ABSTRACT

New drug candidates remained under consideration by the pharmaceutical industries to cure new arising diseases. To fulfill the requirement of new drug candidates, synthetic chemistry has added much in this regard. A large number of bioactive compounds have been synthesized by different fields of Chemistry which emphasize the significance of synthetic chemistry in the field of pharmacy. The presented work is also about the synthesis of some new bioactive molecules by coupling different bioactive functionalities. The valuable biological activities of derivatives of indole, sulfonamide, hydrazones and 1,3,4-oxadiazole prompted us to synthesize some new compounds comprising amalgamation of these functionalities; and to demonstrate their antibacterial, % hemolytic activities and enzyme inhibitory potentials supported by the computational docking simulations.

The presented work has been extended into different eight (8) schemes. In the first scheme the starting compound, 2-(1*H*-indol-3-yl)acetic acid (**1**) was converted to 2-(1*H*-indol-3-yl)acetohydrazide (**3**) in two steps through formation of ethyl 2-(1*H*-indol-3-yl)acetate (**2**). First step includes refluxing of **1** with conc. H_2SO_4 in ethanol and second step includes stirring of **2** with hydrazine and methanol at room temperature for 10-13 hrs. Further, the compound **3** was stirred with (un)/substituted benzoyl/thiophen-2-ylcarbonyl halides (**4a-e**) in a basic aqueous medium to synthesize five 2-(1*H*-indol-3-yl)-*N*'-[(un)/substituted benzoyl/2-thiophenylcarbonyl] acetohydrazides (**5a-e**, Scheme-1).

Ten compounds were synthesized as *N*'-[2-(1*H*-indol-3-yl)acetyl]arylsulfonohydrazides (**7a-j**, Scheme-2) by reacting parent compound **3** with arylsulfonyl halides (**6a-j**) in a basic aqueous medium, and fifteen compounds were synthesized by reacting aromatic aldehydes (**8a-o**) and compound **3** in methanol with a few drops of glacial acetic acid to yield 2-(1*H*-indol-3-yl)-*N*'-[(un)/substituted phenylmethylidene] acetohydrazides (**9a-o**, Scheme-3).

The compound **3** was also refluxed with CS_2 in ethanol having dissolved KOH to synthesize 2-(1*H*-indol-3-ylmethyl)-1,3,4-oxadiazol-5-thiol (**10**, Scheme-4) which was further reacted with various alkyl/aryl/aralkyl halides (**11a-u**) in *N,N*-dimethylformamide (DMF) and sodium hydride (NaH) to synthesize nineteen 2[(alkyl/aralkyl)thio]-5-[(1*H*-indol-3-yl)methyl]-1,3,4-oxadiazole (**12a-u**, Scheme-4).

Different alkyl/aryl/aralkyl amines (**13a-w**) were reacted with 2-bromoacetyl bromide (**14**) to synthesize 2-bromo-*N*-(substituted)acetamides (**15a-w**, Scheme-5) and alkyl/aryl/aralkyl amines (**13a-s**) with 3-bromopropanoyl bromide (**17**) to synthesize 3-bromo-*N*-(substituted)propanamides (**18a-s**, Scheme-7) as electrophiles.

The compound **10**, in DMF and NaH, was stirred with 2-bromo-*N*-(substituted) acetamides (**15a-w**) to synthesize twenty three *N*-Substituted-2-({5-[(1*H*-indol-3-yl)methyl]-1,3,4-oxadiazol-2-yl}sulfanyl)acetamides (**16a-w**, Scheme-6).

Twenty one compounds were synthesized as *N*-Substituted-3-({5-[(1*H*-indol-3-yl)methyl]-1,3,4-oxadiazol-2-yl}sulfanyl)propanamides (**19a-s**, Scheme-8), by reaction of 3-bromo-*N*-(substituted)propanamides (**18a-s**) with 2-(1*H*-indol-3-ylmethyl)-1,3,4-oxadiazol-5-thiol (**10**) in DMF and NaH.

The structural characterization has been well supported by spectral data of IR (Infra Red), ^{1}H-NMR (Proton Nuclear Magnetic Resonance), ^{13}C-NMR (Carbon-13 Nuclear Magnetic Resonance) and EIMS (Electron Impact Mass Spectrometry). Some of the ^{1}H-NMR, ^{13}C-NMR, EIMS and IR spectra of synthesized compounds are also presented for the obvious perceptive of signals. The physical data of all the compounds is also provided which included color, state, yield, melting points (in case of solids), molecular formula and molecular mass.

The biological evaluation of these compounds included enzyme inhibitory activity against three enzymes including lipoxygenase (LOX), α-glucosidase & butyrylcholinesterase (BChE) and antibacterial activity against five bacterial strains including three gram-negative (*Escherichia coli, Pseudomonas aeruginosa* and *Salmonella typhi*) and two gram-positive (*Bacillus subtilis, Staphylococcus aureus*) bacteria; and finally evaluation of % hemolytic activity. The enzyme inhibition data is also explicated in detail through molecular docking studies. The reference standards used were baicalein for LOX, acarbose for α-glucosidase, eserine for BChE, ciprofloxacin for antibacterial, Triton X-100 and PBS (phosphate buffer saline) for % hemolytic evaluation.

Some compounds were found active and showed excellent or good results in various studies mentioned above. The biological activity data in comparison of each scheme with the reference standard drugs is presented in results and discussion section