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RESEARCH ARTICLE

Synthesis and *In Vitro* Antibacterial Activity of Nitrogen and Sulphur Containing Thiadiazole Derivatives

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ABSTRACT

Thiadiazole and Triazoles heterocyclic compounds were reported with wide range of biological activities. Hence it was planned to synthesize and screen for their antibacterial and antifungal (*in vitro*) activity. Azoles like Thiadiazole and Triazoles have been reported to play an important role as antibacterial, antifungal and anti-inflammatory activity. 2-(2-benzyl-4-chlorophenoxy) acetohydrazide derivatives were synthesized and screened for antibacterial activity and antifungal activity. Some thiadiazole like 2-[(2-benzyl-4-chlorophenoxy) methyl]-5-(4-Nitrophenyl)-1, 3, 4-thiadiazole (BA) and 2-[(2-benzyl-4-chlorophenoxy) methyl]-5-(4-Flurophenyl)-1, 3, 4-thiadiazole (BB) etc. were synthesized by a sequence of reactions starting from Con.H_2SO_4 and 2-[(2-benzyl-4-chlorophenoxy) acetyl]-N-(4-Nitrophenyl) hydrazine carbothioamide (AA) and 2-[(2-benzyl-4-chlorophenoxy) acetyl]-N-(4-flurophenyl) hydrazine carbothioamide(AB). The antibacterial and antifungal activities of carbothioamide derivatives, was tested by disc diffusion method (Mueller Hinton Agar (M173) medium). All the compounds tested against bacteria showed comparable or less antibacterial activities than the reference drug. Differences in their activity depend on the substitution of different groups. More specifically, best antibacterial activity & antifungal activity among synthetic analogues was shown by compound AA, AB, AC, BA, BB, and BC, possess very good activity against *Staphylococcus aureus*, Gram negative *Escherichia coli, and Pseudomonas aeruginosa* with Gentamycin at 100 µg/ml were used as standard drugs for antibacterial activities.

KEYWORDS

Antibacterial Activity, Carbothioamide derivatives, Ethyl bromo Acetate, Thiadiazole; 2-(3-Hydroxy-benzoyl) Benzoic Acid

INTRODUCTION

Thiadiazole and Triazoles heterocyclic compounds were reported with wide range of biological activities. Thiadiazole, Carbothioamide and its derivatives are important heterocyclic in organic and biochemistry. Many Thiadiazole derivatives have shown interesting biological properties such as antibacterial, anti-inflammatory, antioxidant, antitumor, antifungal and immune suppressant activities. Thiadiazole derivatives are prepared by using 2-(2-benzyl-4-chlorophenoxy) acetohydrazide. These 2-(2-benzyl-4-chlorophenoxy) acetohydrazide derivatives are screened for antibacterial activity and antifungal activity. It reveals that Thiadiazole posses broad spectrum activity such as antimicrobial[1-4], anti-inflammatory[5], analgesic[6], antitumorial[7], antihypertensive[8], anticonvulsant and antiviral[9]. Since the past few decades, the

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literature has been enriched with progressive findings about the synthesis and pharmacological activities of various substituted Thiadiazole derivatives. There are antifungal and antibacterial agent having different structure and used in the treatment of fungal and bacterial infection. Heterocyclic compounds containing N and S gives a variety of biological activities; antimicrobial activity[10]. Nitrogen containing heterocyclic compounds and Sulphur containing heterocyclic compounds has received considerable attention due to their wide range of pharmacological activity[11]. During the past decades, the human population affected with life-threatening infectious diseases. Due to this reason, it is imperative to design and develop new antibacterial or antifungal agents for examples; 2-(2-benzyl-4-chlorophenoxy) acetohydrazide derivative exhibit diverse biological activities, Triazoles and Thiadiazole give antibacterial activity.

MATERIAL AND METHODS

Materials

2-benzyl-4-chlorophenol, Ethyl bromo acetate, Aromatic isothiocyanates, Pyridine, Hydrazine Hydrate, Sodium hydroxide, Ethanol, Con.Hydrochloric acid, Con. Sulphuric acid i.e. H_2SO_4 etc. All reagents were purchased from Atmaja chemicals, Aurangabad. All chemicals were of analytical grade.

Method

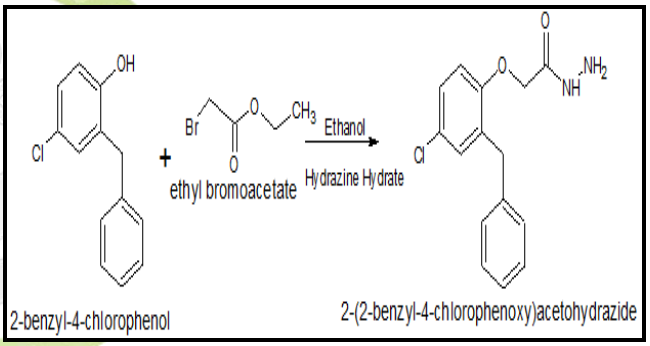
All thiadiazole and Carbothioamide derivatives were synthesized by conventional method.

Experimental Section[17-20]

Melting points were determined by open tube capillary method. The purity of the compounds was checked on thin layer chromatography (TLC) plates (silica gel G) in chloroform: acetone (8:2) and chloroform: methanol (8:2) solvent systems, the spots were located under iodine vapors and UV light. IR spectra were obtained on a Perkin Elmer Spectrum1 FT-IR instrument (KBr pellets). Perkin Elmer Spectrum1 FT-IR instrument consists of globar and mercury vapor lamp as sources. ^{1}H-NMR spectra were recorded by a Bruker AVANCE III 500 MHz (AV 500) spectrometer using TMS as internal standard in DMSO-d_6/$CDCl_3$ and mass spectra was obtained on JEOL GCMATE II GC-MS are presented as m/z. The synthetic route for the title compounds is shown in Scheme 1, 2 and 3.

General procedure for Synthesis of 2-(2-benzyl-4-chlorophenoxy) acetohydrazide (ADH): [Scheme 1]

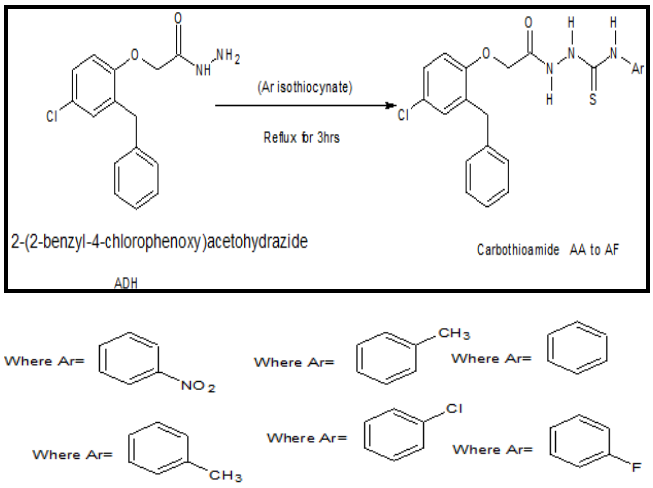
A mixture of 2-benzyl-4-chlorophenol (0.5g) and Ethyl bromo acetate (0.5g) was react with each other in the presence of Ethanol (15 ml) and hydrazine hydrate and reflux for 3 hrs and then Completion of the reaction were confirmed by TLC. The mixture was cooled by addition of ice. The precipitate formed was washed with water and recrystalized from ethanol and then it gives 2-(2-benzyl-4-chlorophenoxy) acetohydrazide (ADH).



Scheme 1: Synthesis of 2-(2-benzyl-4-chlorophenoxy) acetohydrazide (ADH) from 2-benzyl-4-chlorophenol (ADH)

General procedure for synthesis of carbothio-amide (AA to AF):[Scheme 2]

A solution of 2-(2-benzyl-4-chlorophenoxy) acetohydrazide (ADH) reacts with different aromatic isothiocyanates like 3-chlorophenyl isothiocyanates and reflux for 3 hrs and then Completion of the reaction were confirmed by TLC. The mixture was cooled by addition of ice. The precipitate formed was washed with water and recrystalized from ethanol and then it gives different derivatives of carbothioamide like 2-[(2-benzyl-4-chlorophenoxy) acetyl]-N-(3-chlorophenyl) hydrazine carbothioamide after addition of 3-chlorophenyl isothiocyanates on 2-(2-benzyl-4-chlorophenoxy) acetohydrazide.



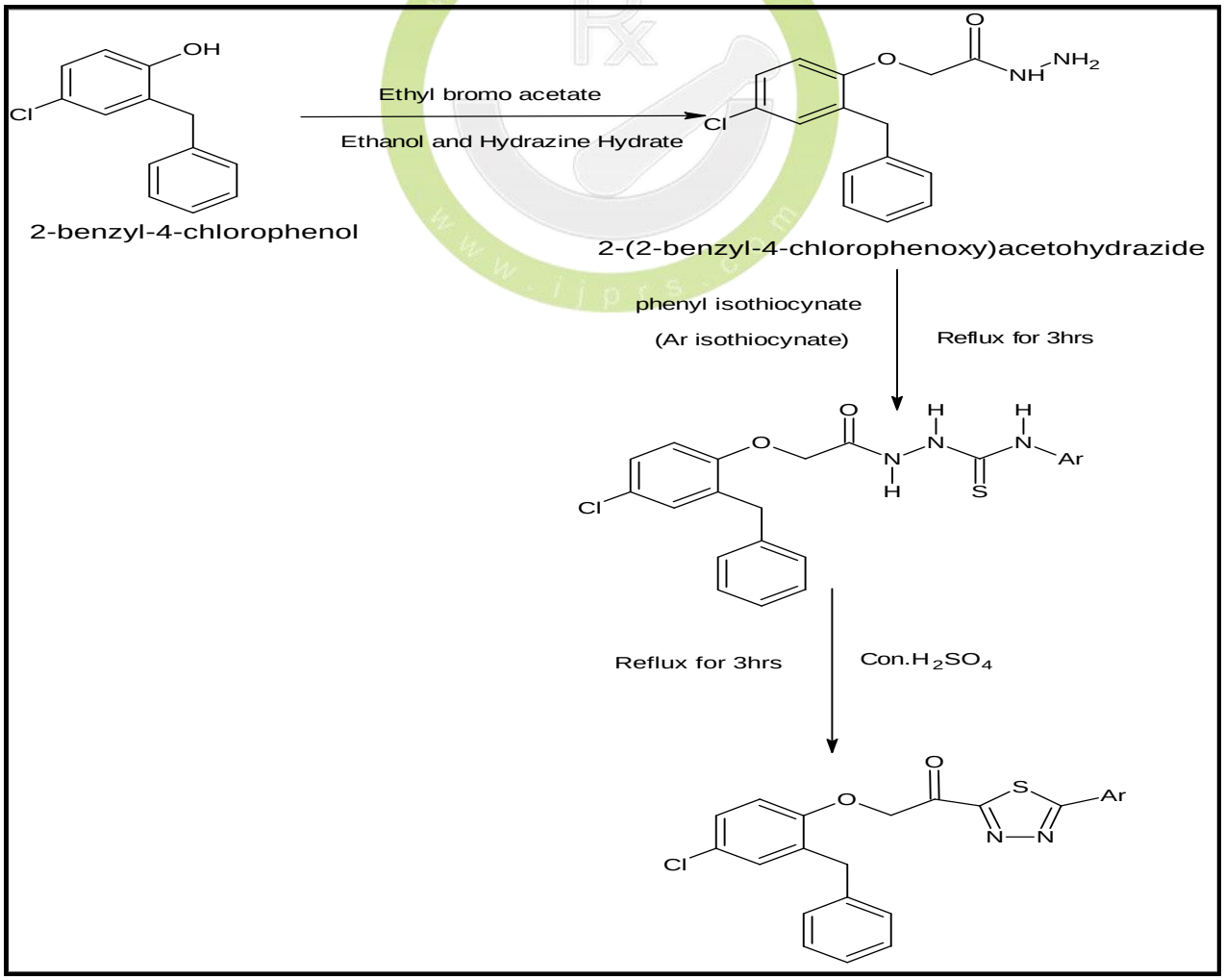
Scheme 2: Synthesis of derivatives of carbothioamide derivatives from 2-(2-benzyl-4-chlorophenoxy) acetohydrazide (ADH) : (AA-AF)

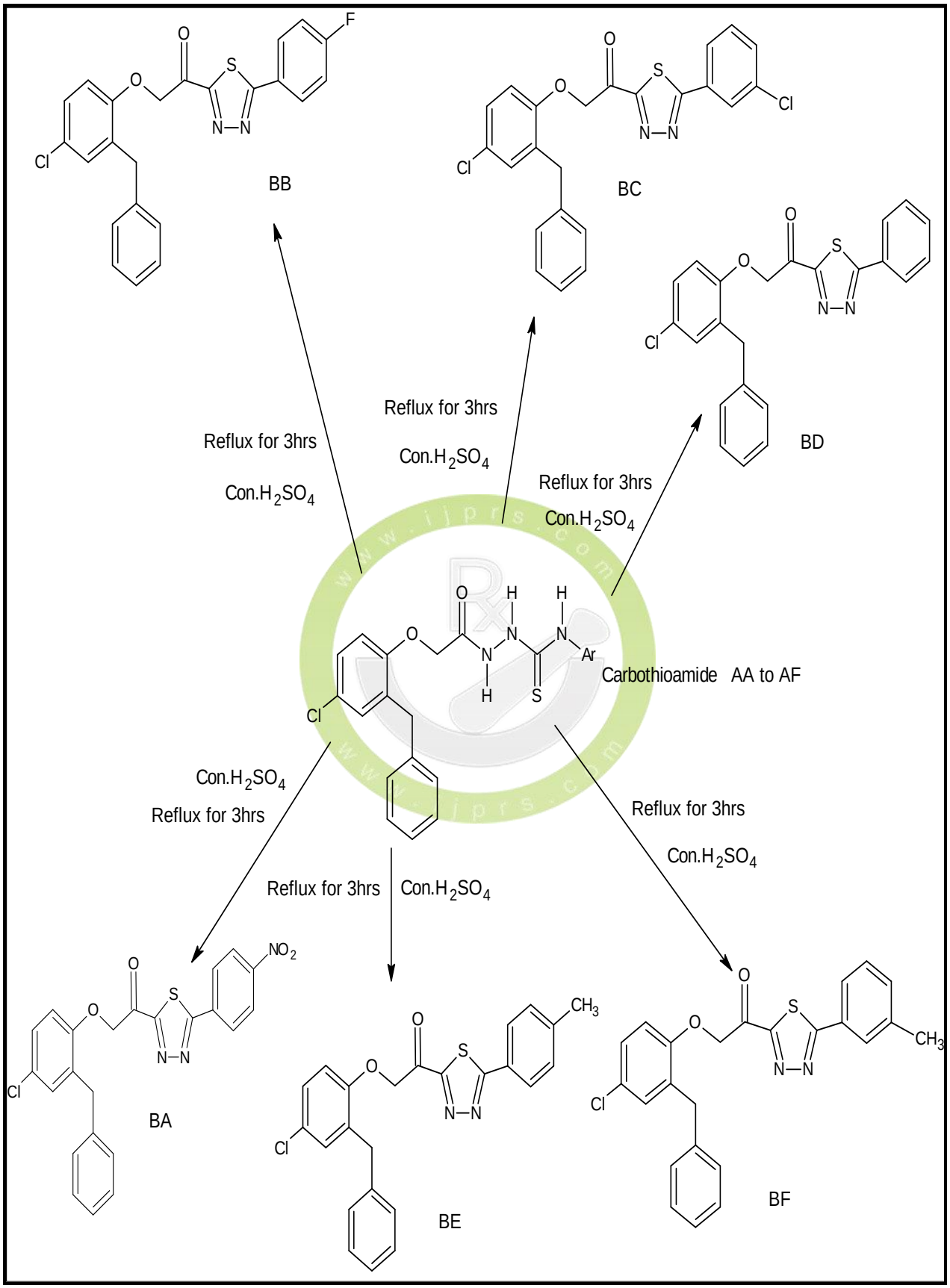
General procedure for synthesis of thiadiazole (BA to BF):[Scheme 3]

A solution of different derivatives of carbothioamide likes 2-[(2-benzyl-4-chlorophenoxy) acetyl]-N-(3-chlorophenyl) hydrazine carbothioamide reacts with Con. H2SO4 and reflux for 3 hrs and then Completion of the reaction were confirmed by TLC. The mixture was cooled by addition of ice. The precipitate formed was washed with water and recrystalized from ethanol and then it gives different derivatives of thiadiazole like 2-[(2-benzyl-4-chlorophenoxy) methyl]-5-(3-chlorophenyl)-1, 3, 4-thiadiazole after addition of 2-[(2-benzyl-4-chlorophenoxy) acetyl]-N-(3-chlorophenyl) hydrazine carbothioamide on Con. H2SO4 and reflux for 3 hrs.

General Scheme of Reaction

General scheme of thiadiazole from 2-(2-benzyl-4-chlorophenoxy) acetohydrazide derivative





Scheme 3: Scheme for thiadiazole from carbothioamide derivatives (BA- BF)

RESULTS

2-(2-benzyl-4-chlorophenoxy) acetohydrazide {ADH}

Colorless solid; $C_{15}H_{19}O_2N_2Cl$; % Yield: 60.15%; Melting Point: 86-88ºC; Rf value: 0.76; FTIR (KBr) ν cm^{-1} : 3063.97 (Ar C-H), 1562.39 (Ar C=C),1631.83 (amide C=O), 1246.06 (Ar C-N), 2946.26 (Aliphatic C-H), 3425.60 (N-H), 775.41 (C-Cl); ^{1}H NMR (400 MHz CDCl3 δ ppm): 7.6-8.2 (m, 3H, aromatic protons), 7.2 (s, 5H, phenyl), 6.4 (s, 3H, NH_2), 6.8 (s, 3H, NH_2), 4.4 (s, 2H, CH_2), 4.8 (s, 2H, CH_2 Phenyl); JEOL GCMATE II GC-MS (m/z) : 289 (M^+), 290 (M^++1). Mol. Wt.: 290

2-[(2-benzyl-4-chlorophenoxy) acetyl]-N-(4-Nitrophenyl) hydrazine carbothioamide (AA)

Colorless solid; $C_{22}H_{19}O_4N_4SCl$; % Yield: 78.9%; Melting Point: 218ºC; Rf value: 0.69; FTIR (KBr) ν cm^{-1} : 3068.85 (Ar C-H), 1591.33 (Ar C=C), 1687.71 (amide C=O), 1234.48 (Ar C-N), 2928.04 (Aliphatic C-H), 3263.86 (N-H), 758.06 (C-Cl); 1HNMR (DMSO, 400MHz): 7.6-8.2 (m, 3H, aromatic protons), 7.2 (s, 5H, phenyl), 4.2 (s, 2H, CH_2), 6.2 (s, 2H, NH_2), 6.8 (s, 1H, NH), 4.2 (s, 2H, CH_2), 7.0 (s, 4H, aromatic NO_2 protons str), 4.8 (s, 2H, CH_2 Phenyl); FABMS (m/z) 469 (M^+), 470 (M^++1). Mol. Wt.: 470

2-[(2-benzyl-4-chlorophenoxy) acetyl]-N-(4-flurophenyl) hydrazine carbothioamide (AB)

Colorless solid; $C_{22}H_{19}O_2N_3SClF$; % Yield: 63%; Melting Point: 222ºC; Rf value: 0.76; FTIR (KBr) ν cm^{-1} : 3063.97 (Ar C-H), 1585.18 (Ar C=C), 1680.05 (amide C=O), 1230.63 (Ar C-N), 2974.33 (Aliphatic C-H), 3373.61(N-H), 761.91 (C-Cl); 1HNMR (DMSO, 400MHz): 7.6-8.2 (m, 3H, aromatic protons), 7.2 (s, 5H, phenyl), 4.2 (s, 2H, CH_2), 6.2 (s, 2H, NH_2), 6.8 (s, 1H, NH), 7.1 (s, 4H, aromatic F protons str), 4.8 (s, 2H, CH_2 Phenyl); JEOL GCMATE II GC-MS (m/z) : 442 (M^+), 443 (M^++1). Mol. Wt.: 443

2-[(2-benzyl-4-chlorophenoxy) acetyl]-N-(3-chlorophenyl) hydrazine carbothioamide (AC)

Colorless solid; $C_{22}H_{19}O_2N_3SCl_2$; % Yield: 85%; MP-178 ºC; Rf value 0.839; FTIR (KBr) ν cm^{-1} : 3041.84 (Ar C-H), 1548.89 (Ar C=C), 1681.98 (amide C=O), 1213.27 (Ar C-N), 2962.05 (Aliphatic C-H), 3211.59 (N-H), 769 (C-Cl); 1HNMR (DMSO, 400MHz): 7.6-8.2 (m, 3H, aromatic protons), 7.2 (s, 5H, phenyl), 4.2 (s, 2H, CH_2), 6.2 (s, 2H, NH_2), 6.8 (s, 1H, NH), 7.3 (s, 4H, aromatic Cl protons str), 4.8 (s, 2H, CH_2 Phenyl); FABMS (m/z) 458 (M^+), 459 (M^++1). Mol. Wt.: 459

2-[(2-benzyl-4-chlorophenoxy) acetyl]-N-phenyl hydrazine carbothioamide (AD)

Colorless solid; $C_{22}H_{19}O_2N_3SCl$; % Yield: 59.27%; Melting Point: 169ºC; Rf value: 0.83; FTIR (KBr) ν cm^{-1} : 3040.84 (Ar C-H), 1548.89 (Ar C=C), 1680.98 (amide C=O), 1213.27 (Ar C-N), 2962.05 (Aliphatic C-H), 3211.59 (N-H), 769 (C-Cl); 1HNMR (DMSO, 400MHz): 7.6-8.2 (m, 3H, aromatic protons), 7.2 (s, 5H, phenyl), 4.2 (s, 2H, CH_2), 6.2 (s, 2H, NH_2), 6.8 (s, 1H, NH), 7.0 (s, 4H, aromatic phenyl protons str), 4.8 (s, 2H, CH_2 Phenyl); JEOL GCMATE II GC-MS (m/z) : 424 (M^+), 425 (M^++1). Mol. Wt.: 425

2-[(2-benzyl-4-chlorophenoxy) acetyl]-N-(4-Methylphenyl) hydrazine carbothioamide (AE)

Colorless solid; $C_{23}H_{21}O_2N_3SCl$; % Yield: 56.43%; Melting Point: 210ºC; Rf value: 0.92; FTIR (KBr) ν cm^{-1} : 3033.74 (Ar C-H), 1591.33 (Ar C=C),1629.26 (amide C=O), 1220.93 (Ar C-N), 2920.32 (Aliphatic C-H), 3390.96 (N-H),751.06 (C-Cl); 1HNMR (DMSO, 400MHz): 7.6-8.2 (m, 3H, aromatic protons), 7.2 (s, 5H, phenyl), 6.2 (s, 2H, NH_2), 6.8 (s, 1H, NH), 4.2 (s, 2H, CH_2), 7.0 (s, 4H, aromatic methyl protons), 2.34 (s, 3H, CH_3), 4.8 (s, 2H, CH_2 Phenyl); JEOL GCMATE II GC-MS (m/z) : 438 (M^+), 439 (M^++1). Mol. Wt.: 439

2-[(2-benzyl-4-chlorophenoxy) acetyl]-N-(3-Methylphenyl) hydrazine carbothioamide (AF)

Colorless solid; $C_{23}H_{21}O_2N_3SCl$; % Yield: 45.43%; Melting Point: 218ºC; Rf value: 0.82; FTIR (KBr) ν cm^{-1} : 3033.74 (Ar C-H), 1591.33 (Ar C=C),1629.26 (amide C=O), 1220.93 (Ar C-N), 2980.32 (Aliphatic C-H), 3335.96 (N-H),783.06 (C-Cl); 1HNMR (DMSO, 400MHz):

7.6-8.2 (m, 3H, aromatic protons), 7.2 (s, 5H, phenyl), 6.2 (s, 2H, NH_2), 6.8 (s, 1H, NH), 4.2 (s, 2H, CH_2), 7.0 (s, 4H, aromatic methyl protons), 2.34 (s, 3H, CH_3), 4.8 (s, 2H, CH_2 Phenyl); FABMS (m/z) 438 (M^+), 439 (M^++1). Mol. Wt.: 439

2-[(2-benzyl-4-chlorophenoxy) methyl]-5-(4-Nitrophenyl)-1, 3, 4-thiadiazole (BA)

Colorless solid; $C_{22}H_{16}O_3N_3SCl$; Yield: 80.43%; Melting Point: 234ºC; Rf value: 0.77; FTIR (KBr) ν cm^{-1} :3061.13 (Ar C-H), 1533.46 (Ar C=C), 1681.98 (amide C=O), 1332.86 (Ar C-N), 2856.07 (Aliphatic C-H), 3311.89 (N-H), 771.05 (C-Cl); 1HNMR (DMSO, 400MHz): 7.6-8.2 (m, 3H, aromatic protons), 7.1 (s, 5H, phenyl), 4.4 (s, 2H, CH_2), 7.0 (s, 4H, aromatic nitro protons), 4.8 (s, 2H, CH_2 Phenyl); JEOL GCMATE II GC-MS (m/z) : 436 (M^+), 437 (M^++1). Mol. Wt.: 437

2-[(2-benzyl-4-chlorophenoxy) methyl]-5-(4-Flurophenyl)-1, 3, 4-thiadiazole (BB)

Colorless solid; $C_{22}H_{16}ON_2SFCl$; % Yield: 67.39%; Melting Point: 276ºC; RF value: 0.79; FTIR (KBr) ν cm^{-1} : 3036.13 (Ar C-H),1583.61 (Ar C=C), 1661.12 (amide C=O), 1257.63 (Ar C-N), 2839.31 (Aliphatic C-H), 3354.31 (N-H), 758.52 (C-Cl); 1HNMR (DMSO, 400MHz): 7.6-8.2 (m, 3H, aromatic protons), 7.2 (s, 5H, phenyl), 4.4 (s, 2H, CH_2),7.0 (s, 4H, aromatic F protons), 4.8 (s, 2H, CH_2 Phenyl); FABMS (m/z) 409 (M^+), 410 (M^++1). Mol. Wt.: 410

2-[(2-benzyl-4-chlorophenoxy) methyl]-5-(3-chlorophenyl)-1, 3, 4-thiadiazole (BC)

Colorless solid; $C_{22}H_{16}ON_2SCl_2$; % Yield: 62.50%; Melting Point: 310ºC; Rf value: 0.84; FTIR (KBr) ν cm^{-1} : 3072.71 (Ar C-H),1537.32 (Ar C=C), 1670.41(amide C=O), 1319.35 (Ar C-N), 2926.11 (Aliphatic C-H), 3267.52 (N-H), 752.28 (C-Cl); 1HNMR (DMSO, 400MHz): 7.6-8.2 (m, 3H, aromatic protons), 7.2 (s, 5H, phenyl), 4.4 (s, 2H, CH_2),7.0 (s, 4H, aromatic Cl protons), 4.8 (s, 2H, CH_2 Phenyl); JEOL GCMATE II GC-MS (m/z) : 425 (M^+), 426 (M^++1). Mol. Wt.: 426

2-[(2-benzyl-4-chlorophenoxy) methyl]-5-(phenyl)-1, 3, 4-thiadiazole (BD)

Colorless solid; $C_{22}H_{17}ON_2SCl_2$; % Yield: 84.78%; Melting Point: 256ºC; Rf value: 0.89; FTIR (KBr) ν cm^{-1} : 2974.77 (Ar C-H), 1599.56 (Ar C=C), 1680.05 (amide C=O), 1392.62 (Ar C-N), 1282.71 (Aliphatic C-N), 2860.88 (Aliphatic C- H), 3309.56 (N-H), 750.18 (C-Cl); 1HNMR (DMSO, 400MHz): 7.6-8.2 (m, 3H, aromatic protons), 7.2 (s, 5H, phenyl), 4.4 (s, 2H, CH_2), 7.0 (s, 4H, aromatic phenyl protons), 4.8 (s, 2H, CH_2 Phenyl); JEOL GCMATE II GC-MS (m/z) : 391 (M^+), 392 (M^++1). Mol. Wt.: 392

2-[(2-benzyl-4-chlorophenoxy) methyl]-5-(4-methylphenyl)-1, 3, 4-thiadiazole (BE)

Colorless solid; $C_{22}H_{17}ON_2SCl_2$; % Yield: 71.14%; Melting Point: 298ºC; Rf value: 0.94; FTIR(KBr) ν cm^{-1} : 3068.85 (Ar C-H), 1591.33 (Ar C=C), 1687.77 (amide C=O), 1360.78 (Ar C-N), 1234.48 (Aliphatic C-N), 2928.04, 2886.07 (Aliphatic C- H), 3394.83 (N-H), 758.05 (C-Cl); 1HNMR (DMSO, 400MHz): 7.6-8.2 (m, 3H, aromatic protons), 7.2 (s, 5H, phenyl), 4.4 (s, 2H, CH_2), 7.1 (s, 4H, aromatic methyl protons), 1.2 (s, 3H, CH_3), 4.8 (s, 2H, CH_2 Phenyl); JEOL GCMATE II GC-MS (m/z) : 406 (M^+), 406 (M^++1). Mol. Wt.: 406

2-[(2-benzyl-4-chlorophenoxy) methyl]-5-(3-methylphenyl)-1, 3, 4-thiadiazole (BF)

Colorless solid; $C_{22}H_{17}ON_2SCl_2$; % Yield: 84.44%; Melting Point: 312ºC; Rf value: 0.94; FTIR (KBr) ν cm^{-1} : 3072.71 (Ar C-H), 1537.32 (Ar C=C), 1670.41 (amide C=O), 1360.78 (Ar C-N), 1319.35 C-N (Aliphatic C-N), 2928.04, 2926.11 (Aliphatic C- H), 3267.52 (N-H), 751.54 (C-Cl); 1HNMR (DMSO, 400MHz): 7.6-8.2 (m, 3H, aromatic protons), 7.2 (s, 5H, phenyl), 4.4 (s, 2H, CH_2), 7.1(s, 4H, aromatic methyl protons), 4.8 (s, 2H, CH_2 Phenyl); JEOL GCMATE II GC-MS (m/z) : 406 (M^+), 406 (M^++1). Mol. Wt.: 406

Pharmacological Studies[21]

In this present work a novel series of Synthesis of 2-(2-benzyl-4-chlorophenoxy) acetohydrazide {ADH} derivatives were synthesized. All the synthesized compounds were screened for their antibacterial activity against activity against both gram positive *S. aureus* and gram negative *E*

.coli bacteria according to disc diffusion method at concentrations of 100 mg/ml Gentamycin was used as standard for comparison of antibacterial activity.

Antibacterial Activity

The compounds ADH, AA to AF and BA to BF were evaluated for their *in vitro* antibacterial activity against various microorganisms gram positive *Staphylococcus aureus*, gram negative *Escherichia coli and Pseudomonas aeruginosa by* in vitro method like disc diffusion method was performed using Mueller Hinton Agar (M173) medium.

Each compound was tested at concentration 100 µg/mL in DMSO. The zone of inhibition was measured after 24 h incubation at 37^0C. Standard: Gentamycin (100 µg/mL of DMSO) (Table-1) revealed that all tested compounds exhibit moderate to good activity against all the tested bacteria.

Moreover, the compounds having AA, AB, AC, BA, BB, and BC the side chain containing aromatic heterocyclic ring which is attached by Cl, F halogen and NO_2 group showed higher activity than aliphatic group which is attached by CH_3 derivatives.

Table 1: Antibacterial activity screening result of synthesized compound measuring the zone of inhibition in millimeter

Comp No.	**Diameter of zone of inhibition (mm)**		
	Escherichia coli	***Staphylococcus aureus***	***Pseudomonas aeruginosa***
	ATCC 25922	**ATCC 25923**	**ATCC 27853**
ADH	15	14	14
AA	19	26	18
AB	19	28	20
AC	18	25	19
AD	15	13	10
AE	14	13	12
AF	15	10	13
BA	19	20	21
BB	17	21	19
BC	18	25	18
BD	14	14	12
BE	15	14	11
BF	13	15	10
Genta mycin	20	36	28

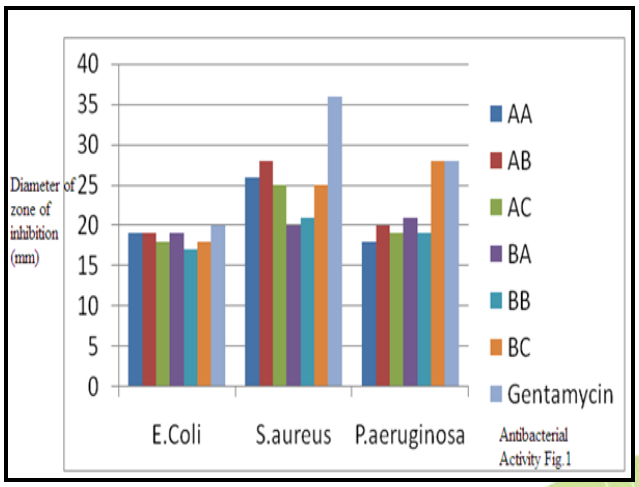
DISCUSSION

In the course of our search for therapeutically useful antimicrobial agent .Our study revealed that all the compounds had stronger antibacterial activity against Gram positive bacteria when compared to Gram negative bacteria. The series contain 13 analogues. Our synthetic strategy for Synthesis of 2-(2-benzyl-4-chlorophenoxy) acetohydrazide {ADH} derivatives is illustrated in general scheme, scheme (1) and scheme (2). Moreover, the compounds having AA, AB, AC, BA, BB, and BC the side chain containing aromatic heterocyclic ring which is attached by Cl, F halogen and NO_2 group showed higher activity than aliphatic group which is attached by CH_3 and phenyl derivatives.

It is interesting to note that a minor change in the molecular structure of investigated compounds may have a pronounced effect on antimicrobial screening e.g. compound AE, AF and BE, BF with methylene group linker has very weak antimicrobial activity. Compounds having AA, AB, AC, BA, BB, and BC the side chain containing aromatic heterocyclic ring which is attached by Cl, F halogen and NO_2 group showed higher activity. The synthesized compounds were screened for their antibacterial activity as shown in Figure 1.

The derivatives AA, AB, AC, BA, BB, and BC showed highly active compound against *E. coli*.

BA, BB showed moderately active compound against *E. coli, S. aureus*. AA, AB, AC , and BC showed moderately active compound against *E. coli, S. aureus*. Standard (Ciprofloxacin) showed highly active against *E. coli, P. aeruginosa* and *S. aureus*.



CONCLUSION

In summary we have synthesized a novel series of 2-(2-benzyl-4-chlorophenoxy) acetohydrazide derivatives compounds and evaluated. The antibacterial activity of the synthesized compounds may be due to the presence side chain containing aromatic heterocyclic ring which is attached by Cl, F halogen and NO_2 group showed higher activity than aliphatic group.

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