups were also introduced for acquiring novel drug candidates having therapeutic potential. Pharmacological screening of novel compounds against five enzymes, i.e., lipoxygenase, α-glucosidase, urease, acetylcholinesterase and butyrylcholinesterase was done and the results were verified by molecular docking.

The current research work has been divided into seven synthetic schemes in order to synthesize 73 compounds. 4-Methoxy benzene sulfonylchloride **(a)** and ethyl piperidine-4-carboxylate **(b)** were reacted to synthesize ethyl 1-[(4-methoxyphenyl sulfonyl]piperidin-4-carboxylate **(1A)**. Compound **(1A)** was refluxed with hydrazine monohydrate to get 1-[(4-methoxyphenyl)sulfonyl]piperidin-4-carbohydrazide **(2A)**. Compound **(2A)** was reacted with CS_2 in presence of KOH to acquire 5-[1-(4-methoxyphenyl)sulfonyl)piperidin-4-yl]-1,3,4-oxadiazol-2-thiol **(3A)**. Ethyl piperidin-3-carboxylate **(c)** was reacted with 4-methoxy benzene sulfonylchloride **(a)** to produce ethyl 1-[(4-methoxyphenyl sulfonyl]piperidin-3-carboxylate **(1B)** which is further reacted with hydrazine monohydrate on reflux to form 1-[(4-methoxyphenyl)sulfonyl]piperidin-3-carbohydrazide **(2B)**. Compound **(2B)** is refluxed with CS_2 and KOH to form 5-[1-(4-methoxyphenyl)sulfonyl)piperidin-3-yl]-1,3,4-oxadiazol-2-thiol **(3B)**. Compound **(3A)** was reacted with various aralkyl

halides **(4a-4j)** by employing both microwave assisted and conventional methods. The products **(5a-5j)** were obtained by filteration. Reaction of 2-bromoacetyl bromide **(7)** with alkyl/aralkyl/aryl amines **(6a-6r)** in an equimolar ratio in 5% Na_2CO_3 solution generated electrophiles **(8a-8r)**. The parent compounds **(3A)** and **(3B)** were reacted with *N*-alkyl/aralkyl/aryl-2-bromoacetamides **(8a-8r)** and **(8a-8d, 8f-8h, 8j-8p, 8r)** to get *N*-alkyl/aralkyl/aryl acetamide derivatives **(9a-9r) and (13a-13o)** of 5-[1-(4-methoxyphenyl)sulfonyl)piperidin-4-yl]-1,3,4-oxadiazol-2-thiol and 5-[1-(4-methoxy phenyl)sulfonyl)piperidin-3-yl]-1,3,4-oxadiazol-2-thiol respectively. Reaction of 2-bromopropionyl bromide **(10)** and different alkyl/aralkyl/aryl amines **(6a-6p)** in equimolar amounts produces electrophiles **(11a-11p)**. *N*-alkyl/aralkyl/aryl propanamide derivatives **(12a-12p)** and **(14a-14n)** of compounds **(3A)** and **(3B)** respectively, were acquired by reacting with *N*-alkyl/aralkyl/aryl proponamides **(11a-11p)** and **(11a-11d, 11f-11i, 11k-11n, 11p, 11r)** respectively. Initial verification of synthesized compounds was done by TLC and then further analysis was made.

Spectroscopic characterization of synthesized compounds was done by ^{13}C-NMR, ^{1}H-NMR and IR spectral data in order to verify available carbon atoms, hydrogen atoms and functional groups respectively. Screening of all synthesized compounds for anti-enzyme potential was performed against five enzymes i.e. lipoxygenase, α-glucosidase, butyryl cholinesterase (BChE) and acetyl cholinesterase (AChE). The majority of compounds showed excellent potential against the target enzymes. Molecular docking studies helped to understand drug interactions with proteins, which further established the understanding of binding constants and active sites. It also provided justification for pharmacodynamics, metabolism and elimination of drugs. Molecular docking verified various functional groups and active sites which impart pharmacological potential to the compounds. All the synthesized compounds are obtained with minimum time and cost by using environmental friendly synthetic routes with high purity and good yield. A comparison of two synthetic modes, i.e., microwave assisted and conventional methods (in terms of % age yield and time required for synthesis) was performed.

Both synthetic and biological evaluation studies helped to identify many compounds with inhibitory potential against target enzymes. Different kinds of diseases are caused due to abnormal secretion of these enzymes. Therefore, compounds having bioactivity may be recommended as novel drug candidates in our drug discovery program against concerned diseases.