and **14g** against *E. coli*, *S. aureus* and *S. typhi*, respectively and also comparable to that of Ciprofloxacin. Among the alkyl/aralkyl *S*-substituted derivatives (**18a-t**) of 4-phenyl-5-(1-tosylpiperidin-4-yl)-4*H*-1,2,4-triazole-3-thiol (**17**), compound **18a** executed better potential against four bacterial strains *S. typhi, E. coli, B. subtilis* and *P. aeruginosa* and **18c** against *S. aureus*. The observed potential was also comparable to the reference. Among the acetamide derivatives (**19a-t**) of 4-phenyl-5-(1-tosylpiperidin-4-yl)-4*H*-1,2,4-triazole-3-thiol (**17**), the most active compounds were **19a** against *S. typhi*, **19d** against *E. coli*, **19o** against *B. subtilis* and **19h** against *P. aeruginosa* with MIC value close to that of the reference.

Lipoxygenase (LOX) inhibition potential was evaluated with reference to Baicalein, the reference standard. The enzyme inhibition activity results are given as % inhibition and concentration for 50% inhibition (IC_{50}) values. Among the alkyl/aralkyl *S*-substituted derivatives (**7a-w**) of 5-(1-(4-methyl phenylsulfonyl)piperidin-4-yl)-1,3,4-oxadiazole-2-thiol (**5**), three the most potent inhibitors of LOX were **7a, 7b** and **7c** with reference of the standard, Baicalein. Among the acetamide derivatives (**11a-v**) of 5-(1-(4-methylphenylsulfonyl)piperidin-4-yl)-1,3,4-oxadiazole-2-thiol (**5**), three the most potent inhibitors of LOX were **11m, 11n** and **11t**. Among the propionamide derivatives (**14a-l**) of 5-(1-(4-methylphenylsulfonyl)piperidin-4-yl)-1,3,4-oxadiazole-2-thiol (**5**), two the most potent inhibitors of LOX were **14e** and **14f**. Among the alkyl/aralkyl *S*-substituted derivatives (**18a-t**) of 4-phenyl-5-(1-tosylpiperidin-4-yl)-4*H*-1,2,4-triazole-3-thiol (**17**), three the most potent inhibitors of LOX were **18a, 18b** and **18c**. Among the acetamide derivatives (**19a-t**) of 4-phenyl-5-(1-tosylpiperidin-4-yl)-4*H*-1,2,4-triazole-3-thiol (**17**), three the most potent inhibitors of LOX were **19g, 19n** and **19r**. The activity of all these compounds was compared to the reference, Baicalein. Furthermore, the molecular docking studies have been discussed in Chapter-4 for LOX inhibition activity.

Overall a number of compounds exhibited moderate LOX inhibition potential as compared to reference standard, Baicalein. Many compounds showed excellent antibacterial potential. The most active compounds against bacterial strains might be suitable as new drug candidates in pharmaceutical industries to develop potent drugs for the different bacterial infection. The most active LOX inhibitors might be further forwarded as new drug candidates for inflammatory diseases.

ABSTRACT

Heterocyclic compounds are being focused by the organic and synthetic chemists because of their wide range of biological and other desirable applications. Five membered heterocyclic moieties, oxadiazoles and triazoles are among the most considered five membered heterocyclic cores for the production of new potential synthetic drugs. The most studied isomers of these heterocyclic moieties are 1,3,4-oxadiazole and 1,2,4-triazole owing to their potent pharmaceutical activities.

Keeping in view the importance of 1,3,4-oxadiazole and 1,2,4-triazole heterocycles, a number of different *S*-substituted derivatives of 1,3,4-oxadiazole-2-thiol and 1,2,4-triazole-3-thiol having 4-methylphenyl sulfonyl piperidine have been synthesized and screened for the evaluation of pharmaceutical potential including antibacterial and enzyme inhibition. The antibacterial potential was evaluated against certain strains of Gram positive and Gram negative bacteria. Enzyme inhibition potential was evaluated against lipoxygenase (LOX) enzyme responsible for inflammation.

The list of ninety seven (97) synthesized derivatives includes fifty seven (57) derivatives of 1,3,4-oxadiazole (**7a-w, 11a-v, 14a-l**) and forty (40) derivatives of 1,2,4-triazole (**18a-t, 19a-t**). The multistep protocols for all of these compounds have been described in five (5) schemes. The compound ethyl 1-tosylpiperidine-4-carboxylate (**3**) was synthesized by the reaction of 4-methylphenyl sulfonyl chloride (**1**) and ethyl isonipecotate (**2**) using 10% aqueous solution of Na_2CO_3 as reaction medium. The compound **3** was further converted into corresponding carbohydrazide (**4**) by hydrated hydrazine in methanol under reflux. 5-(1-(4-Methylphenylsulfonyl) piperidin-4-yl)-1,3,4-oxadiazole-2-thiol (**5**) was synthesized from compound (**4**) by reflux in ethanol in the presence of carbon disulfide (CS_2) in basic medium. Twenty three (23) alkyl/aralkyl derivatives of 1,3,4-oxadiazole-2-thiol having 4-methylphenyl sulfonyl piperidine were synthesized (**7a-w, Scheme-1**) by the reaction of **5** and **6a-w**. *N*-Substituted alkyl/aralkyl amines (**8a-v**) were made to react with 2-bromoacetyl bromide (**9**) to synthesize 2-bromo-*N*-substituted acetamides (**10a-v**) as electrophiles. The synthesized 1,3,4-oxadiazole-2-thiol (**5**) was further derivatized by these electrophiles (**10a-v**) to synthesize twenty two (22) *N*-substituted acetamide derivatives (**11a-v, Scheme-2**). *N*-substituted alkyl/aralkyl amines (**8a-g,j,m,n,p,v**) were made to react with 3-bromopropionyl bromide (**12**) to synthesize 3-bromo-*N*-substituted propanamides (**13a-l**). Again the synthesized 1,3,4-oxadiazole-2-thiol (**5**)

was derivatized with these electrophiles (**13a-l**) to synthesize twelve (12) *N*-substituted propanamides (**14a-l, Scheme-3**). Compound **4** was refluxed with isothiocyanatobenzene (**15**) in methanol to produce *N*-phenyl-2-(1-4-methylphenylsulfonylpiperidine-4-carbonyl)hydrazine carbothioamide (**16**). The compound **16** was cyclized to 4-phenyl-5-(1-tosylpiperidin-4-yl)-4*H*-1,2,4-triazole-3-thiol (**17**) using 10% aqueous solution of NaOH as reaction medium. The synthesized 1,2,4-triazole-3-thiol (**17**) was used to produce twenty (20) derivatives (**18a-t, Scheme-4**) on reaction with different alkyl/aralkyl halides (**6a-t**) in a polar aprotic medium. The synthesized electrophiles, 2-bromo-*N*-substituted acetamides (**10a-s,u**), were stirred with the synthesized 1,2,4-triazole-3-thiol (**17**) to yield twenty (20) different *N*-substituted acetamide derivatives (**19a-t, Scheme-5**).

Structures of all the synthesized compounds were confirmed using Infra Red (IR) spectroscopy, Proton Nuclear Magnetic Resonance (^{1}H-NMR) spectroscopy, Carbon-13 Nuclear Magnetic Resonance (^{13}C-NMR) spectroscopy and Electron Impact Mass Spectrometry (EIMS) data. Ring formation of 1,3,4-oxadiazole and 1,2,4-triazole was confirmed through ^{13}C-NMR. The determined physical data of all the target compounds includes physical state, color, yield, melting point, molecular formula and molecular mass which are given in results section (Chapter-4).

The synthesized compounds were screened for antimicrobial potential against Gram-positive and Gram-negative bacterial strains. The results of antibacterial potential are given as % inhibition and minimum inhibitory concentration (MIC) values. Among the alkyl/aralkyl *S*-substituted derivatives (**7a-w**) of 5-(1-(4-methyl phenylsulfonyl)piperidin-4-yl)-1,3,4-oxadiazole-2-thiol (**5**), compounds **7a**, **7c** and **7m** remained the most active against *P. aeruginosa*, *S. aureus* and *E. coli* respectively and compound **7o** against both of *S. typhi* and *B. subtilis*. All of these (**7a, 7c, 7m, 7o**) showed antibacterial activity comparable to that of the reference standard, Ciprofloxacin. Among the acetamide derivatives (**11a-v**) of 5-(1-(4-methylphenylsulfonyl)piperidin-4-yl)-1,3,4-oxadiazole-2-thiol (**5**), compounds **11c** and **11s** exhibited proficient activity against *S. typhi* and *P. aeruginosa,* respectively and compound **11d** against three strains including *E. coli*, *S. aureus* and *B. subtilis*. These three most active compounds also showed activity comparable to that of Ciprofloxacin. Among the propanamide derivatives (**14a-l**) of 5-(1-(4-methylphenylsulfonyl) piperidin-4-yl)-1,3,4-oxadiazole-2-thiol (**5**), compounds **14b** showed efficient activity against *B. subtilis* and *P. aeruginosa*; compounds **14d, 14f**