ABSTRACT

Heterocyclic sulfonamides (sulfa drugs) are compounds having a diverse array of pharmacological properties. Since their discovery they have gained tremendous attention of the researchers working around the world because of the valuable biological activities. The presented research effort was intended to synthesize *N*/*O*-substituted derivatives of synthesized parent sulfonamide compounds and to unveil their effective enzyme inhibitory potential against 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 *N* and *O*-substituted derivatives of different sulfonamides was expressed in the form of four major reaction schemes. The synthetic route depicted herein involved initially the synthesis of parent sulfonamides, which was done by the treatment of different aromatic amines with various aliphatic/aromatic sulfonyl chlorides in aqueous medium at RT & pH = 9-10, maintained by adding sodium carbonate **(Scheme 1, 3, 5)**. These parent molecules were further subjected to the synthesis of *N*-substituted derivatives of aromatic sulfonamides **(Scheme 2, 4, 7)** and *O*-substituted derivatives of RSO_2NCH_3R' **(Scheme 6)**. The **Scheme 6** was initiated by the formation of an electrophile *via* nucleophilic acylation reaction of 2,3-dihydro-1,4-benzodioxin-6-amine **(1)** with 2-bromoacetyl bromide at 0 °C to RT under stirring in mild alkaline media. The second phase of **Scheme 6** included the synthesis of various 2-(4-(substituted-sulfonamido)phenoxy)-*N*-(2,3-dihydrobenzo[1,4]dioxin-6-yl)acetamides in *N,N*'-dimethyl formamide in the presence of LiH. The predictable structures have been established on the basis of modern spectrosopic techniques i.e. FTIR, ^{1}H-NMR and EIMS analysis. The synthesized derivatives were screened against acetylcholinesterase (AChE), butyrylcholinesterase (BChE) and lipoxygenase (LOX) and α-glucosidase enzymes; most of them were found to be active against cholinesterases and lipoxygenase enzymes. The influence of the

amalgamation of sulfamoyl functionality along with benzodioxane ring system with alkyl/aralkyl halides and 2-bromo-*N*-substituted acetamide on the inhibitory action of these enzymes was also studied. It was ascertained that *N* & *O*-substituted derivatives were promising entrant for inhibiting lipoxygenase enzyme particularly, some of them were found to be moderately to reasonably good active against cholinesterases. Moreover anti-bacterial studies were performed with the synthesized derivatives and compounds pertaining to **Scheme 5, 6 & 7** portrayed admirable antibacterial activity as evident from their MIC values 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, butyrylcholinesterase and lipoxygenase enzymes. The results obtained were in high agreement with the observed good potency of *N* & *O*-substituted derivatives of benzodioxane containing sulfonamides. So, our results revealed that the most of the synthesized molecules can serve as very valuable therapeutic agents.