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Synthesis and Biological Screening of *S*-Substituted Derivatives of 5-{1-[(4-Chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl Sulfide

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In present research, a novel series of *S*-substituted derivatives of 5-[1-(4-chlorophenylsulfonyl)-3-piperidinyl]-1,3,4-oxadiazole-2-thiol (**5a-f**) was synthesized by multistep protocol starting from ethyl-3-piperidine carboxylate (**a**) geared up with 4-chlorobenzene sulfonyl chloride (**b**). The resulted ethyl-1-(4-chlorophenyl)sulfonyl piperidine-3-carboxylate (**1**) was subsequently converted into carbohydrazide (**2**) and then 2,5-disubstituted-1,3,4-oxadiazole by intermolecular cyclization. The compound 5-[1-(4-chlorophenylsulfonyl)-3-piperidinyl]-1,3,4-oxadiazole-2-thiol (**3**) was derivatized by different alkyl halides. All the synthesized compounds were characterized by IR, EIMS, ^{1}H NMR analysis and screened for antibacterial activity and enzyme inhibition potential against lipoxygenase enzyme.

Keywords: Sulfonamides, Antibacterial activity, Lipoxygenase activity, Spectral analysis.

INTRODUCTION

Currently researchers are keenly interested to synthesize medicinally potent molecules with better efficacy against different microbial ailments[1]. In the present situation, as microbes have developed resistance for antimicrobial drugs in use and different side effects have been encountered like hypersensitivity, toxicity, local tissue irritation and resistance *etc*., it has become unavoidable to produce and explore therapeutically lead molecules that can work with more efficiency and minimize the side effects[2]. Under this scenario a large variety of heteroatom rings have been synthesized and explored for development of most efficient and safe antibacterial and antifungal drugs. Literature survey revealed that sulfa drugs bearing sulfamoyl group (-NSO_2) and 1,3,4-oxadiazole heterocycle moiety have potential as antiviral[3], antifungal [4], antidepressant, anticancer[5], antioxidant, ulcerogenic[6], antimicrobial, anti-mycobacterial[7] and antiinflammatory[8,9] agents.

EXPERIMENTAL

The melting points of all synthesized derivatives were recorded on Gallenkamp digital melting point apparatus and were uncorrected. Thin layer chromatography was utilized to check the purity of all synthesized compounds. Structure elucidation was brought out by spectral data. The IR spectra were recorded with the help of Jasco FTIR spectrometer by applying KBr pellet method. Bruker spectrometers were utilized to record ^{1}H NMR operating at 300 and 400 MHz using chloroform-d_1 as solvent. Mass spectra were recorded on JMS-HX 110 spectrometer.

Synthesis of ethyl-1-[(4-chlorophenyl)sulfonyl] piperidine-3-carboxylate (1): Ethyl-1-[(4-chlorophenyl)sulfonyl] piperidine-3-carboxylate was synthesized by treating ethyl piperidine-3-carboxylate (a) (0.05 mol) with 4-chlorobenzene sulfonyl chloride (0.05 mol) in basic aqueous media under dynamic pH control. By the help of TLC using *n*-hexane and EtOAc as mobile phase purity of the compound was assured. Cold distilled water was used to quench the precipitates.

Synthesis of 1-[(4-chlorophenyl)sulfonyl]piperidine-3-carbohydrazide (2): 1-[(4-Chlorophenyl)sulfonyl]piperidine-3-carbohydrazide was synthesized from compound **1** (0.04 mol) on reaction with hydrazine hydrate (0.04 mol) in methanol (40 mL) under reflux for 2-3 h. Reaction progress was checked by TLC. Excess of methanol was distilled off and cold water was used to obtain the precipitates.

Synthesis of 5-[1-(4-chlorophenylsulfonyl)-3-piperidinyl]-1,3,4-oxadiazole-2-thiol (3): To synthesize parent compound **3**, the compound **2** (0.05 mol) was refluxed with CS_2 (0.05 mol) and KOH (0.075 mol) in alcoholic media (45 mL) in 100 mL round bottom flask for 4-5 h. Reaction progress was monitored by TLC. On reaction completion distilled water and dil. HCl was introduced to reaction contents and precipitates were collected.

Synthesis of *S*-substituted derivatives of 5-{1-[(4-chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl

sulfide: Compound **3** (0.001 mol) was treated with equimolar alkyl halide **4a-f** (0.001 mol) in the presence of NaH (0.001 mol) using DMF as reaction media to synthesize S-alkyl substituted derivatives of 5-{1-[(4-chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl sulfide. To quench the precipitates cold distilled water was used and filtered the precipitates.

Antibacterial activity: Antibacterial screening was performed following the protocols reported in literature[10,11].

Lipoxygenase assay: Lipoxygenase activity was screened by the protocol reported in literature[12,13] with slight modifications.

Statistical analysis: All the measurements were done in triplicate and statistical analysis was performed by Microsoft Excel 2010. Results are presented as mean ± sem.

Spectral characterization of all synthesized derivatives

5-[1-[(4-Chlorophenyl)sulfonyl]-3-piperidinyl]-1,3,4-oxadiazole-2-thiol (3): White amorphous solid; Yield: 85 %; m.p. 145-146 °C; m.f. $C_{13}H_{14}N_3O_3S_2Cl$; mol. mass: 359 g mol^{-1}; IR (KBr, ν_{max}, cm^{-1}): 3033 (Ar-H), 2252 (S-H stretching), 1591 (C=N stretching), 1524 (Ar C=C stretching), 1327 (-SO_2 stretching); ^{1}H NMR ($CDCl_3$, 300 MHz, δ/ppm): 7.70 (d, *J* = 8.4 Hz, 2H, H-2" & H-6"), 7.52 (d, *J* = 8.7 Hz, 2H, H-3" & H-5"), 3.90 (dd, *J* = 11.7, 3.6 Hz, 1H, H_e-2'), 3.65 (br.d, *J* = 11.7 Hz, 1H, H_a-2'), 3.10-3.02 (m, 1H, H-3'), 2.65 (br.t, *J* = 9.9 Hz, 1H, H_e-6'), 2.49 (td, *J* = 11.4, 3.0 Hz, 1H, H_a-6'), 2.10-2.06 (m, 1H, H_a-5'), 1.90-1.82 (m, 1H, H_a-4'), 1.81-1.70 (m, 1H, H_e-5'), 1.69-1.58 (m, 1H, H_e-4'); EIMS (*m/z*): 359 $[M]^+$, 300 $[C_{12}H_{13}ClN_2O_3S]^{\bullet+}$, 284 $[C_{12}H_{13}ClN_2O_2S]^{\bullet+}$, 286 $[C_{12}H_{13}ClNO_3S]^+$, 258 $[C_{11}H_{13}ClNO_2S]^+$, 175 $[C_6H_4ClO_2S]^+$, 111 $[C_6H_4Cl]^+$.

5-{1-[(4-Chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl 2-bromoethyl sulfide (5a): White amorphous solid; Yield: 84 %; m.p. 140-142 °C; m.f. $C_{15}H_{17}N_3O_3S_2BrCl$; mol. mass: 466 g mol^{-1}; IR (KBr, ν_{max}, cm^{-1}): 3018 (Ar-H), 1583 (C=N stretching), 1558 (Ar C=C stretching), 1342 (-SO_2 stretching); ^{1}H NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.70 (d, *J* = 8.4 Hz, 2H, H-2" & H-6"), 7.49 (d, *J* = 8.4 Hz, 2H, H-3" & H-5"), 3.96-3.94 (m, 1H, H_e-2'), 3.71-3.62 (m (merged with piperidine ring), 5H, H_a-2', H-1"' & H-2"'), 3.21-3.15 (m, 1H, H-3'), 2.71-2.62 (m, 1H, H_e-6'), 2.51-2.43 (m, 1H, H_a-6'), 2.15-2.12 (m, 1H, H_a-5'), 2.02-1.97 (m, 1H, H_a-4'), 1.92-1.86 (m, 1H, H_e-5'), 1.79-1.70 (m, 1H, H_e-4'); EIMS (*m/z*): 466 $[M]^+$, 359 $[C_{13}H_{14}ClN_3O_3S_2]^{\bullet+}$, 291 $[M\text{-}C_6H_4ClSO_4]^+$, 284 $[C_{12}H_{13}ClN_2O_2S]^{\bullet+}$, 258 $[C_{11}H_{13}ClNO_2S]^+$, 175 $[C_6H_4ClO_2S]^+$, 107 $[C_2H_4Br]^+$.

5-{1-[(4-Chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl isopropyl sulfide (5b): Dull green sticky; yield: 75 %; m.f.: $C_{16}H_{20}N_3O_3S_2Cl$; mol. mass: 401 g mol^{-1}; IR (KBr, ν_{max}, cm^{-1}): 3021 (Ar-H), 1577 (C=N stretching), 1541 (Ar C=C stretching), 1318 (-SO_2 stretching); ^{1}H NMR ($CDCl_3$, 300 MHz, δ/ppm): 7.66 (d, *J* = 8.4 Hz, 2H, H-2" & H-6"), 7.50 (d, *J* = 8.4 Hz, 2H, H-3" & H-5"), 3.90 (dd, *J* = 8.7, 3.6 Hz, 1H, H_e-2'), 3.85 (septet, *J* = 6.9 Hz, 1H, H-1"'), 3.62 (br.d, *J* = 11.7 Hz, 1H, H_a-2'), 3.11-3.03 (m, 1H, H-3'), 2.67 (br.t, *J* = 10.2 Hz, 1H, H_e-6'), 2.43 (td, *J* = 11.4, 3.0 Hz, 1H, H_a-6'), 2.11-2.06 (m, 1H, H_a-5'), 1.90-1.82 (m, 1H, H_a-4'), 1.81-1.75 (m, 1H, H_e-5'), 1.74-1.58 (m, 1H, H_e-4'), 1.44 (d, *J* = 6.9 Hz, 6H, H-2"' & H-3"'); EIMS (*m/z*): 401 $[M]^+$, 359 $[C_{13}H_{14}Cl\text{-}N_3O_3S_2]^{\bullet+}$, 284 $[C_{12}H_{13}ClN_2O_2S]^{\bullet+}$, 226 $[M\text{-}C_6H_4ClSO_4]^+$, 175 $[C_6H_4ClO_2S]^+$.

5-{1-[(4-Chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl *sec*-butyl sulfide (5c): Greenish sticky solid; yield: 77 %; m.f. $C_{17}H_{22}N_3O_3S_2Cl$; mol. mass: 415 g mol^{-1}; IR (KBr, ν_{max}, cm^{-1}): 3018 (Ar-H), 1584 (C=N stretching), 1547 (Ar C=C stretching), 1331 (-SO_2 stretching); ^{1}H NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.69 (d, *J* = 8.4 Hz, 2H, H-2" & H-6"), 7.49 (d, *J* = 8.4 Hz, 2H, H-3" & H-5"), 4.91-4.82 (m, 1H, H-1"'), 3.97 (dd, *J* = 12.0, 3.6 Hz, 1H, H_e-2'), 3.68 (dist. dd, *J* = 13.2, 6.4 Hz, 1H, H_a-2'), 3.19-3.12 (m, 1H, H-3'), 2.62 (br.t, *J* = 11.2 Hz, 1H, H_e-6'), 2.42 (td, *J* = 11.2, 2.8 Hz, 1H, H_a-6'), 2.15-2.11 (m, 1H, H_a-5'), 2.01-1.96 (m, 2H, H-2"'), 1.86-1.67 (m, 3H, H_e-5', H-4'), 1.45 (d, *J* = 6.8 Hz, 3H, H-4"'), 1.01 (t, *J* = 7.6 Hz, 3H, H-3"'); EIMS (*m/z*): 415 $[M]^+$, 359 $[C_{13}H_{14}ClN_3O_3S_2]^{\bullet+}$, 286 $[C_{12}H_{13}ClNO_3S]^+$, 240 $[M\text{-}C_6H_4ClSO_4]^+$, 111 $[C_6H_4Cl]^+$.

5-{1-[(4-Chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl 1-methylbutyl sulfide (5d): Light green sticky solid; yield: 79 %; m.f. $C_{18}H_{24}ClN_3O_3S_2$; mol. mass: 429 g mol^{-1}; IR (KBr, ν_{max}, cm^{-1}): 3011 (Ar-H), 1589 (C=N stretching), 1540 (Ar C=C stretching), 1338 (-SO_2 stretching); ^{1}H NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.68 (d, *J* = 8.8 Hz, 2H, H-2" & H-6"), 7.50 (d, *J* = 8.4 Hz, 2H, H-3" & H-5"), 4.02 (br.d, *J* = 12.0 Hz, 1H, H_e-2'), 3.77 (hex., *J* = 6.8 Hz, 1H, H-1"'), 3.69 (br.d, *J* = 12.0 Hz, 1H, H_a-2'), 3.19-3.14 (m, 1H, H-3'), 2.62 (td, *J* = 11.6, 3.6 Hz, 1H, H_e-6'), 2.41 (br.t, *J* = 11.2 Hz, 1H, H_a-6'), 2.16-2.13 (m, 1H, H_e-5'), 2.02-1.97 (m, 4H, H-2"' & H-3"'), 1.86-1.61 (m, 3H, H_a-5' & H-4'), 1.45 (d, *J* = 6.8 Hz, 3H, H-5"'), 0.92 (t, *J* = 7.2 Hz, 3H, H-4"'); EIMS (*m/z*): 429 $[M]^+$, 359 $[C_{13}H_{14}ClN_3O_3S_2]^{\bullet+}$, 286 $[C_{12}H_{13}ClNO_3S]^+$, 254 $[M\text{-}C_6H_4ClSO_4]^+$, 111 $[C_6H_4Cl]^+$.

5-{1-[(4-Chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl 3-phenylpropyl sulfide (5e): White solid; yield: 83 %; m.p. 65-66 °C; m.f. $C_{22}H_{24}N_3O_3S_2Cl$; mol. mass: 477 g mol^{-1}; IR (KBr, ν_{max}, cm^{-1}): 3024 (Ar-H), 1583 (C=N stretching), 1557 (Ar C=C stretching), 1344 (-SO_2 stretching); ^{1}H NMR ($CDCl_3$, 300 MHz, δ/ppm): 7.70 (d, *J* = 8.4 Hz, 2H, H-2" & H-6"), 7.48 (d, *J* = 8.4 Hz, 2H, H-3" & H-5"), 7.27 (d, *J* = 7.2 Hz, 2H, H-2"' & H-6"'), 7.20-7.15 (m, 3H, H-3"' to H-5"'), 4.01 (br.d, *J* = 11.7 Hz, 1H, H_e-2'), 3.68 (br.d, *J* = 11.7 Hz, 1H, H_a-2'), 3.22 (t, *J* = 7.2 Hz, 2H, H-9"'), 3.17-3.12 (m, 1H, H-3'), 2.75 (t, *J* = 7.5 Hz, 2H, H-7"'), 2.61 (br.t, *J* = 10.8 Hz, 1H, H_e-6'), 2.38 (td, *J* = 11.4, 2.7 Hz, 1H, H_a-6'), 2.11 (qui, *J* = 7.2 Hz, 2H, H-8"'), 1.90-1.53 (m, 4H, H-4' & H-5'); EIMS (*m/z*): 477 $[M]^+$, 359 $[C_{13}H_{14}ClN_3O_3S_2]^{\bullet+}$, 302 $[M\text{-}C_6H_4ClSO_4]^+$, 284 $[C_{12}H_{13}ClN_2O_2S]^{\bullet+}$, 258 $[C_{11}H_{13}ClN\text{-}O_2S]^+$, 175 $[C_6H_4ClO_2S]^+$, 119 $[C_9H_{11}]^+$, 111 $[C_6H_4Cl]^+$.

5-{1-[(4-Chlorophenyl)sulfonyl]-3-piperidinyl}-1,3,4-oxadiazol-2-yl 1,3-dioxolan-2-ylmethyl sulfide(5f): Light yellow sticky material; yield: 89 %; m.f. $C_{17}H_{20}N_3O_5S_2Cl$; mol. mass: 445 g mol^{-1}; IR (KBr, ν_{max}, cm^{-1}): 3022 (Ar-H), 2235 (S-H stretching), 1587 (C=N stretching), 1549 (Ar C=C stretching), 1343 (-SO_2 stretching); ^{1}H NMR ($CDCl_3$, 400 MHz, δ/ppm): 7.68 (d, *J* = 8.4 Hz, 2H, H-2" & H-6"), 7.50 (d, *J* = 8.4 Hz, 2H, H-3" & H-5"), 5.24 (t, *J* = 4.0 Hz, 1H, H-5"'), 4.00 (t, *J* = 7.2 Hz, 2H, H-2"'), 3.91 (dd, *J* = 8.4, 3.6 Hz, 1H, H_e-2'), 3.89 (t, *J* = 7.2 Hz, 2H, H-3"'), 3.65 (br. d, *J* = 11.2 Hz, 1H, H_a-2'), 3.44 (d, *J* = 4.0 Hz, 2H, H-6"'), 3.10-3.02 (m, 1H, H-3'), 2.66 (br.t, *J* = 10.4 Hz, 1H, H_e-6'), 2.49 (td, *J* = 11.2, 2.4 Hz, 1H, H_a-6'), 2.16-2.09 (m, 1H, H_a-5'), 1.92-1.87 (m, 1H,

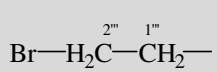
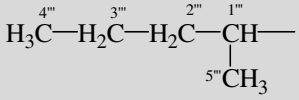
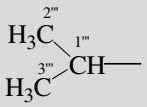
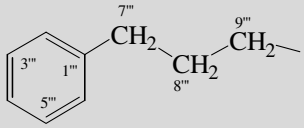
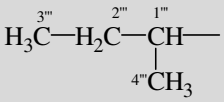
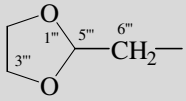
H_a-4'), 1.83-1.76 (m, 1H, H_e-5'), 1.74-1.59 (m, 1H, H_e-4'); EIMS (*m/z*): 445 $[M]^+$, 359 $[C_{13}H_{14}ClN_3O_3S_2]^{\bullet+}$, 286 $[C_{12}H_{13}ClNO_3S]^+$, 270 $[M\text{-}C_6H_4ClSO_4]^+$, 258 $[C_{11}H_{13}ClN\text{-}O_2S]^+$, 175 $[C_6H_4ClO_2S]^+$, 111 $[C_6H_4Cl]^+$.

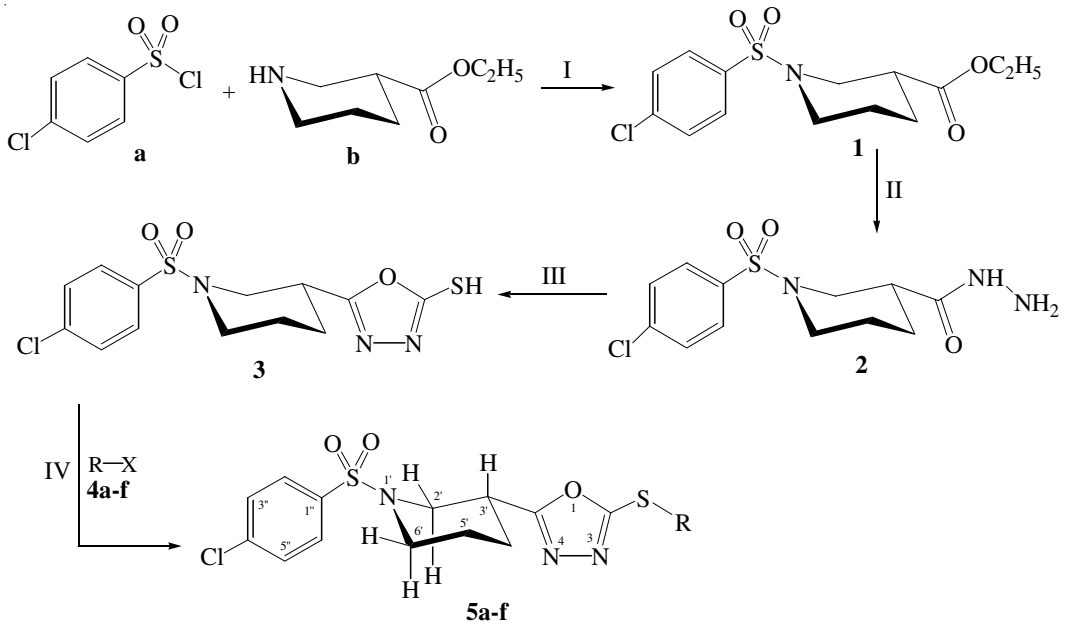
RESULTS AND DISCUSSION

In present paper, a series of *S*-substituted derivatives of 5-[1-(4-chlorophenylsulfonyl)-3-piperidinyl]-1,3,4-oxadiazole-2-thiol (Table-1) was synthesized to introduce new biologically active molecules that can be helpful in drug development programs against different resistant microbes. The target compounds **5a-f** were synthesized by following the multistep protocols (**Scheme-I**) in continuation of already reported projects[14-16] and screened for lipoxygenase inhibitory potential and antibacterial activity. The predicted structures of all the derivatives were corroborated by different analytical techniques like ^{1}H NMR, EIMS and IR data.

Compound **5e** was obtained as white amorphous solid in 83 % yield with melting point range 87-89 °C, which is uncorrected. The molecular formula for compound **5e** was $C_{22}H_{24}N_3O_3S_2Cl$ and corresponding molecular mass 477 g/mol. In IR spectra characteristic absorption bands at 3024 (aromatic C-H str.), 1583 (C=N str.), 1557 (C=C str.) and 1344 (sulfonyl str.) cm^{-1} confirmed the presence of these groups and help to confirm the structure of compound **5e**. In ^{1}H NMR, the aromatic region of the spectra showed four signals at different chemical shift values, two relatively deshielded doublets appeared at ppm 7.70 (*J* = 8.4 Hz, 2H) and 7.48 (*J* = 8.4 Hz, 2H) indicated the presence of 4-chlorophenyl sulfonyl group while a doublet at ppm 7.27 (*J* = 7.2 Hz, 2H), relatively in shielded region due to ortho protons of mono substituted phenyl ring and a multiplet at 7.20-7.15 (m, 3H, H-3''' to H-5''') confirmed the presence of phenyl group. The characteristic two triplets and one quintet for 1,3-disubstituted propane fragment appeared in aliphatic region at 3.22 (t, *J* = 7.2 Hz, 2H, H-9'''), 2.75 (t, *J* = 7.5 Hz, 2H, H-7''') and 2.11 (quin, *J* = 7.2 Hz, 2H, H-8''') due to attachment to thiol group of 1,3,4-oxadiazole-2-thiol moiety, phenyl group and methylene group that is flagged by two methylene, respectively. The signals for the protons of piperidine ring appeared at ppm 4.01 (br.d, *J* = 11.7 Hz, 1H, H_e-2'), 3.68 (br.d, *J* = 11.7 Hz, 1H, H_a-2'), 3.17-3.12 (m, 1H, H-3'), 2.61 (br.t, *J* = 10.8 Hz, 1H, H_e-6'), 2.38

TABLE-1
DIFFERENT *S*-SUBSTITUTED ALKYL GROUPS

Compound	R	Compound	R
5a		**5d**	
5b		**5e**	
5c		**5f**	



Scheme-I: Outline for the synthesis of *S*-substituted derivatives of 5-(1-(4-chlorophenylsulfonyl)piperidin-3-yl)-1,3,4-oxadiazole-2-thiol. Reagents and conditions: (I) 5 % Na_2CO_3 soln./H_2O/pH = 9-10/stirring for 3-4 h. (II) N_2H_4/MeOH/stirring for 5-6 h (III) CS_2/KOH/EtOH/refluxing for 6 h (IV) DMF/NaH/stirring for 2-3 h

TABLE-3
ANTIBACTERIAL ACTIVITY (%) INHIBITION FOR TESTED COMPOUNDS

Codes	Inhibition (%)				
	S. typhi (-)	*E. coli* (-)	*P. aeruginosa* (-)	*B. subtilis* (+)	*S. aureus* (+)
5a	70.64 ± 1.45	55.23 ± 3.29	55.20 ± 1.22	68.84 ± 2.07	55.20 ± 0.80
5b	62.17 ± 1.39	63.73 ± 0.36	57.00 ± 4.20	38.00 ± 5.00	57.26 ± 0.32
5c	64.23 ± 0.14	45.69 ± 2.82	55.71 ± 1.53	67.07 ± 4.65	44.00 ± 5.00
5d	67.86 ± 1.15	49.77 ± 1.32	52.19 ± 0.46	72.93 ± 1.52	39.30 ± 1.40
5e	49.18 ± 1.80	57.31 ± 1.56	49.95 ± 3.01	42.78 ± 2.17	51.40 ± 2.20
5f	76.36 ± 1.45	48.29 ± 5.00	50.82 ± 3.67	69.55 ± 4.90	43.20 ± 2.00
Ciprofloxacin	91.79 ± 1.45	90.87 ± 0.56	92.13 ± 0.97	91.18 ± 1.22	90.45 ± 2.98

TABLE-4
ANTIBACTERIAL ACTIVITY (MIC VALUES) FOR TESTED COMPOUNDS

Codes	MIC				
	S. typhi (-)	*E. coli* (-)	*P. aeruginosa* (-)	*B. subtilis* (+)	*S. aureus* (+)
5a	10.46 ± 1.34	15.11 ± 1.25	17.26 ± 3.00	11.04 ± 2.36	15.67 ± 5.00
5b	16.72 ± 1.21	15.80 ± 5.00	17.26 ± 1.50	-	18.25 ± 1.21
5c	9.05 ± 1.64	-	17.27 ± 1.00	13.85 ± 3.57	-
5d	10.53 ± 4.31	-	18.91 ± 2.42	10.90 ± 2.86	-
5e	-	18.19 ± 3.27	-	-	18.51 ± 3.58
5f	10.37 ± 5.00	-	18.54 ± 3.17	11.69 ± 4.00	-
Ciprofloxacin	7.15 ± 1.29	7.90 ± 1.87	8.21 ± 1.21	7.12 ± 2.11	8.00 ± 2.98

(td, J = 11.4, 2.7 Hz, 1H, H_a-6') and 1.90-1.53 (m, 4H, H-4' & H-5'). In EIMS spectra molecular ion peak appeared at *m/z* 477 while base peak appeared at *m/z* 175. All this analytical data assured the structure of compound **5e**. In similar manner, the structures of all the synthesized derivatives were established.

Enzyme inhibitory potential: All the derivatives were screened for lipoxygenase inhibitory activity and results are depicted in Table-2. It is apparent that compound **5d** revealed excellent inhibitory potential against lipoxygenase enzyme with IC_{50} value of 20.72 ± 0.34 comparable to that of standard Baicalein with IC_{50} 22.41 ± 1.31 μM that is probably due to the electrophilic substitution of phenylpropyl group to the parent molecule. It indicated that small amount of compound **5e** is required to cause 50 % inhibition as compared to reference standard Baicalein. Other members of this series were not found to be good inhibitor.

TABLE-2
LIPOXYGENASE INHIBITORY ACTIVITIES

Code	Conc.	Inhibition (%)	IC_{50} (μM)
5a	0.5	34.89 ± 1.76	–
5b	0.5	44.23 ± 0.43	> 500
5c	0.5	43.69 ± 0.98	> 500
5d	0.5	95.71 ± 0.96	20.72 ± 0.34
5e	0.5	69.45 ± 0.44	324.98 ± 2.45
5f	0.5	19.34 ± 0.56	–
Baicalein	0.5	93.79 ± 1.27	22.41 ± 1.3

Antibacterial activity: The results of antibacterial activity of the series are shown in terms of % inhibition and MIC_{50} values in Tables 3 and 4. Different compounds were found to be active against different bacterial strains. If one compound revealed promising activity against one bacterial strain it may not be active in case of some other bacterial strain/s. compound **5c** was found to be good inhibitor against *S. typhi* with % inhibition 64.23 ± 0.14 and MIC_{50} 9.05 ± 1.64 μ mol that is close to that of standard Ciprofloxacin 7.15 ± 1.29. Compound **5a** and **5f** showed good % inhibition against *S. typhi* 70.64 ± 1.45 and 76.36 ± 1.45, respectively but MIC_{50} values were not so good 10.46 ± 1.34 and 10.37 ± 5.00, respectively. Compound **5a**, **5b** and **5e** showed relatively good %inhibition value against *E. coli* strain but MIC_{50} values are not so appreciable. Compound **5d** revealed relatively good %inhibition and MIC_{50} value 72.93 ± 1.52 and 10.90 ± 2.86, respectively against *B. subtilis*.

REFERENCES

1. P.C. Sharma and S. Jain, *Acta Pharm. Sciencia*, **50**, 35 (2008).
2. P.C. Sharma and S. Jain, *Acta Pol. Pharm. Drug Res*., **65**, 551 (2008).
3. S. Wagle, A.A. Vasudeva and N.K. Suchetha, *Indian J. Chem*., **47B**, 439 (2008).
4. B.S. Holla, K.N. Poojary, B. Kalluraya and P.V. Gowda, *Indian J. Heterocycl. Chem*., **5**, 273 (1996).
5. S.S. Shafi and T.R. Radhakrishnan, *Indian J. Heterocycl. Chem*., **5**, 133 (1995).
6. T.M. Tan, Y. Chen, K.H. Kong, J. Bai, Y. Li, S.G. Lim, H. Ang and Y. Lam, *Antiviral Res*., **71**, 7 (2006).
7. K. Matsumoto, Y. Kawamura, Y. Yasuda, T. Tanimoto, K. Matsumoto, T. Yoshida and J. Shoji, *J. Antibiot. (Tokyo)*, **42**, 1465 (1989).
8. F.A. Omar, N.M. Mahfouz and M.A. Rahman, *Eur. J. Med. Chem*., **31**, 819 (1996).
9. B.N. Goswami, J.C.S. Kataky and J.N. Baruah, *J. Heterocycl. Chem*., **21**, 1225 (1984).
10. M. Kaspady, V.K. Narayanaswamy, M. Raju and G.K. Rao, *Lett. Drug Des. Discov*., **6**, 21 (2009).
11. C.-R. Yang, Y. Zhang, M.R. Jacob, S.I. Khan, Y.-J. Zhang and X.-C. Li, *Antimicrob. Agents Chemother*., **50**, 1710 (2006).
12. H.C. Clapp, A. Banerjee and S.A. Rotenberg, *Biochemistry*, **24**, 1826 (1985).
13. S. Baylac and P. Racine, *Int. J. Aromatherap*., **13**, 138 (2003).
14. Aziz-ur-Rehman, A. Fatima, N. Abbas, M. A. Abbasi, K.M. Khan, M. Ashraf, I. Ahmad and S. A. Ejaz, *Pak. J. Pharm. Sci*., **26**, 345 (2013).
15. Aziz-ur-Rehman, A. Fatima, M.A. Abbasi, S. Rasool, A. Malik, M. Ashraf, I. Ahmad and S. A. Ejaz, *J. Saudi Chem. Soc*.; doi:10.1016/j.jscs.2013.02.006.
16. H. Khalid, Aziz-ur-Rehman, M.A. Abbasi, A. Malik, S. Rasool, K. Nafeesa, I. Ahmad and S. Afzal, *J. Saudi Chem. Soc*.; doi:10.1016/j.jscs.2013.05.001.