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Synthesis of Some *N*-Substituted Sulfonamides Derived from Moringine as Lipoxygenase Inhibitors

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ABSTRACT
Sulfonamides belong to an emerging class having good inhibitory effects. In the present work, a series of *N*-substituted derivatives of *N*-benzyl-4-chlorobenzenesulfonamide have been synthesized. The reaction of moringine (benzylamine; **1**) with 4-chlorobenzenesulfonyl chloride (**2**) in aqueous medium yielded the parent molecule, *N*-benzyl-4-chlorobenzenesulfonamide (**3**). Alkyl/aralkyl halides, **4a-m**, were reacted with **3** in polar aprotic medium to produce *N*-substituted derivatives, **5a-m**. These synthesized products were characterized by ^{1}H-NMR, IR and EI-MS spectra and screened against lipoxygenase (LOX) enzyme. These were found to be moderate inhibitors of this enzyme and could find their use as therapeutic agent for various inflammatory ailments.

Keywords: Moringine, Sulfonamide, Lipoxygenase, EI-MS, IR and ^{1}H-NMR.

1. INTRODUCTION
Sulfamoyl -SO_2-NH- moiety is present in many biologically active compounds. These are known as sulfonamides and extensively used because of their low cost, low toxicity and excellent activity against common bacterial diseases. The synergetic action of sulfonamides with trimethoprim has brought about vast resurgence of sulfonamide usage everywhere over the last decade[1-4]. Many of the chemotherapeutic sulfonamide derivatives are widely used as antibacterial and antiviral agents[5,6]. Sulfonamides have shown multiple applications in biological systems such as, anticancer, anticonvulsant etc[2,5,7-9]. Structurally modified sulfonamide is considered as important potential inhibitors of histone deacetylase (HDAC) cease tumor cell growth *in vivo* in animal cultures[10,11]. Due to bacteriostatic activity, sulfonamides are specialized for treatment of urinary-tract infection. To control many diseases in animals and aquaculture, sulfonamides are employed[12-14]. The mechanism of action of sulfonamide includes incorporation of 4-aminobenzoic acid in folic acid pathway, as it blocks the foliate synthetase enzyme. In this respect, it offers hindrance to folic acid synthesis in bacteria, which consequently creates hurdle in production of purines[2-14].

Lipoxygenases are implied in arachidonic acid metabolism and generation of various biologically active lipids which own a primary role in inflammation. These support a large number of physiological processes and necessitate in the development of several pathological conditions such as arthritis and cancer. Lipoxygenases are, therefore, likely objectives for rational medicine design[15-21].

In continuation of our previous work[22,23], to search out some therapeutic agents with low toxicity, here we report the facile and benign synthesis of sulfonamides starting from moringine as lipoxygenase inhibitors for the ailment of various inflammatory diseases.

2. RESULTS AND DISCUSSION
The basic purpose of this research was to inaugurate the different synthesized compounds having valuable potential inhibition against lipoxygenase enzyme. The synthesized compounds were screened against this enzyme selectively because of its role in the inflammatory diseases[15-21] and also our quondam work on the inhibition of this enzyme[15,24,25]. We used different alkyl/aralkyl groups for the substitution at nitrogen of sulfonamide to elucidate the structure-activity relationship of the synthesized compound with the applied lipoxygenase enzyme. Some of the electrophiles utilized bear halogens, this was because of better reported inhibition potential of the halogenated compounds[26].

2.1 *Chemistry*
First a parent, that is, *N*-benzyl-4-chlorobenzenesulfonamide (**3**) was prepared by the reaction of moringine (benzyl amine) with 4-chlorobenzenesulfonyl chloride on stirring for an excellent yield. The product was precipitated and separated after the addition of the hydrochloric acid. Second, the parent product **3** was further processed to achieve a series of new *N*-alkyl/aralkyl substituted sulfonamides, **5a-m**. The products were accomplished after the addition of a weak base in a polar aprotic solvent along with excess of distilled water.

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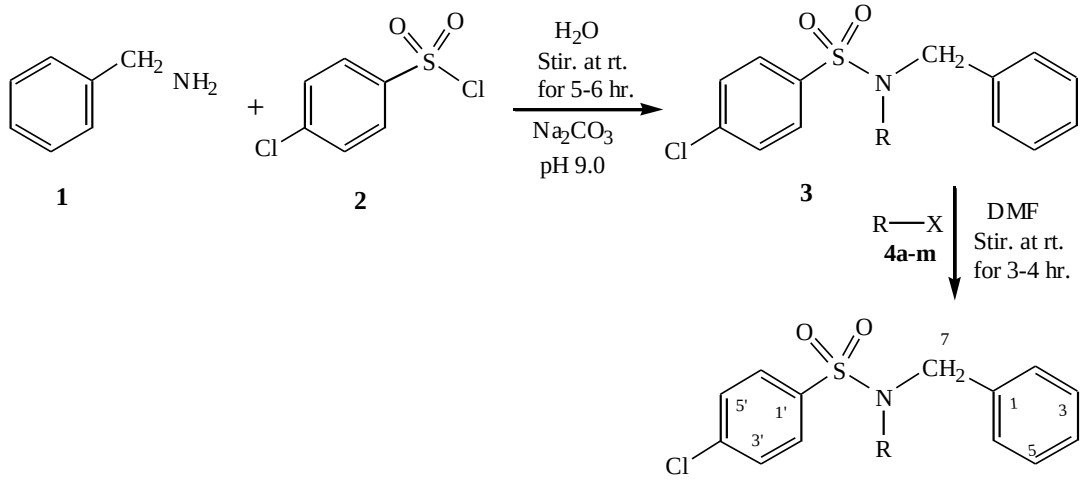

1 **2** **3** **5a-m**

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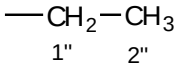
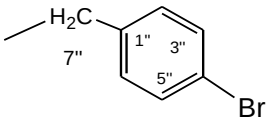
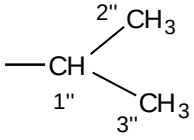
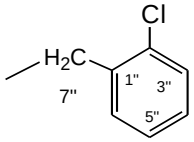
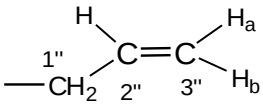
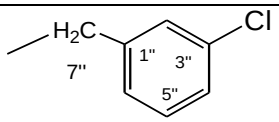
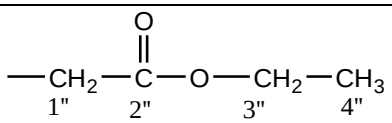
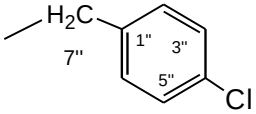
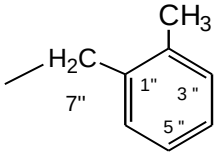
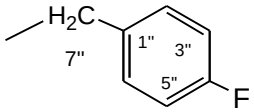
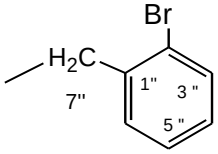
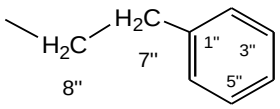
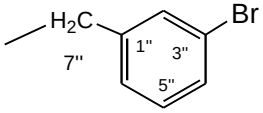
5a		**5h**	
5b		**5i**	
5c		**5j**	
5d		**5k**	
5e		**5l**	
5f		**5m**	
5g			

Scheme-1: Synthesis of *N*-substituted sulfonamides, **5a-m**

The products were separated by filtration and by solvent extraction in some cases. The sulfonamide **3** was accomplished in good yield with white amorphous appearance with sound support of HR-MS by *m/z* 281.7578 owing to molecular formula $C_{13}H_{12}ClNO_2S$ (Calcd. for 281.7807). The molecular formula was also supported by counting the number of protons in its ^{1}H-NMR spectrum. Two *ortho* coupled doublets appearing in its ^{1}H-NMR spectrum at δ 7.71 and 7.45 were characteristics of the protons H-2' & H-6' and H-3' & H-5' respectively owing to 4-chlorobenzenesulfonyl moiety.

The other signal in aromatic region appearing at δ 7.16-7.25 was a multiplet of five protons which was assigned as H-2 to H-6 owing to phenyl ring of moringine. Furthermore, in aliphatic region a broad singlet at δ 4.65 (CH_2-7) was due to methylene protons attached to nitrogen of sulfamoyl group. The IR and EI-MS data of this parent molecule also thoroughly supported the above inferred structural units. The whole discussion collectively confirmed **3**, *N*-Benzyl-4-chlorobenzenesulfonamide[27]. Similarly the structures of *N*-benzyl-4-chlorobenzenesulfonamide derivatives were elucidated.

2.2 *Structural Characterization*

2.2.1 *N-Benzyl-4-chlorobenzenesulfonamide (3)*

White amorphous powder; Yield: 88%; m.p.: 108-112°C; HR-MS: $[M]^+$ 281.7578 (Calcd. for $C_{13}H_{12}ClNO_2S$; 281.7807); ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 7.77 (d, *J* = 8.4 Hz, 2H, H-2', H-6'), 7.45 (d, *J* = 8.4 Hz, 2H, H-3', H-5'), 7.15-7.25 (m, 5H, H-2 to H-6), 4.65 (br s, 2H, CH_2-7); IR (KBr): ν_{max} (cm^{-1}): 3380 (N-H), 3056 (Ar-H), 1530 (Ar C=C), 1410 (-SO_2-), 1140 (C-N), 710 (C-Cl); EIMS: *m/z* 283 $[M+2]^+$, 281 $[M]^+$, 246 $[M-Cl]^+$, 217 $[M-SO_2]^+$, 190 $[M-CH_2C_6H_5]^+$, 170 $[M-C_6H_4Cl]^+$.

2.2.2 *N-Benzyl-N-ethyl-4-chlorobenzenesulfonamide (5a)*

White amorphous powder; Yield: 90%; m.p.: 56-60°C; HR-MS: $[M]^+$ 309.8110 (Calcd. for $C_{15}H_{16}ClNO_2S$; 309.8305); ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 7.76 (d, *J* = 8.0 Hz, 2H, H-2', H-6'), 7.47 (d, *J* = 8.0 Hz, 2H, H-3', H-5'), 7.24-7.28 (m, 5H, H-2 to H-6), 4.33 (br s, 2H, CH_2-7), 3.18 (q, *J* = 7.2 Hz, 2H, CH_2-1''), 0.92 (t, *J* = 7.2 Hz, 3H, CH_3-2''); IR (KBr): ν_{max} (cm^{-1}): 3058 (Ar-H),1535 (Ar C=C), 1415 (-SO_2-), 1145 (C-N), 712 (C-Cl); EIMS: *m/z* 311 $[M+2]^+$, 309 $[M]^+$, 280 $[M-C_2H_5]^+$, 274 $[M-Cl]^+$, 245 $[M-SO_2]^+$, 218 $[M-CH_2C_6H_5]^+$, 198 $[M-C_6H_4Cl]^+$.

2.2.3 *N-Benzyl-N-(1-methylethyl)-4-chlorobenzenesulfonamide (5b)*

White amorphous powder; Yield: 84%; m.p.: 94-98°C; HR-MS: $[M]^+$ 323.8376 (Calcd. for $C_{16}H_{18}ClNO_2S$; 323.8567); ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 7.61 (d, *J* = 8.4 Hz, 2H, H-2', H-6'), 7.42 (d, *J* = 8.4 Hz, 2H, H-3', H-5'), 7.24-7.36 (m, 5H, H-2 to H-6), 4.36 (br s, 2H, CH_2-7), 4.12-4.15 (m, 1H, H-1''), 0.96 (d, *J* = 6.8 Hz, 6H, CH_3-2'', CH_3-3''); IR (KBr): ν_{max} (cm^{-1}): 3054 (Ar-H), 1540 (Ar C=C), 1440 (-SO_2-), 1143 (C-N), 715 (C-Cl); EIMS: *m/z* 325 $[M+2]^+$, 323 $[M]^+$, 288 $[M-Cl]^+$, 280 $[M-C_3H_7]^+$, 259 $[M-SO_2]^+$, 232 $[M-CH_2C_6H_5]^+$, 214 $[M-C_6H_4Cl]^+$.

2.2.4 *N-Benzyl-N-(2-propenyl)-4-chlorobenzenesulfonamide (5c)*

White amorphous powder; Yield: 80%; m.p.: 48-52°C; HR-MS: $[M]^+$ 321.8217 (Calcd. for $C_{16}H_{16}ClNO_2S$; 321.8412); ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 7.76 (d, *J* = 8.0 Hz, 2H, H-2', H-6'), 7.46 (d, *J* = 8.0 Hz, 2H, H-3', H-5'), 7.24-7.27 (m, 5H, H-2 to H-6), 5.44 (m, 1H, H-2''), 5.08 (dd, *J* = 9.6, 1.5 Hz, 1H, H_b-3''), 5.00 (dd, *J* = 17.2, 1.5 Hz, 1H, H_a-3''), 4.33 (br s, 2H, CH_2-7), 3.75 (d, *J* = 6.0 Hz, 2H, CH_2-1''); IR (KBr): ν_{max} (cm^{-1}): 3080 (C=C), 3055 (Ar-H), 1533 (Ar C=C), 1435 (-SO_2-), 1145 (C-N), 708 (C-Cl); EIMS: *m/z* 323 $[M+2]^+$, 321 $[M]^+$, 307 $[M-CH_2]^+$, 286 $[M-Cl]^+$, 280 $[M-C_3H_5]^+$, 257 $[M-SO_2]^+$, 230 $[M-CH_2C_6H_5]^+$, 212 $[M-C_6H_4Cl]^+$.

2.2.5 *N-Benzyl-N-[(ethoxycarbonyl)methyl)]-4-chlorobenzenesulfonamide (5d)*

White amorphous powder; Yield: 80%; m.p.: 54-56°C; HR-MS: $[M]^+$ 367.8471 (Calcd. for $C_{17}H_{18}ClNO_4S$; 367.8517); ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 7.81 (d, *J* = 8.4 Hz, 2H, H-2', H-6'), 7.47 (d, *J* = 8.4 Hz, 2H, H-3', H-5'), 7.24-7.29 (m, 5H, H-2 to H-6), 4.47 (br s, 2H, CH_2-7), 4.00 (q, *J* = 7.2 Hz, 2H, CH_2-3''), 3.90 (br s, 2H, CH_2-1''), 1.13 (t, *J* = 7.2 Hz, 3H, CH_3-4''); IR (KBr): ν_{max} (cm^{-1}): 3050 (Ar-H), 1740 (C=O), 1530 (Ar C=C), 1435 (-SO_2-), 1170 (C-O), 1138 (C-N), 716 (C-Cl); EIMS: *m/z* 369 $[M+2]^+$, 367 $[M]^+$, 338 $[M-C_2H_5]^+$, 332 $[M-Cl]^+$, 322 $[M-OC_2H_5]^+$, 303 $[M-SO_2]^+$, 294 $[M-C_3H_5O_2]^+$, 280 $[M-C_4H_7O_2]^+$, 276 $[M-CH_2C_6H_5]^+$, 258 $[M-C_6H_4Cl]^+$.

2.2.6 *N-Benzyl-N-(2-methylbenzyl)-4-chlorobenzenesulfonamide (5e)*

White amorphous powder; Yield: 96%; m.p.: 82-85°C; HR-MS: $[M]^+$ 385.9075 (Calcd. for $C_{21}H_{20}ClNO_2S$; 385.9208); ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 7.72 (d, *J* = 8.4 Hz, 2H, H-2', H-6'), 7.45 (d, *J* = 8.4 Hz, 2H, H-3', H-5'), 6.95-7.15 (m, 9H, H-2 to H-6, H-3'' to H-6''), 4.33 (br s, 2H, CH_2-7), 4.30 (br s, 2H, CH_2-7''), 2.05 (s, 3H, CH_3-2''); IR (KBr): ν_{max} (cm^{-1}): 3057 (Ar-H), 1528 (Ar C=C), 1439 (-SO_2-), 1142 (C-N), 717 (C-Cl); EIMS: *m/z* 387 $[M+2]^+$, 385 $[M]^+$, 370 $[M-CH_3]^+$, 350 $[M-Cl]^+$, 321 $[M-SO_2]^+$, 294 $[M-CH_2C_6H_5]^+$, 280 $[M-CH_2C_6H_4CH_3]^+$, 276 $[M-C_6H_4Cl]^+$.

2.2.7 *N-Benzyl-N-(2-bromobenzyl)-4-chlorobenzenesulfonamide (5f)*

White amorphous powder; Yield: 89%; m.p.: 83-86°C; HR-MS: $[M]^+$ 450.7764 (Calcd. for $C_{20}H_{17}BrClNO_2S$; 450.7915); ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 7.70 (d, *J* = 8.4 Hz, 2H, H-2', H-6'), 7.43 (d, *J* = 8.4 Hz, 2H, H-3', H-5'), 7.38 (d, *J* = 7.2 Hz, 1H, H-3''), 7.05-7.17 (m, 8H, H-2 to H-6, H-4'' to H-6''), 4.44 (br s, 2H, CH_2-7''), 4.39 (br s, 2H, CH_2-7); IR (KBr): ν_{max} (cm^{-1}): 3055 (Ar-H), 1534 (Ar C=C), 1439 (-SO_2-), 1139 (C-N), 711 (C-Cl), 550 (C-Br); EIMS: *m/z* 352 $[M+2]^+$, 450 $[M]^+$, 359 $[M-CH_2C_6H_5]^+$, 415 $[M-Cl]^+$, 386 $[M-SO_2]^+$, 341 $[M-C_6H_4Cl]^+$, 280 $[M-CH_2C_6H_4Br]^+$.

2.2.8 *N-Benzyl-N-(3-bromobenzyl)-4-chlorobenzenesulfonamide (5g)*

White amorphous powder; Yield: 75%, m.p.: 49-52°C; HR-MS: $[M]^+$ 450.7764 (Calcd. for $C_{20}H_{17}BrClNO_2S$; 450.7915); ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 7.73 (d, *J* = 8.4 Hz, 2H, H-2', H-6'), 7.46 (d, *J* = 8.4 Hz, 2H, H-3', H-5'), 7.33 (br s, 1H, H-2''), 6.98 (d, *J* = 7.2 Hz, 1H, H-4''), 7.05-7.23 (m, 7H, H-2 to H-6, H-5'', H-6''), 4.32 (s, 2H, H-7''), 4.26 (s, 2H, H-7); IR (KBr): ν_{max} (cm^{-1}): 3055 (Ar-H), 1534 (Ar C=C), 1439 (-SO_2-), 1139 (C-N), 715 (C-Cl), 550 (C-Br); EIMS: *m/z* 452 $[M+2]^+$, 450 $[M]^+$, 359 $[M-CH_2C_6H_5]^+$, 415 $[M-Cl]^+$, 386 $[M-SO_2]^+$, 341 $[M-C_6H_4Cl]^+$, 280 $[M-CH_2C_6H_4Br]^+$.

2.2.9 ***N-Benzyl-N-(4-bromobenzyl)-4-chlorobenzenesulfonamide (5h)***

White greenish granules; Yield: 80%; m.p.: 92-94^{o}C; HR-MS: $[M]^+$ 450.7764 (Calcd. for $C_{20}H_{17}BrClNO_2S$; 450.7915); ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 7.73 (d, *J* = 8.4 Hz, 2H, H-2', H-6'), 7.46 (d, *J* = 8.4 Hz, 2H, H-3', H-5'), 7.33 (d, *J* = 8.0 Hz, 2H, H-3", H-5"), 7.22 (d, *J* = 8.8 Hz, 2H, H-2", H-6"), 6.90-7.01 (m, 5H, H-2 to H-6), 4.29 (br s, 2H, CH_2-7"), 4.24 (br s, 2H, CH_2-7); IR (KBr): ν_{max} (cm^{-1}): 3055 (Ar-H), 1534 (Ar C=C), 1439 (-SO_2-), 1139 (C-N), 713 (C-Cl), 550 (C-Br); EIMS: *m/z* 452 $[M+2]^+$, 450 $[M]^+$, 359 $[M-CH_2C_6H_5]^+$, 415 $[M-Cl]^+$, 386 $[M-SO_2]^+$, 341 $[M-C_6H_4Cl]^+$, 280 $[M-CH_2C_6H_4Br]^+$.

2.2.10 ***N-Benzyl-N-(2-chlorobenzyl)-4-chlorobenzenesulfonamide (5i)***

White amorphous powder; Yield: 80%; m.p.: 54-56^{o}C; HR-MS: $[M]^+$ 406.3254 (Calcd. for $C_{20}H_{17}Cl_2NO_2S$; 406.3305); ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 7.69 (d, *J* = 8.4 Hz, 2H, H-2', H-6'), 7.42 (d, *J* = 8.4 Hz, 2H, H-3', H-5'), 7.32 (d, *J* = 7.2 Hz, 1H, H-3"), 7.06-7.17 (m, 8H, H-2 to H-6, H-4" to H-6"), 4.46 (br s, 2H, CH_2-7"), 4.39 (br s, 2H, CH_2-7); IR (KBr): ν_{max} (cm^{-1}): 3057 (Ar-H), 1535 (Ar C=C), 1441 (-SO_2-), 1141 (C-N), 709 (C-Cl); EIMS: *m/z* 408 $[M+2]^+$, 406 $[M]^+$, 315 $[M-CH_2C_6H_5]^+$, 370 $[M-Cl]^+$, 342 $[M-SO_2]^+$, 296 $[M-C_6H_4Cl]^+$, 280 $[M-CH_2C_6H_4Cl]^+$.

2.2.11 ***N-Benzyl-N-(3-chlorobenzyl)-4-chlorobenzenesulfonamide (5j)***

White amorphous powder; Yield: 85%; m.p.: 78-86^{o}C; HR-MS: $[M]^+$ 406.3254 (Calcd. for $C_{20}H_{17}Cl_2NO_2S$; 406.3305); ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 7.73 (d, *J* = 8.4 Hz, 2H, H-2', H-6'), 7.46 (d, *J* = 8.4 Hz, 2H, H-3', H-5'), 7.22 (br s, 1H, H-2"), 6.94 (br d, *J* = 7.2 Hz, 1H, H-4"), 7.04-7.16 (m, 7H, H-2 to H-6, H-5", H-6"), 4.32 (br s, 2H, CH_2-7"), 4.26 (br s, 2H, CH_2-7); IR (KBr): ν_{max} (cm^{-1}): 3057 (Ar-H), 1535 (Ar C=C), 1441 (-SO_2-), 1141 (C-N), 707 (C-Cl); EIMS: *m/z* 408 $[M+2]^+$, 406 $[M]^+$, 315 $[M-CH_2C_6H_5]^+$, 370 $[M-Cl]^+$, 342 $[M-SO_2]^+$, 296 $[M-C_6H_4Cl]^+$, 280 $[M-CH_2C_6H_4Cl]^+$.

2.2.12 ***N-Benzyl-N-(4-chlorobenzyl)-4-chlorobenzenesulfonamide (5k)***

White amorphous powder; Yield: 72%, m.p.: 94-98^{o}C; HR-MS: $[M]^+$ 406.3254 (Calcd. for $C_{20}H_{17}Cl_2NO_2S$; 406.3305); ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 7.73 (d, *J* = 8.4 Hz, 2H, H-2', H-6'), 7.46 (d, *J* = 8.4 Hz, 2H, H-3', H-5'), 7.16-7.22 (m, 5H, H-2 to H-6), 7.00 (d, *J* = 8.0 Hz, 2H, H-3", H-5"), 6.98 (d, *J* = 8.0 Hz, 2H, H-2", H-6"), 4.29 (br s, 2H, CH_2-7"), 4.26 (br s, 2H, CH_2-7); IR (KBr): ν_{max} (cm^{-1}): 3057 (Ar-H), 1535 (Ar C=C), 1441 (-SO_2-), 1141 (C-N), 719 (C-Cl); EIMS: *m/z* 408 $[M+2]^+$, 406 $[M]^+$, 315 $[M-CH_2C_6H_5]^+$, 370 $[M-Cl]^+$, 342 $[M-SO_2]^+$, 296 $[M-C_6H_4Cl]^+$, 280 $[M-CH_2C_6H_4Cl]^+$.

2.2.13 ***N-Benzyl-N-(4-flourobenzyl)-4-chlorobenzenesulfonamide (5l)***

White amorphous powder; Yield: 81%; m.p.: 86-88^{o}C; HR-MS: $[M]^+$ 389.8708 (Calcd. for $C_{20}H_{17}ClFNO_2S$; 389.8891); ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 7.73 (d, *J* = 8.4 Hz, 2H, H-2', H-6'), 7.46 (d, *J* = 8.4 Hz, 2H, H-3', H-5'), (br s, 2H, H-3", H-5"), 7.02 (br s, 2H, H-2", H-6"), 6.87-6.91 (m, 5H, H-2 to H-6), 4.29 (br s, 2H, CH_2-7"), 4.27 (br s, 2H, CH_2-7); IR (KBr): ν_{max} (cm^{-1}): 3059 (Ar-H), 1537 (Ar C=C), 1443 (-SO_2-), 1143 (C-N), 712 (C-Cl); EIMS: *m/z* 391 $[M+2]^+$, 389 $[M]^+$, 298 $[M-CH_2C_6H_5]^+$, 354 $[M-Cl]^+$, 325 $[M-SO_2]^+$, 280 $[M-CH_2C_6H_4F]^+$, 280 $[M-C_6H_4Cl]^+$.

2.2.14 ***N-Benzyl-N-(2-phenylethyl)-4-chlorobenzenesulfonamide (5m)***

White amorphous powder; Yield: 89%; m.p.: 90-92^{o}C; HR-MS: $[M]^+$ 385.9074 (Calcd. for $C_{21}H_{20}ClNO_2S$; 385.9215); ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 7.72 (d, *J* = 8.4 Hz, 2H, H-2', H-6'), 7.44 (d, *J* = 8.4 Hz, 2H, H-3', H-5'), 6.92-7.30 (m, 10H, H-2 to H-6, H-2" to H-6"), 4.33 (br s, 2H, CH_2-7), 3.29 (t, *J* = 7.6 Hz, 2H, CH_2-8"), 2.62 (t, *J* = 7.6 Hz, 2H, CH_2-7"); IR (KBr): ν_{max} (cm^{-1}): 3055 (Ar-H), 1529 (Ar C=C), 1438 (-SO_2-), 1140 (C-N), 713 (C-Cl); EIMS: *m/z* 387 $[M+2]^+$, 385 $[M]^+$, 350 $[M-Cl]^+$, 294 $[M-CH_2C_6H_5]^+$, 280 $[M-CH_2C_6H_4Cl]^+$, 276 $[M-C_6H_4Cl]^+$, 221 $[M-SO_2]^+$.

2.3 ***Biological activity***

In continuation of our previous efforts on such sulfonamides[27] to find their possible therapeutic potential against various diseases, here, the screening of the parent compound **3** and synthesized derivatives **5a-m** against lipoxygenase (LOX) enzyme demonstrated that most of them were active against this enzyme, Table 1. The molecule, **5c** was found to be good inhibitor against lipoxygenase (LOX) having IC_{50} value of 52.31±0.41 µmoles/L, taking baicalein as reference bearing IC_{50} of 22.4±1.3 µmoles/L, the most credibly due to substitution of allyl group in the parent compound showing π-π interaction with binding site of enzyme. The other good inhibitors were **5e**, **5f**, **5h** and **5m** having IC_{50} values of 92.31±0.21, 85.21±0.47, 75.31±0.11 and 64.71±0.47 µmoles/L respectively, relative to baicalein. The activity of the synthesized compounds against the enzyme obeys the following order, **5c** > **5m** > **5h** > **5f** > **5e** > **5i** > **5j**. Four of the synthesized compounds, **5d**, **5g**, **5k** and **5l** were found to be the least active against the enzyme and three, **3**, **5a** and **5b** were found to be inactive plausibly because of simple alkyl chains present in the molecule.

Table-1: Lipoxygenase (LOX) enzyme inhibition studies (mean ± SEM).

Compound No.	Lipoxygenase (LOX) enzyme		
	Conc. (mM)	(%age) Inhibition	(IC_{50}) µmoles/L
3	0.5	33.16±0.35	-
5a	0.5	42.28±0.11	-
5b	0.5	43.07±0.62	-
5c	0.5	96.89±0.58	52.31±0.41
5d	0.5	52.67±0.78	>400
5e	0.25	67.05±0.98	92.31±0.21
5f	0.25	72.44±0.68	85.21±0.47
5g	0.5	54.09±0.47	>400
5h	0.25	78.96±0.55	75.31±0.11
5i	0.5	77.21±0.18	103.61±0.34
5j	0.5	67.98±0.33	157.41±0.51
5k	0.5	57.69±0.44	>400
5l	0.5	60.14±0.41	>400
5m	0.25	83.63±0.17	64.71±0.47
Control (Baicalein)	0.5	93.79±1.27	22.4±1.3

3. CONCLUSION

The synthesized molecules were obtained with better yields and their structures were corroborated through ^{1}H-NMR, EIMS and IR spectra. The molecule **5c** was found to possess relatively low IC_{50} value and so the most active among the whole series. The better inhibitors can be further evaluated for *in vivo* activity and these might be helpful in drug discovery especially for inflammatory diseases.

4. EXPERIMENTAL

4.1 *General*

Purity of compounds during reaction and after reaction was verified through TLC (Thin Layer Chromatography) using coated plates of silica gel G-25-UV_{254} with EtOAc and *n*-hexane as mobile phase. Compounds were characterized by melting points on Griffin-George instrument, ^{1}H NMR spectra in $CDCl_3$ at 400 MHz on Bruker spectrometer, IR spectra in KBr on Jasco-320-A spectrophotometer and EIMS spectra on JMS-HX-110 spectrometer.

4.2 *Synthesis of N-Benzyl-4-chlorobenzenesulfonamide (3)*

Nucleophilic substitution reaction of equimolar mixture of sulfonyl chloride and amine was carried out. 4-Chlorobenzenesulfonyl chloride (**2**, 10.0 mmol) and Moringine (**1**, 10.0 mmol) were mixed with 25 mL distilled water in a 100 mL RB flask. The pH of reaction mixture was monitored and kept 9-10 by sodium carbonate solution. The reaction contents were set to stir and supervised by TLC for 5-6 hours. The reaction mixture was acidified by concentrated HCl till pH of 5-6. The coagulated precipitates were filtered off, washed and dried.

4.3 *General synthesis of N-Alkyl/aralkyl-N-benzyl-4-chlorobenzenesulfonamide (5a-m)*

The compound **3** (0.1 mmol) was dissolved in dimethylformamide (DMF) (10.0 ml) and lithium hydride (0.1 mmol) was introduced. After stirring for 0.5 hour, alkyl/aralkyl halides (0.1 mmol) were added and stirred for 3-4 hours. The reaction was supervised by TLC. A weak base was added to make basic pH of 9. The formed products were collected through filtration or extraction after addition of cold distilled water.

4.4 *Lipoxygenase inhibition assay*

Lipoxygenase enzyme inhibition activity was performed by a reported method[28] with minor differences.

4.5 *Statistical analysis*

The measurements were performed in triplicate and statistically analyzed by Microsoft Excel 2010. Results are presented as mean ± SEM.

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