ABSTRACT

The understanding of universe has also been decorated efficiently by the chemistry like the other sciences. The organic chemistry has launched the tentative challenges in the broad spectrum to understand the chemistry of life. A chemist facilitates the humanity in all the disciplines of life especially in the field of health and care based on the pharmacological efficiencies. Here, we do not aim at discussing the skeleton of chemical sciences but actually we want to equip the thinking to realize the demands of organic chemistry. An organic chemist is always in attempts to design unique synthetic molecules or to extract natural products to quench his thirst for the study of interaction of these molecules with life. Even from a common observer it is evident that the running medicines have entered in the inefficient process from therapeutics point of view because of development of resistance and tolerance by the threatening agents. The current time extremely claims the synthetic chemists to design, discover and invent more potent therapeutic compounds to ensure the well-being, health, care and happiness of humanity like the other advancements on this sphere.

The literature survey of synthetic chemistry is witness for the need of more potent and biologically active compounds. This is the motivational force which has compelled us to design heterocyclic compounds having 1,3,4-oxadiazole, 1,2,4-triazole and azinane with minimum cost, better yield and active pharmacological applications. Based on the applicability of these compounds, placement of wide variety of substituents has been designed to evaluate them for their pharmacological profile against different enzymes (acetyl cholinesterase, α-glucosidase and urease), various bacterial strains (*S. typhi (-), E. coli (-), P. aeruginosa (-), S. aureus (+) and B. subtilis (+)*) supported by the molecular docking to understand their active sites responsible for their pharmacological profile. BSA binding studies were also in progress parallel to the other investigations to check the binding constant which in turn justifies the pharmacodynamics and efficiency of designed drugs.

The current research was organized in twelve schemes to design unique, biologically active compounds. The first scheme was furnished with the synthesis 5-(1-(4-chlorophenylsulfonyl)piperidin-4-yl)-1,3,4-oxadiazole-2-thiol (**5a**) and 5-(1-(4-nitrophenylsulfonyl)piperidin-4-yl)-1,3,4-oxadiazole-2-thiol (**5b**) by the moieties of 4-chlorophenylsulfonyl chloride (**1a**) and 4-nitrophenylsulfonyl chloride (**1b**) treated with ethyl piperidine-4-carboxylate (**2**) to generate ethyl 1-(4-(chloro/nitro)phenyl

sulfonyl)piperidine-4-carboxylate (**3a-b**). Ethyl 1-(4-(chloro/nitro)phenylsulfonyl) piperidine-4-carboxylate (**3a-b**) was treated with hydrazine monohydrate to produce 1-(4-(chloro/nitro)phenylsulfonyl)piperidine-4-carbohydrazide (**4a-b**) respectively. Carbohydrazides were finally converted into their respective 1,3,4-oxadiazoles. A series of 27 *N*-substituted-2-bromoacetamides (**10a-z, 10aa**) (scheme **3**) and a series of 17 *N*-substituted-2-bromopropanamide (**15b, 15c, 15e-g, 15j, 15m, 15o-t, 15v-x, 15aa**) (scheme 7) were synthesized in the aqueous medium by the reaction of 2-bromoacetyl bromide (**9**), 2-brompropionyl bromide (**14**) and different substituted/ unsubstituted alkyl/aralkyl/phenyl/aryl amines. Both 5-(1-(4-chlorophenylsulfonyl) piperidin-4-yl)-1,3,4-oxadiazole-2-thiol (**5a**) and 5-(1-(4-nitrophenylsulfonyl) piperidin-4-yl)-1,3,4-oxadiazole-2-thiol (**5b**) were treated with alkyl/aryl/aralkyl halides (**6a-z**) to synthesize twenty six 2-(alkyl/arylthio)-5-(1-(4-chlorophenyl sulfonyl)piperidin-4-yl)-1,3,4-oxadiazole (**7a-z**) (scheme **2**) and fifteen 2-(alkyl/aryl thio)-5-(1-(4-nitrophenylsulfonyl)piperidin-4-yl)-1,3,4-oxadiazole (**12b-g, 12i, 12k-n, 12p, 12r, 12y, 12aa**) (scheme **5**) respectively. Twenty six 2-(5-(1-(4-chlorophenyl sulfonyl)piperidin-4-yl)-1,3,4-oxadiazol-2-ylthio)-*N*-(substituted) acetamide (**11a-z**) (scheme **4**) and sixteen 2-(5-(1-(4-nitrophenylsulfonyl)piperidin-4-yl)-1,3,4-oxadiazol-2-ylthio)-*N*-(substituted)acetamides (**13b, 13e-g, 13j, 13m, 13o, 13r-v, 13x-z, 13aa**) (sheme **6**) were synthesized by treatment of different *N*-substituted-2-bromoacetamides (**10a-z, 10aa**) (scheme **3**) in the presence of DMF with 5-(1-(4-chlorophenylsulfonyl)piperidin-4-yl)-1,3,4-oxadiazole-2-thiol (**5a**) and 5-(1-(4-nitro phenylsulfonyl)piperidin-4-yl)-1,3,4-oxadiazole-2-thiol (**5b**) respectively. By the reaction of *N*-substituted-2-bromopropanamide (**15b, 15c, 15e-g, 15j, 15m, 15o-t, 15v-x, 15aa**) (scheme 7) and 5-(1-(4-nitrophenylsulfonyl)piperidin-4-yl)-1,3,4-oxadiazole-2-thiol (**5b**), twelve 2-(5-(1-(4-nitrophenylsulfonyl)piperidin-4-yl)-1,3,4-oxadiazol-2-ylthio)-*N*-(substituted)propanamides (**16b, 16e-g, 16j, 16m, 16q, 16s-t, 16v, 16w, 16aa**) (scheme **8**) were synthesized. Scheme **9** was based on the synthesis of 5-(1-(4-nitrophenylsulfonyl)piperidin-4-yl)-4-phenyl-4*H*-1,2,4-triazole-3-thiol (**19**) through the reaction of 1-(4-nitrophenylsulfonyl)piperidine-4-carbohydrazide (**4b**) and phenylisothiocyanate (**17**) in the presence of ethanol through the formation of an intermediate 2-(1-(4-nitrophenylsulfonyl)piperidine-4-carbonyl)-*N*-phenylhydrazine carbothioamide (**18**) product which was cyclized into aimed product 5-(1-(4-nitrophenylsulfonyl)piperidin-4-yl)-4-phenyl-4*H*-1,2,4-triazole-3-thiol (**19**) of scheme **9**. 5-(1-(4-Nitrophenylsulfonyl)piperidin-4-yl)-4-phenyl-4*H*-1,2,4-triazole-3-thiol (**19**)

was reacted at room temperature with equimolar quantities of alkyl/aryl/aralkyl halides (**6b-e, 6g-j, 6l, 6o-p, 6r, 6t, 6x, 6z, 6aa, 6bb**), *N*-substituted-2-bromo acetamides (**10a, 10c-g, 10j, 10m, 10o-p, 10r-t, 10v, 10x-z, 10aa**) (scheme **3**) and *N*-substituted-2-bromopropanamide (**15c, 15f-g, 15j, 15m, 15o-s, 15v-x**) (scheme **7**) to synthesize seventeen 4-(5-(substituted)thio)-4-phenyl-4*H*-1,2,4-triazol-3-yl)-1-(4-nitrophenylsulfonyl)piperidine (**20b-e, 20g-j, 20l, 20o-p, 20r, 20t, 20x, 20z, 20aa, 20bb**) (scheme **10**), eighteen *N*-(substituted)-2-(5-(1-(4-nitrophenylsulfonyl)piperidin-4-yl)-4-phenyl-4*H*-1,2,4-triazol-3-ylthio)acetamides (**21a, 21c-g, 21j, 21m, 21o-p, 21r-t, 21v, 21x-z, 21aa**) (scheme **11**) and fourteen *N*-(substituted)-2-(5-(1-(4-nitrophenylsulfonyl)piperidin-4-yl)-4-phenyl-4*H*-1,2,4-triazol-3-ylthio)propionamides (**22c, 22f-g, 22j, 22m, 22o-s, 22v-x**) (scheme **12**) respectively.

The whole library of synthesized compounds was spectroscopically characterized by using IR, ^{1}H-NMR, ^{13}C-NMR and EIMS spectral information to justify the available main functional groups, hydrogen atoms, carbon atoms and the fragmentation pattern of the structures of synthesized compounds.

All the synthesized compounds were screened against five different bacterial strains in order to judge their antibacterial potential and almost half were found active. Compounds of current research were also subjected to check their anti-enzymatic potential against AChE, α-glucosidase and urease enzyme. Almost all the compounds were found to be excellent active agents against these enzymes. Anticancer and anti-inflammatory activities of all the synthesized molecules were also tested in search of some unique drug candidates but unluckily no compound was found active against these activities. The chemistry of active sites and different functionalities responsible for the best pharmacological potential of all the synthesized compounds was verified through docking studies. In addition to it, the evaluation of protein drug interaction assisted us in understanding the various binding sites and binding constant to justify the stay of the drugs in the body, their circulation, metabolism, elimination and pharmacodynamics. The sketched library of the compounds in the twelve various schemes were synthesized efficiently with high yield and purity through environment friendly protocol with minimum cost and time. The following synthetic as well as biological screening studies resulted in the identification of a list of compounds (**54**) with broad spectrum of biological and pharmacological applications. These compounds may be admitted by the pharmacological world as new unique cost effective and human friendly therapeutic agents for the betterment of humanity.