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SYNTHESIS AND ANTIMICROBIAL ACTIVITIES OF NOVEL 1,3,4-THIADIAZOLE BEARING CARBOXAMIDES DERIVATIVES

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ABSTRACT:

A novel series of [(5-{[4-(acetylamino) phenoxy] methyl}-1,3,4-thiadiazol-2-yl)sulfanyl] N-substituted 2-acetamide & 2/3-propanamide have been synthesized by condensation of sodium salts ofN-{4-[(5-sulfanyl-1,3,4-thiadiazole-2-yl)methoxy]phenyl} acetamide with differently substituted carboxamidesunder Schotten-Baumann reaction conditions. The structures of all the derivatives were confirmed by spectral techniques like IR, 1H NMR and mass spectroscopy. All the derivatives were screened for antibacterial and antifungal activity studies. Compounds bearing electron withdrawing substituents showed significant activity comparable with that of the standard drugs

Keywords: 1,3,4-thiadiazole; carboxamides; antibacterial; antifungal activity.

Introduction

Five-membered 1,3,4-thiadiazole heterocyclic ring has received considerable attention because of its unique bioisosteric properties and an unusually wide spectrum of biological activities.Inductive effect of sulfur makes 1,3,4-thiadiazole a very weak base and have comparatively high aromatic property.[1] Members of this ring system have found their way in to such diverse applications as pharmaceuticals, oxidation inhibitors, cyanide dyes, metal complexing agents. During recent years there has been intense investigation of different classes of thiadiazole compounds, many of which known to possess interesting biological properties.Acetazolimide containing 1,3,4-thiadiazole nucleus is the well known carbonic anhydrase inhibitor used in glaucoma,[2] epileptic seizures,[3] hemiplegic migraine[4] etc. Thiadiazole derivatives with significant biological activities are reported in literature. Some 1,3,4-thiadiazole derivatives displays diverse pharmacological activities including antimicrobial,[5] anti-cancer,[6] antifungal,[7] antituberculosis[8], local anaesthetic[9],antiglaucoma[10], anticonvulsant[11], anti-inflammatory[12], antidepressant and anxiolytic[13], antihypertensive[14], antiviral[15], and antioxidant[16] activity.More than 1400 different species of microorganisms are reported in literature up to now which includes bacteria, fungi, viruses, protozoa and helminthes affecting human being which often results in death. Interestingly, only 20 of them (mostly bacteria) accounts for around two thirds of the casualties.[17] Although highly developed countries experiencing fall in death from 16 million in 1990 to approximately 15 million and forecasting

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13 million in 2050, death rate is still high in developing countries because of tuberculosis, pneumonia, malaria, HIV/AIDS, diarrhea and many other diseases.[18-19] Considering the recent pandemic because of COVID-19 and similar pandemic threat in future and issue of raising antibiotics resistance, discovering new effective antibacterial/antiviral drugs and the development of modern therapies are two challenges of top importance.

Hence, considering the biological potential of 1,3,4-thiadiazole and in search of new antibacterial we have planned to condense 1,3,4 thiadiazole moiety with differently substituted carboxamides and screen them for antibacterial and antifungal activities.

Result and Discussion

Chemistry

The synthetic routes for targeted structures are shown in (**Scheme I**&**II**).Ethyl-4-acetamido phenoxy acetate**(5)**obtained by reacting p-acetamido phenol **(4)**with ethylbromoacetate which when refluxed with hydrazine hydrate afforded N-[4-(hydrazinyl methoxy) phenyl] acetamide**(6).** Compound **(7)** was obtained from the reaction of N-[4-(hydrazinyl methoxy) phenyl] acetamide **(6)** with carbon disulfide in basic media in good yield. Compound (**7)** on treatmentwith cold concentrated H_2SO_4 afforded compound **(8)**.

Starting thiol (**8**)was converted to the corresponding sodium salt and the resultant salt was subjected for *Schotten-Baumann* reaction upon an addition of various N-substituted chloroacetamides, α-chloropropionamides and β-chloropropionamides in water. The reaction was carried out at 60-70 ^{0}C for 36 hours and yielded desired structures (**9, 10 & 11**) respectively.IR absorption bands at 3320 cm^{-1} (N-H), 2459 cm^{-1} (S-H), 2949 cm^{-1} (C-H) and 1535 cm^{-1} (C-N str) confirms the structure of N-{4-[(5-sulfanyl-1,3,4-thiadiazole-2-yl)methoxy]phenyl} acetamide (**8**). Being acidic nature hydrogen of SH can be easily substituted in basic reaction conditions. Formation of 2- & 3- [(5-{[4 (acetylamino) phenoxy] methyl}-1,3,4-thiadiazol-2-yl)sulfanyl] N-substituted acetamide & propanamide(**9, 10 &11**) was confirmed by recording their IR, ^{1}H NMR and mass spectra. IR spectrum of thiadiazole (**9a**) displayed absorption at 3430cm^{-1}owing to N-H stretching of amide, absorption band at 3110cm^{-1}attributed to aromatic stretching and broad absorption stretching at 1640 cm^{-1}appeared because of amide carbonyl group (C=O).

The ^{1}H NMR spectrum of **9a**displayed multiplet in the region of δ, 6.80–7.6attributed to aromatic proton, two singlet for two amide protons (-CONH) were observed in the region of δ, 9.9 and δ, 10.01 respectively. Similarly singlet of two protons in the region of δ, 3.50 corresponding to $–CH_2$ of acetamide, a singlet at δ, 2.2corresponding to three protons of the methyl group and a singlet of two methylene proton ($O-CH_2$) in the region of δ, 5.2were recorded.The mass spectrum of **8a** showed molecular ion peak at m/z 415.48$(M+1)^+$ which is in agreement with the molecular formula $C_{19}H_{18}N_4O_3S_2$. Similarly the spectral values for all the compounds and C, H, N analyses are given in the experimental part.

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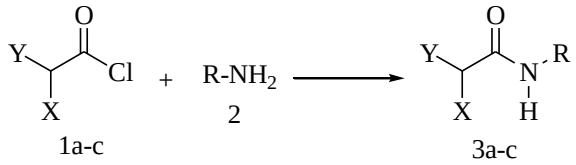
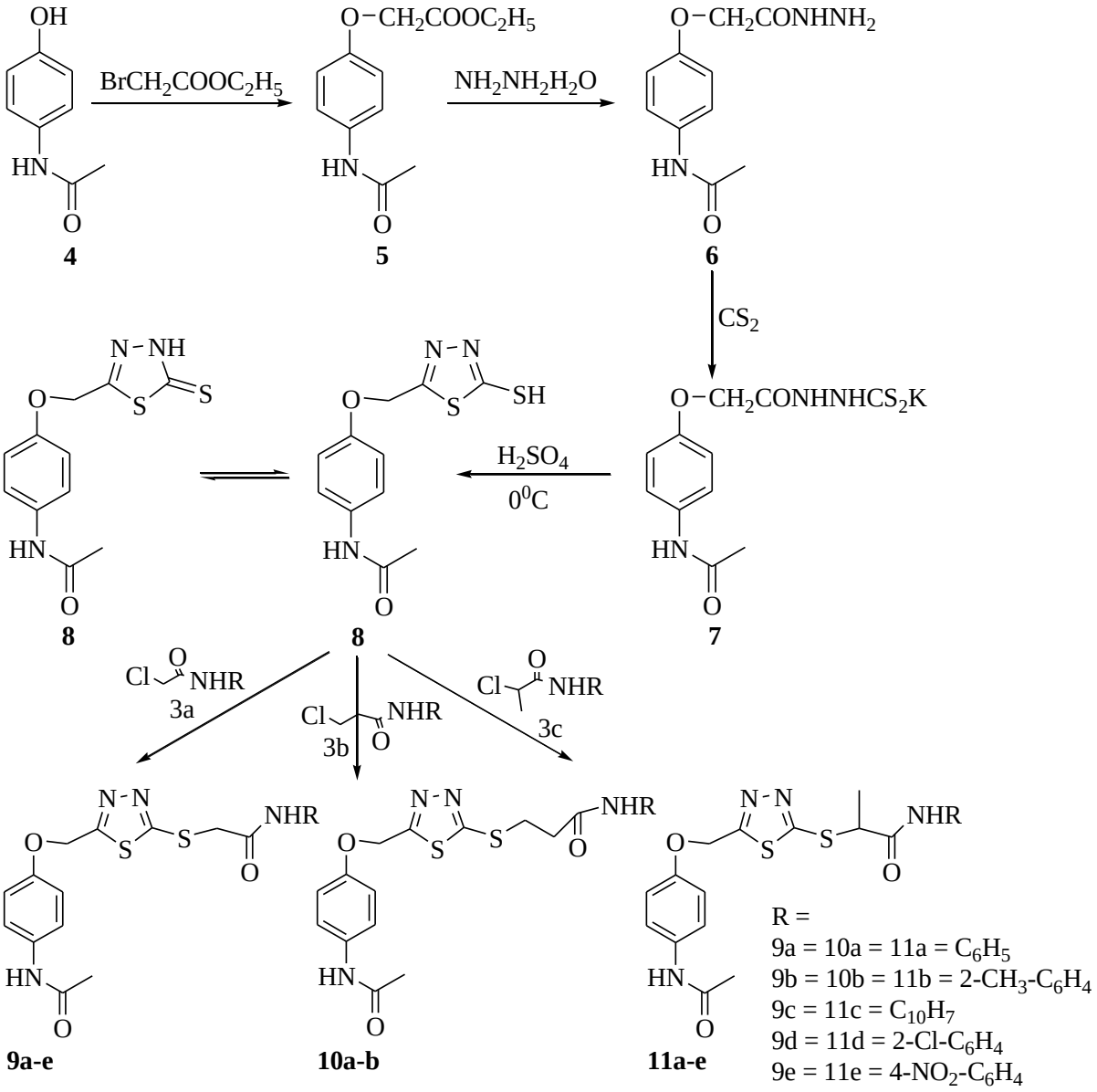


1a=Chloroacetamide; (3a); X=H, Y=-Cl
1b=beta-chloropropionamide; (3b); X=H, Y=-CH_2Cl
1c=alpha-chloropropionamide; (3c); X=-CH_3, Y=-Cl

Reaction Scheme-I



Reaction Scheme-II

Antibacterial and antifungal activity

All the newly synthesized compounds (**9**,**10**,and **11)** were evaluated for antibacterial activity against pathogenic bacteria *Staphylococcus aureus* (gram positive) and *Escherichia coli* (gram

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negative)and for antifungal activity against the two fungi namely *Aspergillus flavus* and *Candida albicans*using minimum inhibitory concentration (MIC) by the serial dilution method. The results of antibacterial activity are provided in Table 1.Most of the compounds exhibited significant antibacterial activity comparable with that of standard drug Norfloxacin. Among the compounds tested, **9d**, **9e**, **11d** and **11e** displayedpromisingantibacterial activity comparable with that of standard drug. The higher activity of the title compounds**9d**, **9e**, **11d** and **11e**could be attributed to the presence of the electron-withdrawing groups such as $–NO_2$ and –Cl. Compound **9a** also exhibited satisfactory antibacterial activity. Antifungal activity was carried out using Fluconazole as the standard. The results of antifungal activity data are also shown inTable 1. Interestingly same pattern for antifungal activity was observed. Compounds bearing electron withdrawing substituents (**9d**, **9e**, **11d** and **11e**) were found to display higher activity and comparable with standard drug.

Experimental

Precoated silica gel plates (Merk, Darmstadt, Germany) were used to check completion of reaction and to check homogeneity of compounds by using solvent system chloroform: methanol (8:2). Visualization was done against UV lamp. Melting points were checked by open capillary tubes and are uncorrected. Shimadzu-8400 FTIR spectrophotometer was used to record IR spectra and Bruker spectrometer was used to record ^{1}H NMR spectra. Elemental analysis was done by Perkin-Elmer 2400 CHN analyzer. Mass spectra were recorded on Shimadzu LCMS spectrometer.All the chemicals were procuredfrom Sigma-Aldrich and SD Fine chemicals.

General procedure for the synthesis of N-substituted-carboxamides, 3a-c

Chloroacetyl chloride (1.16 mol) was dissolved in benzene and p-Chloro aniline (0.8 mol) was suspended in resultant solution. The mixture was held on reflux and checked for complete evaporation of hydrogen chloride gas. After evaporation of solvent under diminished pressure residual material of chloroacetamide (**3a**) resulted was cooled and recrystallized from 70 % ethanol. In the same way, various N-substituted β-chloropropionamides (**3b**) and α-chloropropionamides (**3c**) were synthesized by condensing different aromatic amines with 3-chloropropanoyl chloride and 2-chloropropanoyl chloride respectively.[20]

Practical procedures

Synthesis of ethyl-4-acetamido phenoxy acetate, 5

A mixture of p-acetamido phenol (**4**) (0.01 mol) & ethylbromoacetate (0.01 mol) was refluxed by using dry acetone in presence of anhydrous potassium carbonate (K_2CO_3) for 6 h. The reaction mixture was cooled & then poured into crushed ice.[21] The solid product obtained (**5**) was filtered, dried & recrystallized using absolute ethanol. Yield 56%, m.p. 98-100 °C.Yellow solid, TLC: R_f value: 0.68 (Ethyl acetate: chloroform, 3:2).

Synthesis of N-[4-(hydrazinyl methoxy) phenyl] acetamide,6

The ethyl-4-acetamido phenoxy acetate (**5**)(0.01 mol) & hydrazine hydrate (0.01mol) was refluxed in the presence of chloroform for 5 h. The reaction mixture was cooled & then poured in to crushed ice. The solid product (**6**) formed, was filtered, dried & recrystallized using absolute ethanol.[21]Yield 84%, m.p. 197-199 °C.

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Synthesis of {[2-({[4-(acetylamino) phenoxy] acetyl} oxy) hydrazinyl] (disulfeniumyl) methyl} potassium, 7

A three-necked 250 ml flask fitted with a thermometer, dropping funnel & a magnetic stirring bar was charged with KOH (6.1 gm, 0.09 mol), anhydrous ethanol (120 ml) & N-[4-(hydrazinyl ethoxy)phenyl]acetamide (**6**) (14.6 gm). The mixture was stirred to obtain a homogeneous solution & then CS_2 (6.9 gm) was slowly added through a dropping funnel. The reaction system was stirred at room temperature for an additional 6 h, filtered and resulting solid was used for the next step without further purification[22]. White crystals, yield 94%, m.p. 118-120 °C.

Procedure for synthesis N-{4-[(5-sulfanyl-1,3,4-thiadiazole-2-yl)methoxy]phenyl} acetamide,8

A three-necked 250 ml flask fitted with a thermometer, dropping funnel & a magnetic stirring bar was first charged with sulfuric acid (80 ml, 98%) and then cooled on ice bath with vigorous stirring. When the temperature reached below -2 ^{0}C, N-[4-(hydrazinyl methoxy) phenyl] acetamide (**7**)(22.9 g, 0.08 mol) was slowly added into it. After completion of the addition, the reaction mixture was kept below 0 °C and stirred for another 5 h. The mixture was poured into ice water (200 ml) when upon a large amount of white solid precipitated which was separated by suction filtration. The cake was dissolved in 10% aqueous NaOH and the insoluble part was removed through filtration. The filtrate was acidified by HCl (36%) to a pH of 2. The resulting white solid was filtered, washed with water and recrystallized from ethanol to yield 14.6g of (**8**)as white crystals[22] yield 81%, m.p. 220-222 °C.TLC: R_f value - 0.64 (Ethyl acetate: chloroform, 1:1). IR (KBr cm^{-1}): 3320.82, 3131.83, 3050.83, 2981.41, 2549.83, 1565.77 cm^{-1}

General procedure for the synthesis of 2- & 3- [(5-{[4 (acetylamino) phenoxy] methyl}-1,3,4-thiadiazol-2-yl)sulfanyl] N-substituted acetamide & propanamide, 9, 10 & 11

To a cool solution of metallic sodium (0.025 mol) in an absolute ethanol; N- {4-[(5-sulfanyl-1,3,4-thiadiazole-2-yl) methoxy] phenyl} acetamide (**8**) (0.025mol) was added with stirring, at about 15 ^{0}C. The solution was filtered. The excess of solvent was removed by heating on water bath and cold water was added to get a clear solution. The solution was again filtered to remove suspended particles. The N-substituted chloroacetamide (**3a**), β-chloropropionamides (**3b**) or α-chloropropionamides (**3c**) (0.025mol) was added in small portion at room temperature over 3 h. with stirring, stirring was continued between 60 to 65 ^{0}C for 24 h. The solid get precipitated out in between the stirring after 24 h. The mixture kept at room temperature for two to three hours. The resultant precipitate was filtered and product collected on Whatman filter paper, dried & recrystallized from absolute ethanol.[23]

2-(5-((4-acetamidophenoxy)methyl)-1,3,4-thiadiazol-2-ylthio)-N-phenylacetamide, 9a:m.p. 140-142 °C. Yield: 64%. IR (KBr): 3430 (N-H), 3110 (Ar-H), 1640 (C=O), 1545 (C=N); ^{1}H NMR: δ 10.01 (s, 1H, NH), 6.8-7.6 (m, 9H, Ar-H), 5.22 (s, 2H, O-CH_2), 3.50 (s, 2H, S-CH_2), 2.21 (s, 3H, CH_3); MS: *m/z* $(M+1)^+$415.48. Anal. Calcd for $C_{19}H_{18}N_4O_3S_2$: C 55.01; H 4.38; N 12.98.Found: C 55.05; H 4.38; N 13.20.

2-(5-((4-acetamidophenoxy)methyl)-1,3,4-thiadiazol-2-ylthio)-N-o-tolylacetamide, 9b:m.p. 205-207 °C. Yield: 68%. IR (KBr): 3580 (N-H), 3130 (Ar-H), 1650 (C=O), 1i70 (C-N str); ^{1}H

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NMR: δ 9.90 (s, 1H, NH), 6.9-7.8(m, 9H, Ar-H), 5.20 (s, 2H, O-CH_2), 3.60 (s, 2H, S-CH_2), 2.60 (s, 3H, CH_3), 2.00 (s, 3H, CH_3); MS: *m/z*$(M+2)^+$434.02. Anal. Calcd for $C_{20}H_{20}N_4O_3S_2$: C 56.02; H 4.52; N 13.56. Found: C 56.07; H 4.70; N 13.70.

2-(5-((4-acetamidophenoxy)methyl)-1,3,4-thiadiazol-2-ylthio)-N-(naphthalen-1-yl) acetamide, 9c:m.p. 158-160 °C. Yield: 74%. IR (KBr): 3390 (N-H), 3137 (Ar-H), 1665 (C=O), 1195 (C-N str); ^{1}H NMR: δ 9.80 (s, 1H, NH), 6.8-7.8 (m, 9H, Ar-H), 5.30 (s, 2H, O-CH_2), 3.60 (s, 2H, S-CH_2), 2.10 (s, 3H, CH_3); MS: *m/z*$(M+1)^+$412.07. Anal. Calcd for $C_{23}H_{20}N_4O_3S_2$: C 59.06; H 4.34; N 12.06. Found: C 59.46; H 4.70; N 13.70.

2-(5-((4-acetamidophenoxy)methyl)-1,3,4-thiadiazol-2-ylthio)-N-(2-chlorophenyl) acetamide, 9d:m.p. 218-220 °C. Yield: 63%. IR (KBr): 3350 (N-H), 2910 (Ar-H), 1663 (C=O), 1175 (C-N str); ^{1}H NMR: δ 9.90 (s, 1H, NH), 6.9-7.9 (m, 9H, Ar-H), 5.30 (s, 2H, O-CH_2), 3.60 (s, 2H, S-CH_2), 2.10 (s, 3H, CH_3); MS: *m/z* $(M+1)^+$413.10. Anal. Calcd for $C_{19}H_{17}ClN_4O_3S_2$: C 50.15; H 3.65; N 12.08. Found: C 50.83; H 3.86; N 12.48.

2-(5-((4-acetamidophenoxy)methyl)-1,3,4-thiadiazol-2-ylthio)-N-(4-nitrophenyl)acetamide, 9e:m.p. 132-134 °C. Yield: 61%. IR (KBr): 3361 (N-H), 3130 (Ar-H), 1661 (C=O), 1180 (C-N str); ^{1}H NMR: δ 9.70 (s, 1H, NH), 6.9-8.3 (m, 9H, Ar-H), 5.30 (s, 2H, O-CH_2), 3.60 (s, 2H, S-CH_2), 2.10 (s, 3H, CH_3); MS: *m/z*$(M+2)^+$ 448.02. Anal. Calcd for $C_{19}H_{17}N_5O_5S_2$: C 49.18; H 3.40; N 15.06. Found: C 49.66; H 3.73; N 15.24.

3-(5-((4-acetamidophenoxy)methyl)-1,3,4-thiadiazol-2-ylthio)-N-phenylpropanamide, 10a:m.p. 186-188 °C. Yield: 61%. IR (KBr): 3321 (N-H), 2922 (Ar-H), 1717 (C=O), 1178 (C-N str); ^{1}H NMR: δ 9.90 (s, 1H, NH), 6.8-7.5 (m, 9H, Ar-H), 5.20 (s, 2H, O-CH_2), 3.1 (t, 2H, CH_2),2.2 (t, 2H, CH_2), 2.1 (s, 3H, CH_3); MS: *m/z*$(M+1)^+$ 427.01. Anal. Calcd for $C_{20}H_{20}N_4O_3S_2$: C 55.21; H 4.89; N 12.33. Found: C 55.99; H 5.01; N 12.66.

3-(5-((4-acetamidophenoxy)methyl)-1,3,4-thiadiazol-2-ylthio)-N-o-tolylpropanamide, 10b:m.p. 260-262 °C. Yield: 60%. IR (KBr): 3380 (N-H), 3137 (Ar-H), 1654 (C=O), 1122 (C-N str); ^{1}H NMR: δ 9.90 (s, 1H, NH), 6.9-7.6(m, 9H, Ar-H), 5.20 (s, 2H, O-CH_2), 3.3 (t, 2H, CH_2),2.3 (t, 2H, CH_2), 2.1 (s, 3H, CH_3),; MS: *m/z* $(M+1)^+$ 413.03. Anal. Calcd for $C_{21}H_{22}N_4O_3S_2$: C 55.66; H 4.65; N 12.92. Found: C 56.06; H 4.70; N 13.06.

2-(5-((4-acetamidophenoxy)methyl)-1,3,4-thiadiazol-2-ylthio)-N-phenylpropanamide, 11a:m.p. 186-186 °C. Yield: 59%. IR (KBr): 3324 (N-H), 3131 (Ar-H), 1662 (C=O), 1178 (C-N str); ^{1}H NMR: δ 9.94 (s, 1H, NH), 6.8-7.7 (m, 9H, Ar-H), 5.30 (s, 2H, O-CH_2), 3.5 (d, 1H, CH),2.00 (s, 3H, CH_3), 1.3 (m, 3H, CH_3),; MS: *m/z*$(M+2)^+$ 448.01. Anal. Calcd for $C_{20}H_{20}N_4O_3S_2$: C 55.84; H 4.60; N 12.96. Found: C 56.06; H 4.70; N 13.07.

2-(5-((4-acetamidophenoxy)methyl)-1,3,4-thiadiazol-2-ylthio)-N-o-tolylpropanamide, 11b:m.p. 188-190 °C. Yield: 83%. IR (KBr): 3248 (N-H), 3059 (Ar-H), 1657 (C=O), 1117 (C-N str); ^{1}H NMR: δ 9.94 (s, 1H, NH), 6.6-7.8 (m, 9H, Ar-H), 5.20 (s, 2H, O-CH_2), 3.5 (d, 1H, CH),2.6 (m, 3H, CH_3), 2.10 (s, 3H, CH_3), 1.2 (m, 3H, CH_3); MS: *m/z*$(M+1)^+$ 427.01. Anal. Calcd for $C_{21}H_{22}N_4O_3S_2$: C 56.24; H 4.90; N 12.14. Found: C 56.99; H 5.01; N 12.66.

2-(5-((4-acetamidophenoxy)methyl)-1,3,4-thiadiazol-2-ylthio)-N-(naphthalen-1-yl) propanamide, 11c:m.p. 144-146 °C. Yield: 62%. IR (KBr): 3295 (N-H), 3137 (Ar-H), 1655

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(C=O), 1181 (C-N str); ^{1}H NMR: δ 9.80 (s, 1H, NH), 6.6-7.8 (m, 9H, Ar-H), 5.20 (s, 2H, O-CH_2), 3.6 (d, 1H, CH),2.10 (s, 3H, CH_3), 1.3 (m, 3H, CH_3),; MS: *m/z* $(M+1)^+$479.28. Anal. Calcd for $C_{24}H_{22}N_4O_3S_2$: C 60.01; H 4.43; N 11.41. Found: C 60.23; H 4.63; N 11.71.

2-(5-((4-acetamidophenoxy)methyl)-1,3,4-thiadiazol-2-ylthio)-N-(2-chlorophenyl) propanamide, 11d:m.p. 120-222 °C. Yield: 64%. IR (KBr): 3305 (N-H), 3134 (Ar-H), 1661 (C=O), 1116 (C-N str); ^{1}H NMR: δ 10.00 (s, 1H, NH), 6.7-8.4 (m, 9H, Ar-H), 5.20 (s, 2H, O-CH_2), 3.5 (d, 1H, CH),2.10 (s, 3H, CH_3), 1.2 (m, 3H, CH_3); MS: *m/z* $(M+1)^+$463.97. Anal. Calcd for $C_{20}H_{19}ClN_4O_3S_2$: C 51.22; H 4.02; N 11.90. Found: C 51.89; H 4.14; N 12.10.

2-(5-((4-acetamidophenoxy)methyl)-1,3,4-thiadiazol-2-ylthio)-N-(4-nitrophenyl) propanamide, 11e:m.p. 198-200 °C. Yield: 58%. IR (KBr): 3361 (N-H), 3115 (Ar-H), 1615 (C=O), 1180 (C-N str); ^{1}H NMR: δ 9.90 (s, 1H, NH), 6.8-8.3 (m, 9H, Ar-H), 5.20 (s, 2H, O-CH_2), 3.5 (d, 1H, CH),2.00 (s, 3H, CH_3), 1.2 (m, 3H, CH_3),; MS: *m/z* $(M+1)^+$474.52. Anal. Calcd for $C_{20}H_{19}ClN_4O_3S_2$: C 50.10; H 3.94; N 14.58. Found: C 50.73; H 4.03; N 14.79.

Antimicrobial activity

Antibacterial and antifungal activities of the entire synthesized compound were evaluated by using minimum inhibitory concentration (MIC)[24] by the serial dilution method[25]. The MIC value expresses the highest dilution of the antibiotic with clear fluid devoid of turbidity. To determine MIC of the antibiotic for the organism, the antibiotic is serially diluted in broth,added a standard drop of the culture prepared for the assay to each of the antibiotic dilutions and incubated for 16–18 h at 37°C. Norfloxacin was used as standard drug and antibacterial screening was done against pathogenic bacteria *Staphylococcus aureus* (gram positive) and *Escherichia coli* (gram negative). Stock solution (1000µg/Ml) of the test compound was prepared by dissolving in dimethylformamide (5 mL). Into 5 mL of nutrient broth 18 h broth culture was inoculated and incubated for 4h at 37°C. An assay was prepared by diluting with labeled test tubes 1–11. An aliquot having 0.5 mL of stock solution test compound was added to the first tube. Mixed well and 0.5 mL of this solution was transferred into second tube. This process was repeated serially to obtain the quantities indicated in each of the test tubes. The eleventh test tube was taken as growth control. A sterilized Pasteur pipette was used to transfer a drop of diluted broth culture of the test organism (0.5 mL) into all the tubes. All the solutions after mixing gently wereincubated for 16–18 h. at 37°C.Minimum inhibitory concentration (MIC) values obtained are tabulated in Table 1. As above same manner antifungal activity of all the synthesized compounds was carried out against fungi*Aspergillus flavus* and *Candida albicans* using Fluconazole as the standard. Data of the activity is provided in Table 1.

Table 1. Antibacterial and antifungal activities of synthesized compound 9, 10, 11

Comp	R	MIC values (µg/ml)			
		Antibacterial activity		Antifungal activity	
		Staphylococcus aureus	*Escherichia coli*	*Candida albicans*	*Aspergillus flavus*
9a	C_6H_5	11.5	11.5	12.25	12.25
9b	o-CH_3-C_6H_4	12.5	12.5	12.5	12.5

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9c	Napthyl	11.5	11.5	11.5	11.5
9d	o-Cl-C_6H_4	7.5	7.5	7.5	7.5
9e	p-NO_2-C_6H_4	6.25	6.25	6.25	6.25
10a	C_6H_5	8.25	8.25	8.25	8.25
10b	o-CH_3-C_6H_4	12.25	12.25	12.25	12.25
11a	C_6H_5	11.5	11.5	11.25	11.25
11b	o-CH_3-C_6H_4	12.0	12.0	12.0	12.0
11c	Napthyl	11.25	11.25	11.25	11.25
11d	o-Cl-C_6H_4	7.25	7.25	7.25	7.25
11e	p-NO_2-C_6H_4	6.25	6.25	6.50	6.50
Norfloxacin	-	3.50	3.50	-	-
Fluconazole	-	-	-	3.25	3.25

Conclusion

The 2- & 3- [(5-{[4 (acetylamino) phenoxy] methyl}-1,3,4-thiadiazol-2-yl)sulfanyl] N-substituted-2-acetamide/2-propanamide/3-propanamide derivatives were synthesized by condensing differently substituted carboxamides with thiadiazole nucleus through sulfur under *Schotten-Baumann* reaction condition. All the derivatives were characterized on the basis of their melting point, IR, 1H NMR and mass spectroscopy and tested for their antibacterial and antifungal activities. Among the present series the compound **9e** exhibited highest antimicrobial activity with MIC value (6.25 (µg/ml). The results of the study indicated that derivatives bearing electron withdrawing substituents were more potent than others.

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