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New sulfonamide and carbamate derivatives of 4-(oxiran-2-ylmethoxy)-9*H*-carbazole: Synthesis, characterization, antimicrobial and antioxidant activities

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ABSTRACT

A series of new N-substituted sulfonamides, 9-(substituted phenylsulfonyl)-4-(oxiran-2-ylmethoxy)-9H-carbazole ***6(a-d)*** *and carbamates, substituted phenyl/aliphatic-4-(oxiran-2-ylmethoxy)-9H-carbazole-9-carboxylate****8(a-f)*** *were synthesized in high yields through simple straight forward reaction of 4-(oxiran-2-ylmethoxy)-9H-carbazole* ***(3)*** *with various substituted sulfonyl chlorides and chloroformates in the presence of sodium hydride as a base. The structures of the synthesized compounds were confirmed by IR, NMR (^{1}H, ^{13}C), mass and elemental analysis data. All the compounds were screenedin vitroantibacterial (Staphylococcus aureus, Bacillus subtilis and Escherichia coli), antifungal (Fusariumoxysporum, Candida albicans and Aspergillusniger) activities and antioxidant activities using DPPH and NO methods. All the compounds exhibited moderate to potent antimicrobial activities and good antioxidant activities.*

Keywords:4-(Oxiran-2-ylmethoxy)-9H-carbazole, Sulfonamides, Carbamates, Antimicrobial activity, Antioxidant activity.

INTRODUCTION

Particularly, microbes that causing the diseases have become resistance to drug therapy and is an increasing public health problem during the last decade. The hospital acquired infections are resistant to the most powerful antibiotics are reserved to treat only the most intractable infections [1].Hence, there is a pressing need to develop multi-drug resistant microbial pathogens for the treatment of infectious diseases.

Carbazole and its derivatives are importantaromatic heterocyclic compounds owing to possession of desirable electronic and charge-transport properties, large π-conjugated system and the various functional groups can be easily introduced into the structurally rigid carbazole ring. These outstanding properties of this particular heterocyclic motif are embedded in large number of natural products and medicinally relevant compounds [2].As an important class of natural alkaloids, carbazole derivatives have been isolated from different sources such as some genera of higher plants, blue-green algae, actinomycetes and filamentous fungi.In addition, number of natural and synthetic carbazole derivatives have been reported to exhibit diverse biological activities like antimicrobial [3-7], antiviral [8], anti-inflammatory [9], antimalarial [10], antitumor [11-13],antidiarrhoeal [14],neuroprotection [15], immune suppression [16] and pancreatic lipase inhibition [17].The carbazole frame work containing carazolol**(1)** is used as antihypertensive drug, carbazomycins A and B**(2a)** inhibit the growth of phytopathogenic fungi and have

antibacterial and anti-yeast activities and Murrayafoline A**(2b)** exhibited strong fungicidal activity against *Cladosporiumcucumerinum* at the dose of 12.5 µg [18] (**Figure-1**). The prevalent interests of chemists have been attracted to these structures due to their biological activities and potential applications as pharmacological agents [19] and focused on search for newer physiologically active compounds.

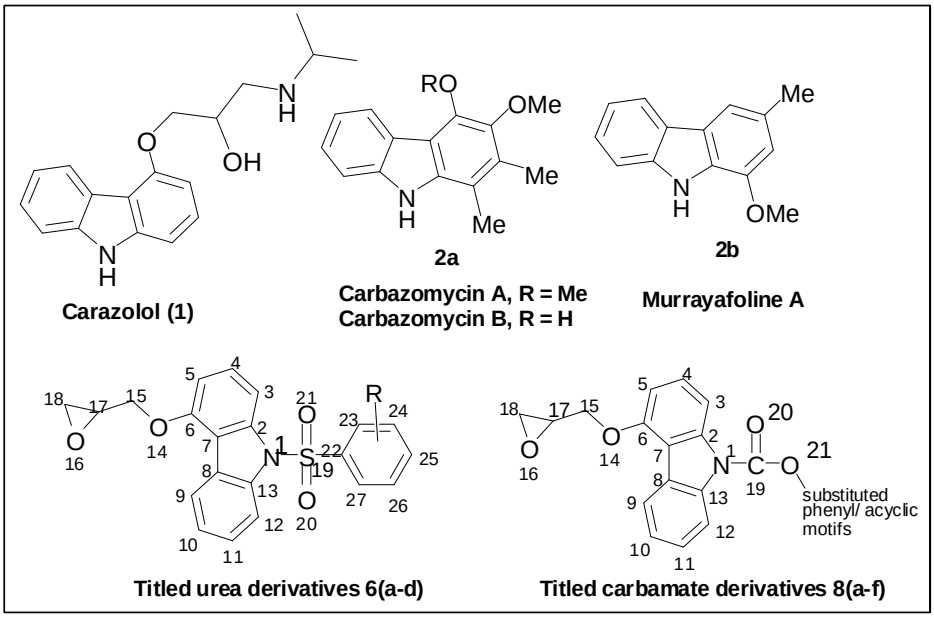


Fig.-1 Some biologically active carbazole derivatives

Further, sulfonamides (-SO_2-N-) are important synthetic, primarily bacteriostatic agents, find use in both human therapy and animal husbandry.Sulfonamide antimicrobials are the unaltered parent compounds or an acetylated metabolite [20] which can be reactivated by bacterial cleavage of the acetyl moiety [21].It was documented that the applications of sulfonamides has greatly extended from their primary function as antitumor [22],hypoglycaemic [23], anti-thyroid [24], anti-carbonic anhydrase [25],anti-inflammatory [26], diuretic [27], COX-inhibitors, the enzyme dihydropteroatesynthetase (DHPS)-the key enzyme involved in folate synthesis, anti-impotent drugs [28] and also used as azo dyes for achieving improved light stability, water solubility and fixation to fiber.Organic carbamates are valuable synthetic intermediates and ubiquitously found in a variety of biologically active compounds. Most of the functionalized carbamate derivatives are considered as interesting medicinally active motifs [29] and these scaffolds could serve as a crucial template in the construction of carbamate derivatives which may be useful in search of potential drug candidates [30].Recently, Mata*et al*.,[31] synthesized the O-alkyl and O-aryl carbamate derivatives of the antimalarial drug primaquine as potential prodrugs that prevent oxidative deamination to the inactive metabolite carboxyprimaquine.

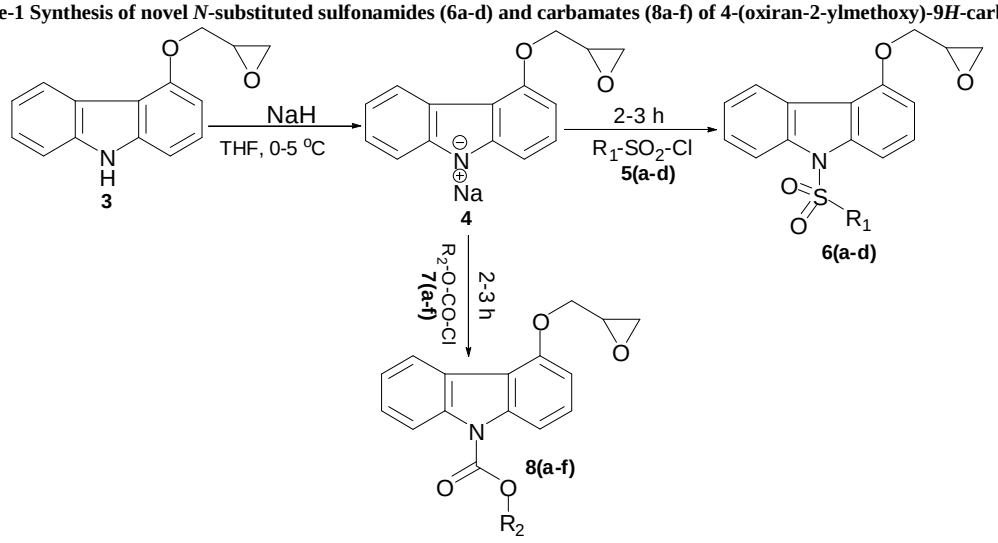
Based on overview outcomesupported by literature,we have directed our attention towards the synthesis of N-substituted sulfonamides, 9-(substituted phenylsulfonyl)-4-(oxiran-2-ylmethoxy)-9*H*-carbazole **6(a-d)** and carbamates, substituted phenyl/aliphatic-4-(oxiran-2-ylmethoxy)-9*H*-carbazole-9-carboxylate **8(a-f)**,with the hope that these new molecules exhibit enhanced biological activity, mainly due to the presence of pharmacologically active heterocyclic compound such as 4-(oxiran-2-ylmethoxy)-9*H*-carbazole(**3)**(carazolol intermediate) and bio-active substituted phenyl/aliphatic sulfonamides and carbamates. The antimicrobial and antioxidant activities of the newly synthesized compounds were evaluated.

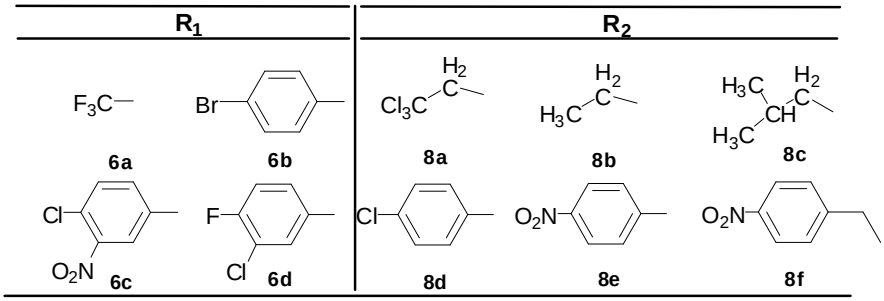
MATERIALS AND METHODS

General. All chemicals were purchased from Merck, Aldrich and S. d. Fine. Chem. (India) and used without further purification. Solvents were distilled from the appropriate drying agents and degassed before use. Melting points were determined in open capillaries on Gunamelting point apparatus and are uncorrected. IR spectra were recorded on JASCO FT-IR 5300 using KBr discs. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker AV-500

spectrometer operating at 400 MHz for ^{1}H-NMR, 100.6 MHz for ^{13}C-NMR. Mass spectra (LC-MS) were recorded on LCMS 201, SHIMADZU, JAPAN (Negative mode). The progress of the reactions was monitored by TLC on Merck silica plates. Results are presented as, chemical shift δ in ppm, J values in Hertz (Hz). Multiplicities are shown as the abbreviations: s (singlet), brs (broad singlet), d (doublet), t (triplet), m (multiplet).

Scheme-1 Synthesis of novel *N*-substituted sulfonamides (6a-d) and carbamates (8a-f) of 4-(oxiran-2-ylmethoxy)-9*H*-carbazole.

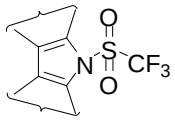
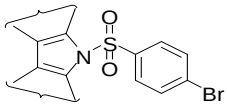
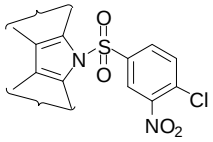
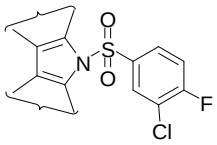
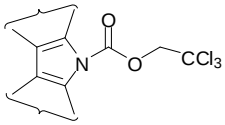
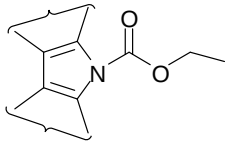
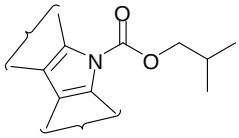
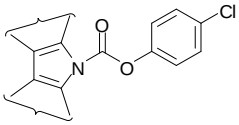
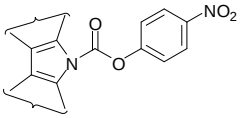
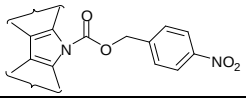




General procedure for the synthesis of title compounds:

4-(Oxiran-2-ylmethoxy)-9*H*-carbazole (**3)**(0.001 mol, 239 mg) was taken in 15 mL of THF and sodium hydride (0.0012 mol, 29 mg) was added. The reaction mixture was stirred for 20 min at 0-5^{o}C to get Na^{+}salt of the compound **3.**4-Chloro-3-nitrobenzenesulfonyl chloride (**5c)** (0.001 mol, 255 mg) was added and the reaction mixture was stirred at 30-40 ^{o}C for 2 h. The progress of the reaction was monitored by TLC. After completion of the reaction, NaCl was removed by filtration and the solvent from the reaction mixture was concentrated under reduced pressure. The crude product was washed with cold water to remove unreacted sulfonyl chloride (**5c)** and salt form of the compound **3.** The residue was recrystallized from ethanol to get pure 9-(4-chloro-3-nitrophenylsulfonyl)-4-(oxiran-2-ylmethoxy)-9H-carbazole **6c**(yield 90%). The rest of the compounds were synthesized using the same successful procedure and the physical characteristics and spectral data are presented in **Table-1** and experimental part respectively.

Table-1 Physical characteristics of the titled sulfonamides (6a-d) and carbamates (8a-f).

Compd	Product	Reaction time (h)	Yield (%)	m.p (°C)
6a		2	91	101-102
6b		3	83	149-151
6c		2	90	180-182
6d		3	85	145-146
8a		3	86	148-150
8b		3	81	110-112
8c		3	80	99-101
8d		3	83	133-134
8e		2	88	135-137
8f		3	83	117-119

4-(Oxiran-2-ylmethoxy)-9-(trifluoromethylsulfonyl)-9H-carbazole (6a):
Light brown solid,Yield 91%. Mol. Wt: 371.04, mp111-112 °C.IR (KBr): 3032 (=C-H, str), 2992 (-C-H, str), 1454 (-C=C, str), 1314 (-SO_2, asymstr), 1160 (-C-O str), 1140 (-SO_2, symstr),1094 (-C-N, str) cm^{-1};^{1}H-NMR (DMSO-d_6, 400 MHz) δ 3.09 (d, 2H, J = 8.0 Hz, -CH-CH_2-O-), 3.68 (m, 1H, -OCH_2-CH-CH_2O-), 4.01 (d, 2H, J = 6.8 Hz, -O-CH_2-CH-), 7.37-7.54 (m, 3H, Ar-H), 7.63-8.24 (m, 4H, Ar-H);^{13}C-NMR (DMSO-d_6, 100.6 MHz): δ 42.5 (C_{18}), 56.4 (C_{17}), 66.8 (C_{15}), 110.8 (C_3), 116.4 ($C_{5,12}$), 119.1 (C_{10}), 121.4 (-CF_3), 124.3 (C_9), 124.9 (C_4), 125.8 ($C_{2,11}$), 128.2 (C_8), 130.2 (C_7), 133.7 (C_{13}), 150.4 (C_6); LC-MS (m/z, %): 370 (M-H^+, 100%). Anal. Calcd. for $C_{16}H_{12}F_3NO_4S$: C, 51.75; H, 3.26; N, 3.77. Found: C, 51.72; H, 3.19; N, 3.75%.

9-(4-Bromophenylsulfonyl)-4-(oxiran-2-ylmethoxy)-9H-carbazole (6b):
Light yellow solid, Yield 83%. Mol. Wt: 457, mp 149-151 ^{o}C. IR (KBr):3017 (=C-H, str), 2986 (-C-H, str), 1450 (-C=C, str), 1348 (-SO_2, asym str), 1183 (-C-O str), 1157 (-SO_2, symstr), 1089 (-C-N, str), 748 (-C-Br str) cm^{-1}; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ 2.93 (d, 2H, J = 8.4 Hz, -CH-CH_2-O-), 3.52 (m, 1H, -OCH_2-CH-CH_2O-), 3.89 (d, 2H, J = 6.8 Hz, -O-CH_2-CH-), 6.82 (d, 2H, J = 7.2 Hz, Ar-H), 7.16 (d, 1H, J = 6.8 Hz, Ar-H), 7.29 (d, 2H, J = 7.8 Hz), 7.31-7.48 (m, 3H, Ar-H), 7.91-8.03 (m, 3H, Ar-H); ^{13}C-NMR (DMSO-d_6, 100.6 MHz) δ 43.12 (C_{18}), 50.8 (C_{17}), 68.7 (C_{15}), 112.6 (C_3), 113.4 (C_5), 115.1 (C_{12}), 117.8 (C_{10}), 122.8 (C_9), 124.4 (C_4), 125.1 ($C_{2,11}$), 127.9 (C_8), 128.2 (C_{25}), 128.9 (C_7), 130.51 ($C_{23,27}$), 131. 4 ($C_{24,26}$), 134.5 (C_{13}), 137.7 (C_{22}), 152.3 (C_6); LC-MS (m/z, %): 458 (M-H$^+$+2, 96.4%), 456 (M-H$^+$, 100%).

9-(4-Chloro-3-nitrophenylsulfonyl)-4-(oxiran-2-ylmethoxy)-9H-carbazole (6c):
Light yellow solid, Yield 90%. Mol. Wt: 458.03, mp 180-182 ^{o}C. IR (KBr):3039 (=C-H, str), 2965 (-C-H, str), 1548 (-NO_2 (aromatic), asym str), 1435 (-C=C, str), 1320 (-SO_2, asym str), 1184 (-C-O str), 1124 (-SO_2, symstr), 1108 (-C-N, str), 846 (-C-Clstr) cm^{-1}; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ 3.01 (d, 2H, J = 8.0 Hz, -CH-CH_2-O-), 3.76 (m, 1H, -OCH_2-CH-CH_2O-), 4.20 (d, 2H, J = 6.8 Hz, -O-CH_2-CH-), 7.24-7.38 (m, 3H, Ar-H), 7.65-7.78 (m, 2H, Ar-H), 7.83 (d, 1H, J = 7.2 Hz, Ar-H), 8.12-8.24 (m, 2H, Ar-H), 8.35 (d, 1H, J = 7.6 Hz, Ar-H), 8.88 (s, 1H, Ar-H); ^{13}C-NMR (DMSO-d_6, 100.6 MHz) δ 44.7 (C_{18}), 55.6 (C_{17}), 68.2 (C_{15}), 115.1 (C_3), 118.1 ($C_{5,12}$), 121.7 (C_{10}), 124.5 (C_9), 125.8 (C_4), 126.9 ($C_{2,11}$), 127.3 (C_8), 130.6 (C_7), 131.0 (C_{27}), 132.8 (C_{24}), 134.3 (C_{13}), 135.1 (C_{23}), 138.2 (C_{22}), 138.8 (C_{25}), 148.7 (C_6), 156.3 (C_{26}); LC-MS (m/z, %): 459 (M-H$^+$+2, 33%), 457 (M-H$^+$, 100%). Anal. Calcd. for $C_{21}H_{15}ClN_2O_6S$: C, 54.97; H, 3.29; N, 6.10; Found: C, 54.85; H, 3.21; N, 6.19%.

9-(4-Chloro-3-fluorophenylsulfonyl)-4-(oxiran-2-ylmethoxy)-9H-carbazole (6d):
Brown solid, Yield 85%. Mol. Wt: 431.04, mp 145-146 ^{o}C. IR (KBr):3012 (=C-H, str), 2976 (-C-H, str), 1423 (-C=C, str), 1335 (-SO_2, asym str), 1169 (-C-O str), 1130 (-SO_2, symstr), 1110 (-C-F, str), 810 (-C-Clstr) cm^{-1}; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ 2.97 (d, 2H, J = 7.6 Hz, -CH-CH_2-O-), 3.53 (m, 1H, -OCH_2-CH-CH_2O-), 3.98 (d, 2H, J = 6.4 Hz, -O-CH_2-CH-), 7.04-7.12 (m, 4H, Ar-H), 7.34 (d, 1H, J = 7.2 Hz, Ar-H), 7.40-7.49 (m, 3H, Ar-H), 7.74 (d, 1H, J = 7.2 Hz, Ar-H), 8.04 (s, 1H, Ar-H); ^{13}C-NMR (DMSO-d_6, 100.6 MHz) δ 42.2 (C_{18}), 51.9 (C_{17}), 65.1 (C_{15}), 111.8 (C_3), 115.7 ($C_{5,12}$), 121.2 (C_{10}), 123.8 (C_9), 124.2 (C_4), 126.4 ($C_{2,11}$), 126.9 (C_8), 131.4 (C_7), 132.1 (C_{27}), 133.2 (C_{24}), 134.4 (C_{13}), 134.8 (C_{23}), 135.6 (C_{22}), 137.1 (C_{25}), 146.2 (C_6), 160.5 (C_{26}); LC-MS (m/z, %): 432 (M-H$^+$+2) (32%), 430 (M-H$^+$, 100%).

2,2,2-Trichloroethyl 4-(oxiran-2-ylmethoxy)-9H-carbazole-9-carboxylate (8a):
White solid, Yield 86%. Mol. Wt: 413, mp 147-150 ^{o}C. IR (KBr):3078 (=C-H, str), 2934 (-C-H, str), 1734 (-C=O, str), 1447 (-C=C, str), 1390 (-C(O)-O-, str), 1132 (-C-O str) cm^{-1}; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ 2.86 (d, 2H, J = 6.8 Hz, -CH-C$\underline{H}_2$-O-), 3.78 (m, 1H, -OCH_2-C$\underline{H}$-CH_2O-), 3.91 (d, 2H, J = 7.2 Hz, -O-C$\underline{H}_2$-), 4.45 (s, 2H, -O-CH_2-CCl_3), 7.19-7.28 (m, 3H, Ar-H), 7.64-7.71 (m, 2H, Ar-H), 8.21 (s, 1H, Ar-H), 8.63 (s, 1H, Ar-H);^{13}C-NMR (DMSO-d_6, 100.6 MHz) δ 43.5 (C_{18}), 46.6 (C_{17}), 68.5 (C_{15}), 72.3 (-$\underline{C}H_2$-COO), 98.2 (-CCl_3), 108.5 (C_5), 109.8 ($C_{3,}$), 113.4 (C_{12}), 117.8 (C_{10}), 121.7 (C_8), 122.4 ($C_{9,4}$), 123.1 (C_{11}), 124.3 (C_2), 128.5 (C_7), 143.8 (C_{13}), 149.1 (C_6), 154.3 (C_{19});LC-MS (m/z, %): 416 (M-H$^+$+4, 28%), 414 (M-H$^+$+2, 86%), 412 (M-H$^+$, 100%); Anal. Calcd. for$C_{18}H_{14}Cl_3NO_4$: C, 52.14; H, 3.40; N, 3.38; Found: C, 51.67; H, 3.29; N, 3.31%.

Ethyl 4-(oxiran-2-ylmethoxy)-9H-carbazole-9-carboxylate (8b):
Light brown solid, Yield 81%. Mol. Wt: 311.12, mp 109-112 ^{o}C. IR (KBr):3031 (=C-H, str), 2918 (-C-H, str), 2874 (-C-H, str), 1726 (-C=O, str), 1434 (-C=C, str), 1367 (-C(O)-O-, str), 1136 (-C-O str) cm^{-1}; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ 1.16 (t, 3H, J = 6.8 Hz, C$\underline{H}_3$-CH_2-O), 2.85 (d, 2H, J = 6.4 Hz, -CH-C$\underline{H}_2$-O-), 3.76 (m, 1H, -OCH_2-C$\underline{H}$-CH_2O-), 3.89 (d, 2H, J = 7.2 Hz, -O-C$\underline{H}_2$-), 4.17 (q, 2H, J = 6.8 Hz, CH_3–C$\underline{H}_2$-O-CO-), 7.13-7.32 (m, 5H, Ar-H), 8.11-8.18 (m, 2H, Ar-H); ^{13}C-NMR (DMSO-d_6, 100.6 MHz) δ 16.4 (-$\underline{C}H_{3alephatic}$), 40.9 ($C_{18}$), 42.3 ($C_{17}$), 61.7 (-O-$\underline{C}H_2$), 68.1 ($C_{15}$), 106.3 ($C_5$), 107.1 ($C_{3,}$), 115.7 ($C_{12}$), 118.2 ($C_{10}$), 120.1 ($C_8$), 123.8 ($C_9$), 124.2 ($C_4$), 124.7 ($C_{11}$), 125.8 ($C_2$), 132.4 ($C_7$), 141.3 ($C_{13}$), 149.7 ($C_6$), 152.5 ($C_{19}$);LC-MS (m/z, %): 310 (M-H$^+$, 100%).

Isobutyl 4-(oxiran-2-ylmethoxy)-9H-carbazole-9-carboxylate (8c):
Brown solid, Yield 80%. Mol. Wt: 339.15, mp 99-101 ^{o}C. IR (KBr):3041 (=C-H, str), 2954 (-C-H, str), 2861 (-C-H, str), 1723 (-C=O, str), 1451 (-C=C, str), 1359 (-C(O)-O-, str), 1134 (-C-O str) cm^{-1}; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ 0.94 (d, 6H, J = 7.8 Hz, ($C\underline{H}_3$)$_2$-CH-), 1.37-1.41 (m, 1H, $(CH_3)_2$-C$\underline{H}$-CH_2-), 2.91 (d, 2H, J = 6.4 Hz, -CH-C$\underline{H}_2$-O-), 3.54 (m, 1H, -OCH_2-C$\underline{H}$-CH_2O-), 3.64 (d, 2H, J = 6.4 Hz, -O-$\underline{CH}_2$-CH-), 3.92 (d, 2H, J = 6.8 Hz, -O-C$\underline{H}_2$-), 7.19-7.25 (m, 4H, Ar-H), 8.09-8.18 (m, 2H, Ar-H), 8.32 (d, 2H, J = 6.4 Hz, Ar-H); ^{13}C-NMR (DMSO-d_6, 100.6 MHz) δ

19.3 (-$\underline{C}H_{3alephatic}$), 24.9 (-$CH_{alephatic}$), 42.1 ($C_{18}$), 46.1 ($C_{17}$), 66.6 ($C_{15}$), 69.2 (-O-$\underline{C}H_2$), 105.6 ($C_5$), 106.8 ($C_3$), 112.8 ($C_{12}$), 117.7 ($C_{10}$), 119.8 ($C_8$), 124.2 ($C_9$), 124.8 ($C_4$), 125.4 ($C_{11}$), 125.9 ($C_2$), 134.9 ($C_7$), 140.6 ($C_{13}$), 148.8 ($C_6$), 150.7 ($C_{19}$);LC-MS (m/z, %): 338 ($M\text{-}H^+$, 100%).

4-Chlorophenyl 4-(oxiran-2-ylmethoxy)-9H-carbazole-9-carboxylate (8d):
White solid, Yield 83%. Mol. Wt: 393.08, mp 133-134 ^oC. IR (KBr):3033 (=C-H, str), 2969 (-C-H, str), 1720 (-C=O, str), 1450 (-C=C, str), 1375 (-C(O)-O-, str), 1148 (-C-O str), 794 (-C-Cl, str) cm^{-1}; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ 2.86 (d, 2H, J = 7.2 Hz, -CH-CH_2-O-), 3.65 (m, 1H, -OCH_2-CH-CH_2O-), 4.12 (d, 2H, J = 6.4 Hz, -O-CH_2-CH-), 7.23 (d, 1H, J = 6.8 Hz, Ar-H), 7.43 (d, 2H, J = 6.8 Hz), 7.52-7.67 (m, 5H, Ar-H), 7.89-8.01 (m, 3H, Ar-H); ^{13}C-NMR (DMSO-d_6, 100.6 MHz) δ 42.5 (C_{18}), 50.2 (C_{17}), 69.3 (C_{15}), 109.2 (C_3), 109.8 (C_5), 118.0 (C_{12}), 119.6 (C_{10}), 123.5 ($C_{8,2'}$), 124.1 ($C_{4,6'}$), 124.9 (C_2), 125.6 (C_{11}), 126.4 (C_9), 131.2 (C_7), 131.9 ($C_{2',3'}$), 134. 6 ($C_{4'}$-Cl), 138.7 (C_{13}), 139.5 (-O-C=O), 150.8 (C_6), 152.2 ($C_{1'}$); LC-MS (m/z, %): 394 ($M\text{-}H^+$+2, 33%), 392 ($M\text{-}H^+$, 100%); Anal. Calcd. for $C_{22}H_{16}ClNO_4$: C, 67.10; H, 4.10; N, 3.56; O, 16.25. Found: C, 66.97; H, 3.91; N, 3.52%.

4-Nitrophenyl 4-(oxiran-2-ylmethoxy)-9H-carbazole-9-carboxylate (8e):
Yellow solid, Yield 88%. Mol. Wt: 404.10, mp 135-137 ^oC. IR (KBr):3046 (=C-H, str), 2954 (-C-H, str), 1731 (-C=O, str), 1524 (-NO_2 (aromatic), asymstr), 1463 (-C=C, str), 1379 (-C(O)-O-, str), 1145 (-C-O str) cm^{-1}; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ 2.94 (d, 2H, J = 7.6 Hz, -CH-CH_2-O-), 3.82 (m, 1H, -OCH_2-CH-CH_2O-), 4.02 (d, 2H, J = 6.4 Hz, -O-CH_2-CH-), 7.21-7.30 (m, 3H, Ar-H), 7.61 (d, 2H, J = 7.2 Hz), 7.68-7.71 (m, 2H, Ar-H), 8.01 (d, 2H, J = 7.2 Hz, Ar-H), 8.13-8.19 (m, 2H, Ar-H); ^{13}C-NMR (DMSO-d_6, 100.6 MHz) δ 44.1 (C_{18}), 50.8 (C_{17}), 69.8 (C_{15}), 108.5 (C_3), 109.1 (C_5), 116.3 (C_{12}), 118.4 (C_{10}), 123.1 ($C_{6',2'}$), 123.9 (C_8), 125.1 (C_4), 125.7 (C_2), 126.3 (C_{11}), 126.9 (C_9), 128.2 ($C_{3',5'}$), 133.6 (C_7), 136.7 (C_{19}), 139.5 (C_{13}), 148.4 ($C_{4'}$-NO_2), 151.1 (C_6), 155.7 ($C_{1'}$); LC-MS (m/z, %): 403 ($M\text{-}H^+$, 100%).

4-Nitrobenzyl 4-(oxiran-2-ylmethoxy)-9H-carbazole-9-carboxylate (8f):
Light brown solid, Yield 83%. Mol. Wt: 418.12, mp 116-119 ^oC.IR (KBr):3048 (=C-H, str), 2949 (-C-H, str), 1737 (-C=O, str), 1536 (-NO_2 (aromatic), asymstr), 1462 (-C=C, str), 1376 (-C(O)-O-, str), 1143 (-C-O str) cm^{-1}; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ 2.90 (d, 2H, J = 7.6 Hz, -CH-CH_2-O-), 3.88 (m, 1H, -OCH_2-CH-CH_2O-), 4.21 (d, 2H, J = 6.4 Hz, -O-CH_2-CH-), 5.23 (s, 2H, -CH_2-O-Ar), 7.11-7.21 (m, 5H, Ar-H), 7.54 (d, 2H, J = 7.2 Hz), 8.04-8.11 (m, 2H, Ar-H), 8.19 (d, 2H, J = 7.2 Hz, Ar-H); ^{13}C-NMR (DMSO-d_6, 100.6 MHz) δ 43.4 (C_{18}), 49.5 (C_{17}), 64.8 (-C-O), 69.1 (C_{15}), 108.4 (C_3), 108.7 (C_5), 115.1 (C_{12}), 118.6 (C_{10}), 123.6 ($C_{4,8}$), 124.4 (C_2), 124.9 (C_{11}), 125.2 (C_9), 126.2 ($C_{3',5'}$), 130.1 ($C_{2',6'}$), 132.3 (C_7), 141.2 ($C_{1'}$), 141.7 (C_{13}), 145.4 ($C_{4'}$-NO_2), 150.7 (C_6), 152.3 (C_{19}); LC-MS (m/z, %): 417 ($M\text{-}H^+$, 100%).

Bioassay

Antibacterial activity

The antibacterial activity of the synthesized sulfonamides**6(a-d)**and carbamates**8(a-f)**were screened against two gram positive bacteria such as *Staphylococcus aureus* and *Bacillus subtilis*and one gram negative bacteria such as *Escherichia coli* by the agar well diffusion method [32].Two different concentrations (100, 200 µg) of the titled compounds were dissolved in 1 mL of DMF. Centrifuged pellets of bacteria from a 24 h old culture containing approximately 104-106 colony forming unit (CFU) per mL was spread on the surface of Muller Hinton Agar (MHA) plates. Nutrient agar medium was prepared by suspending nutrient agar 20 g in one liter of distilled water (p^H 7.0), autoclaved and cooled to 45 ^oC. Then it was seeded with 10 mL of prepared inoculate to have 106 CFU/mL. Petri dishes were prepared by pouring 75 mL of seeded nutrients agar. Wells were created in medium with the help of a sterile metallic borer and test solution was added. Experimental plates were incubated for 24 h and antibacterial activity was assayed by measuring zones of inhibition in diameter around the well. Ciprofloxacin was used as a standard drug for antibacterial assay. The zone of inhibition of the tested solution was compared with standard. The bacterial assays were performed in triplicate and results are given in **Table-2**.

Table-2 Antibacterial zone of inhibition (mm) of the synthesized sulfonamides (6a-d) and carbamates (8a-f).

Compd	Bacterial culture and zone of inhibition in mm					
	S.aureus		*B.subtilis*		*E. coli*	
	100	200	100	200	100	200
6a	15.6	21.4	14.8	22.1	16.3	21.5
6b	10.6	17.0	12.4	19.7	10.3	18.2
6c	8.4	13.8	8.1	15.4	10.2	14.9
6d	14.7	20.1	15.4	21.6	13.8	20.5
8a	16.5	21.6	14.3	20.6	15.1	20.4
8b	10.8	14.3	11.5	17.4	11.1	15.9
8c	8.8	13.2	13.8	23.5	12.4	18.7
8d	11.4	15.5	11.5	18.7	10.3	16.8
8e	13.7	19.9	14.6	22.3	14.1	21.3
8f	9.7	14.8	10.7	16.6	11.3	16.2
Stand[a]	23.0		25.0		24.0	

Standard - . Ciprofloxacin – tested at 200 µg/mL

Antifungal activity

The antifungal activity of the newly synthesized sulfonamides**6(a-d)**and carbamates**8(a-f)**have been evaluated against three fungal pathogens such as*Aspergillusniger*, *Candicaalbicans*and *Fusariumoxysporium* by the poison plate technique [33]. Test compounds were dissolved in dimethylformamide (DMF) (10 mL) before mixing with Potato Dextrose Agar (PDA, 90 mL). The final concentration of the compounds in the medium was fixed at 200 µg/ mL. Three kinds of fungi were incubated in PDA at 25 ± 1 °C for 5 days to get new mycelium for antifungal assay. Then a mycelia disk of approximately 0.45 cm diameter cut from the culture medium was picked up with a sterilized inoculation needle and inoculated in the center of PDA plate. The inoculated plates were incubated at 25 ± 1°C for 5 days. Acetone in sterilized distilled water served as control, while Fluconazole was used as a standard. The radial growth of the fungal colonies was measured on the sixth day. The *in vitro* inhibiting effects of the test compounds on the fungi were calculated by the formula CV =A-B/A, where **A** represents the diameter of fungi growth on untreated PDA, **B** represents the diameter of fungi on treated PDA and **CV** represents the rate of inhibition. All the experiments were carried out in triplicates and the results were expressed as zone of inhibition in mm and presented in **Table-3**.

Table-3Antifungal zone of inhibition (mm) of the synthesized sulfonamides(6a-d) and carbamates(8a-f).

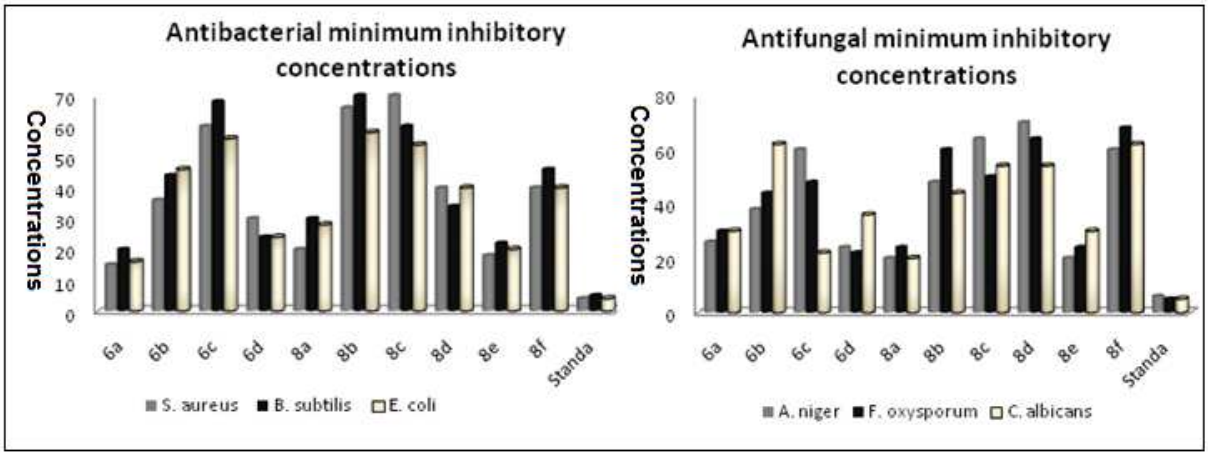
Compd	Fungal culture and zone of inhibition in mm					
	A. niger		*F. oxysporum*		*C. albicans*	
	100	200	100	200	100	200
6a	14.2	20.1	15.3	21.6	13.7	19.9
6b	11.7	18.1	11.1	17.2	9.8	16.5
6c	10.8	15.6	10.2	16.1	14.2	19.1
6d	15.1	20.0	15.2	21.3	12.6	18.7
8a	15.3	21.2	16.7	21.4	15.5	18.6
8b	11.4	16.5	11.2	17.0	10.7	18.2
8c	10.3	17.1	12.5	17.3	10.3	16.4
8d	9.6	14.9	10.1	16.3	12.8	17.9
8e	14.2	20.2	13.6	21.6	13.4	20.6
8f	11.8	16.3	10.7	17.4	10.2	16.4
Stand[a]	22.0		23.0		22.0	

Standard - Fluconazole – tested at 200 µg/mL

Minimum Inhibitory Concentrations:

Micro-broth-dilution method[34] was used for the determination of minimum inhibitory concentration (MIC) of the tested samples.The minimum concentration, at which there was no visually detectable bacterial growth, was taken as MIC.Test compounds concentrations of 0.1-2 µg /mL in steps of 80µg/mL were evaluated. Specifically 0.1 mL of standardized inoculum (1-2 x 10^7 CFU/mL) was added to each test tube. The tubes were incubated aerobically at 37 ^oC for 24 hfor bacterial test samples and 48-72 h for fungal test samples. Control was maintained for each test sample. The lowest concentration (the highest dilution) of test compound that produced no visible signs of bacterial growth (no turbidity) when compared with the control tubes was regarded as MIC(**Graph-1**).

Graph-1 Antibacterial and antifungal minimum inhibitory concentrations (MICs) of sulfonamides (6a-d) and carbamates (8a-f).



Anti oxidant activity:

DPPH radical scavenging activity

The radical in the 1,1-diphenyl-1-picrylhydrazyl (DPPH) gives a strong absorption maximum at 517 nm and is purple in color. The absorbance of DPPH reduces, when the radical of the DPPH becomes paired with an electron or acceptance of the hydrogen radical from the antioxidant. 1 mL of various concentrations of the test compounds (25, 50, 75 and 100 µg/mL) in methanol were prepared and magnetic stirrer was used to make homogeneous solution. After making the desired concentrations, 4 mL of 0.004% (w/v) methanol solution of DPPH was applied on each test tube by using pipette. The room temperature was recorded and the test tube was incubated at 27 ^{o}Cfor 30 min to complete the reaction. The absorbance was read against blank at 517 nm. The percent of inhibition of free radical production from DPPH was calculated by the following equation and presented in **Table-4**.

$$\%\ of\ scavinging = [(A\ control - A\ sample)/A\ control] \times 100$$

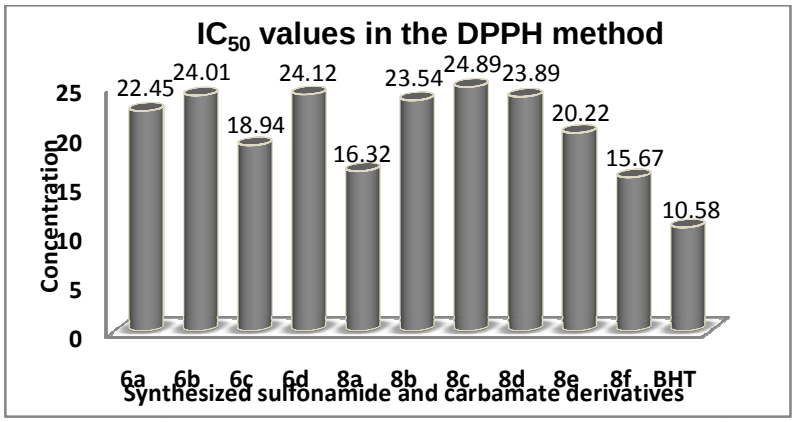
Where A control is the absorbance of the control reaction (containing all reagents except the test compound) and A sample is the absorbance of the test compound. The experiment was carried out in triplicate.

Table-4The *in vitro* antioxidant activity of the synthesized sulfonamides (6a-d) and carbamates(8a-f) in DPPH method.

Comp	Concentration (µg/mL)			
	25	50	75	100
6a	53.57 ± 1.06	63.78 ± 0.87	67.14 ±1.32	71.01 ±1.05
6b	52.74 ± 1.73	58.25 ± 1.02	61.37 ± 0.92	67.81 ± 1.60
6c	64.70 ± 1.44	68.41 ± 1.21	73.84 ±1.56	77.52 ± 0.95
6d	52.34 ± 0.65	59.23 ± 0.89	65.32 ± 1.10	69.42 ± 0.86
8a	68.59 ± 0.26	74.21 ± 0.43	77.85 ± 0.65	81.92 ± 0.70
8b	59.73 ± 1.17	64.48 ± 1.24	68.94 ± 0.88	72.16 ± 0.95
8c	51.42 ± 0.63	58.68 ± 0.85	66.54 ± 0.43	76.41 ± 0.64
8d	54.56 ± 0.81	58.93 ± 0.32	66.74 ± 1.24	70.53 ± 1.30
8e	61.28 ± 1.44	68.82 ± 1.05	72.18 ± 0.42	77.32 ± 0.81
8f	68.19 ± 0.19	72.34 ± 0.95	79.63 ± 0.46	84.34 ± 1.10
BHT	71.42 ± 0.12	77.54 ± 0.38	89.27 ± 0.44	97.12 ± 0.53
Blank	–	–	–	–

(–) Showed no scavenging activity. Values were the means of three replicates ±SD
Butylated hydroxyl toluene (BHT)- Standard

Graph 2.*In vitro* antioxidant IC_{50} values for the synthesized sulfonamide (6a-d) and carbamate (8a-f) derivatives in DPPH method



Nitric oxide (NO) scavenging activity

Nitric oxide scavenging activity was measured by slightly modified methods of Green *et al*. and Marcocci*et al*. Nitric oxide radicals (NO) were generated from sodium nitroprusside. Sodium nitroprusside (1 mL, 10 mM) and 1.5 mL of phosphate buffer saline (0.2 M, pH 7.4) were added to different concentrations (25, 50, 75 and 100 µg/mL) of the test compounds and incubated for 150 min at 25^{o}C and 1 mL of the reaction mixture was treated with 1 mL of Griess reagent (1% sulfanilamide, 2% H_3PO_4 and 0.1% naphthylethylenediaminedihydrochloride). The absorbance of the chromatophore was measured at 546 nm. Butylated hydroxyl toluene was used as standard. Nitric oxide scavenging activity was calculated by the following equation and presented in **Table-5**.

$$\%\ of\ scavinging = [(A\ control - A\ sample)/A\ control] \times 100$$

Where A control is the absorbance of the control reaction (containing all reagents except the test compound) and A sample is the absorbance of the test compound. The experiment was carried in triplicate.

Table-5The *in vitro* antioxidant activity of the synthesized sulfonamides (6a-d) and carbamates(8a-f) in nitric oxide (NO) method.

Compd	Concentration (µg/mL)			
	25	50	75	100
6a	47.26 ± 0.88	59.84 ± 1.07	65.14 ± 1.41	69.93 ± 1.27
6b	50.54 ± 0.79	55.58 ± 0.34	61.27 ± 0.87	66.56 ± 1.10
6c	68.39 ± 0.90	70.61 ± 1.39	74.18 ± 0.95	79.42 ± 1.21
6d	49.23 ± 0.76	55.24 ± 0.45	59.78 ± 1.01	64.87 ± 0.79
8a	71.84 ± 0.17	76.29 ± 0.35	79.65 ± 0.54	86.23 ± 1.34
8b	55.46 ± 0.41	61.13 ± 0.56	66.32 ± 1.78	70.89 ± 0.10
8c	56.68 ± 0.54	60.34 ± 0.39	65.67 ± 1.02	69.54 ± 0.21
8d	52.23 ± 1.03	57.87 ± 0.86	61.43 ± 0.67	66.53 ± 0.51
8e	61.64 ± 1.39	64.49 ± 1.24	69.03 ± 0.71	72.28 ± 1.08
8f	65.15 ± 0.58	69.39 ± 0.65	72.26 ± 0.10	79.76 ± 0.72
BHT	73.72 ± 0.18	81.96 ± 0.36	89.32± 0.52	96.41 ± 0.69
Blank	–	–	–	–

(–) Showed no scavenging activity. Values were the means of three replicates ±SD
Butylated hydroxyl toluene (BHT)- Standard

RESULTS AND DISCUSSION

Chemistry. The starting material, 4-(oxiran-2-ylmethoxy)-9*H*-carbazole(**3)**was used in the direct substitution reaction with various substituted phenyl/aliphaticsulfonylchlorides**5(a-d)**and substituted phenyl/aliphatic chloroformates**7(a-f)** in THF using NaH as a strong base at 5 ^{o}C to 40 ^{o}C to afford 9-(substituted phenyl/aliphatic sulfonyl)-4-(oxiran-2-ylmethoxy)-9*H*-carbazoles**6(a-d)** and substituted phenyl/aliphatic-4-(oxiran-2-ylmethoxy)-9*H*-carbazole-9-carboxylates**8(a-f)** respectively. Progress of the reaction was monitored by TLC using ethyl acetate and hexane (1:2). After completion of the reaction, the NaCl was filtered off and the solvent was removed in a rotaevaporator. The crude products obtained were purified by recrystallization from ethanol. The yields of the titled compounds are in the range of 80-91%.

Structures of the titled sulfonamide **6(a-d)** and carbamate**8(a-f)**derivatives were confirmed by IR, ^{1}H, ^{13}C NMR, mass and elemental analysis data and presented in the experimental part. In IR spectra of the titled compounds, the disappearance of intensive band at 3340 for –N-H str in the starting material **3** andappearance of the intensive bands in the region of 1310-1375 cm^{-1} for the -SO_2 asymmetric stretching, 1085-1135 cm^{-1} for the –SO_2 symmetric stretching were observed in the compounds **6(a-d).** The compounds **8(a-f)**showed strong bands in the ranges of 1690-1760 and 1120-1185 cm^{-1} corresponding to -C=O and –C-O str respectively. Appearance of these bands confirmed the formation of sulfonamide and carbamate derivatives. In ^{1}H NMR spectra of the title compounds, the disappearance of the chemical shift value at 10.7 ppm for carbazole–NH proton of the starting material and the chemical shift values observed in the region of 6.5-8.6 ppm for the aromatic protons confirmed the formation of synthesized compounds. Further, the observed chemical shift values of the corresponding carbons of the titled compounds in ^{13}C NMR spectra and molecular and fragmented ion peaks in the mass spectra have given further evidence for the structural elucidation of the compounds.

Pharmacology. All the newly synthesized compounds were evaluated for their antibacterial activity against *Staphylococcus aureus*, *Bacillus subtilis* and *Escherichia coli* using agar well diffusion method [32], antifungal activity against *Aspergillusniger*, *Fusarium oxysporum and Candida albicans*using the poison plate technique method [33]. Minimum inhibitory concentrations were also determined using micro-broth dilution method [34] and antioxidant activity using DPPH [35] and –NO method [36]. Ciprofloxacin, Fluconazole and BHT drugs were used as standards for antibacterial, antifungal and antioxidant activities respectively. The results of the antibacterial and antifungal activities are tabulated in **Table-2** and **Table-3** respectively and MICs arerepresented in **Graph-1**. Antioxidant data are presented in **Table-4** for DPPH method and **Table-5** for NO method and IC_{50} values are shown in **Graph-2**.

The antimicrobial data revealed that majority of the titled compounds exhibited good antibacterial and antifungal activities, where as compounds **6a**, **6d**, **8a** and **8e** showed excellent antibacterial and antifungal activity against tested strains at lower minimum inhibitory concentrations. Likewise, compound **6b** exhibited good activity against *E. coli*, compound **8c** showed potent activity against *B. subtilis* and the compound **6c** showed high activity against *C. albicans*. The data indicated that a change in the substituent might be affected the antimicrobial activity of the synthesized compounds **6(a-d)** and **8(a-f)**. Among the synthesized compounds, the functional groups such as *p*-NO_2 in **6a** and **8e**, *p*-Cl-*m*-NO_2 in **6c**against *C. albicans*, *p*-Br in **6b**against *E. coli*, *p*-F-*m*-Cl in **6d**, CCl_3 in **8a** and isobutyl in **8c** against *B. subtilis* might be responsible for good activity. Further, the antioxidant activity data disclosed that all the compounds showed moderate to good activity. Compounds **6c**, **8a** and **8f** showed potent antioxidant activity in two methods. The presence of strong electron withdrawing groups such as –NO_2, -Cl in **6c** and –CCl_3 in **8a**, –NO_2 in **8f** might be the cause to exhibit enhanced antioxidant activity.

CONCLUSION

In summary, a series of carbazole-based (carazolol intermediate) sulfonamide and carbamate derivatives were designed and synthesized in high yields. Antimicrobial and antioxidant activities of the titled compounds were evaluated. The biological data showed that compounds **6a**, **6d**, **8a** and **8e** showed excellent antibacterial and antifungal activitiesagainst tested strains at lower minimum inhibitory concentrations and compound **6b** exhibited good activity against *E. coli*, compound **8c** showed potent activity against *B. subtilis* and the compound **6c** showed high activity against *C. albicans*. The compounds **6c**, **8a** and **8f** showed potent antioxidant activity. In overall, the titled compounds efficiently worked as antimicrobial agents. The results paved the way for investigation of new potential lead compounds in the study of antimicrobial agents.

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