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Synthesis and Antimicrobial Evaluation of 1-(Substituted Phenyl)-3-(5-(Substituted-1H-Indol-3-Yl)-1,3,4-Thiadiazol-2-Yl) Thiourea.

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KEYWORDS

Antimicrobial, Synthesis, Staphylococcus

ABSTRACT:

The antibacterial activity of a novel series of 1-(Substituted phenyl)-3-(5-(Substituted-1H-indol-3-yl)-1,3,4-thiadiazol-2-yl) thiourea compounds was assessed through synthesis and screening. The antibacterial activity of each newly created substance was tested against Gram positive bacteria. As organisms for antifungal activity, Bacillus subtilis, Staphylococcus aureus, and Gram-negative species Pseudomonas aeruginosa, E. coli, and Candida albicans, A. niger species were employed. Strong action against the test bacteria and fungus was demonstrated by compounds 4c and 4e, which were apparent as promising compounds for more research. It was discovered that compounds with halogen and methyl substituents were more biologically active.

Keywords: Thiadiazole, antibacterial, antifungal.

Introduction

One of the main infections that kill millions of patients globally is microbial infection, which is brought on by different kinds of fungus and bacteria [1]. The ongoing issue of microbial resistance to antibiotics is making it harder to treat microbial infections, such as bacterial, fungal, and tubercular infections. As a result, there is a constant need for new generations of anti-infective agents, and particularly new antimicrobial agents, to effectively treat microbial infections [2]. One of the most crucial areas of research nowadays is the need to develop novel chemicals to combat this resistance [3].

When atoms from at least two distinct elements make up a compound's ring, it is said to be heterocyclic. Homocyclic compounds, whose rings are composed of a single element, are the opposite of heterocyclic compounds. Due to its many biological applications, heterocyclic chemistry has drawn attention ever since the quest for synthetic molecules with therapeutic significance began. Analogues with therapeutic importance that are utilised in the treatment of a range of illnesses were created by substituting heterocyclic compounds at different places [4-5]. Particularly, substances containing the 1, 3, 4-thiadiazole nucleus are recognised for their special anti-inflammatory and antibacterial properties [6-7]. The thiazole molecule can be bio-isosterically replaced by thiadiazole. It can therefore be employed in antibiotic formulations because it functions similarly to third and fourth generation cephalosporins. The names 1,2,3 Thiadiazole (1), 1,2,4 Thiadiazole (2), 1,2,5 Thiadiazole (3), and 1,3,4 Thiadiazole (4) are the different isomers of thiadiazole [8–9]. Antimicrobial [10], analgesic [11], anti-inflammatory [12], anti-tubercular [14], anticancer [13], diuretic [16], anthelmintic [15], antidepressant [18], anti-Helicobacter pylori [19], and anticonvulsant [20] properties have all been linked to thiadiazoles. Thiadiazoles are not carcinogenic and are readily broken down by regular biochemical processes [21]. We were inspired by these studies to create novel thiadiazole compounds that would work against a range of microorganism strains [22]. The antibacterial activity of all the compounds has been tested against two strains of fungal bacteria, A. niger and C. albicans, as well as two strains of Gramme positive bacteria, S. aureus and B. subtilis, and two strains of Gramme negative bacteria, E. coli and P. aeruginosa. Against these pathogens, some of the synthesised compounds demonstrated strong antibiotic activity, even matching that of ciprofloxacin and miconazole.

Experimental Section

General Procedure for the Synthesis of Indole Substituted 2-Amino-1,3,4-thiadiazoles (3)

To a stirred solution of thiosemicarbazide (5, 0.5mmol) and acetic acid (0.5 mmol) in H_2O (1ml) was added a solution of the aldehyde (3, 0.5 mmol) in MeOH (1 ml). After being stirred at room temperature for 30 min, the solvent was evaporated under reduced pressure, and the resulting residue was redissolved in 1,4-dioxane (5 mL), followed by addition of potassium carbonate (1.6mmol) and iodine (0.75 mmol) in sequence. The reaction

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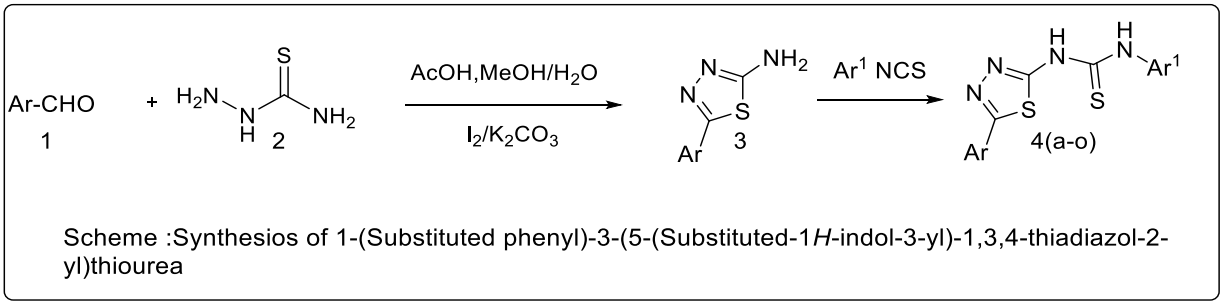
mixture was heated to reflux under nitrogen atmosphere until the conversion was complete (monitored by TLC, 1−4 h). After being cooled to room temperature, it was treated with 5% $Na_2S_2O_3$ (20 mL) and extracted with EtOAc (16 ml x 3). The combined organic layer was dried over anhydrous sodium sulphate and concentrated. The given residue was purified through silica gel column chromatography using a mixture of EtOAc and petroleum ether as eluent to afford the corresponding 2-amino-1,3,4-thiadiazoles.

(Substituted phenyl)-3-(5-(Substituted-1H-indol-3-yl)-1,3,4-thiadiazol-2-yl) thiourea.4(a-o)

To a stirred solution of 2- amino-1,3,4-thiadiazoles(0.01mole) which is dissolved in alcohol was refluxed in the presence of Phenylisothiocyanate (0.05mole) for 4hrs and progress of the reaction was monitored by TLC (1-4hrs). After being Cooled to room temperature reaction mixture was poured into an ice mixture, filtered by using a Buckner funnel, and kept for drying. Recrystallized the product by using ethanol.

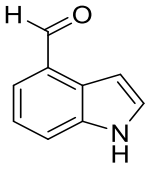
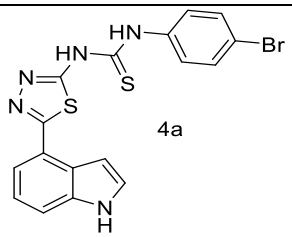
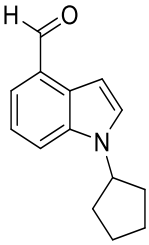
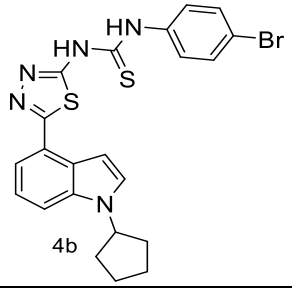
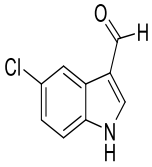
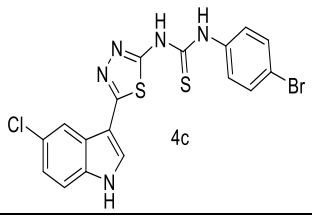
General Procedure for the Synthesis of 1-



Scheme :Synthesios of 1-(Substituted phenyl)-3-(5-(Substituted-1*H*-indol-3-yl)-1,3,4-thiadiazol-2-yl)thiourea

Scheme 1 Synthesis of 1-(Substituted phenyl)-3-(5-(Substituted-1H-indol-3-yl)-1,3,4-thiadiazol-2-yl) thiourea.4(a-o)

Table-I: Physicochemical characteristics of synthesized 1-(Substituted phenyl)-3-(5-(Substituted-1H-indol-3-yl)-1,3,4-thiadiazol-2-yl) thiourea. derivatives

Entry	Aldehyde (Ar)	Ar^1	Product	Yield (%)	Elemental Analysis			Melting Point (^OC)
					C	H	N	
01		4-BrC_6H_4	 4a	77	47.45 (47.44)	2.81 (2.80)	16.27 (16.26)	188
02		4-BrC_6H_4	 4b	70	53.01 (52.99)	4.04 (4.01)	14.05 (14.03)	186
03		4-BrC_6H_4	 4c	69	43.93 (43.92)	2.39 (2.38)	15.07 (15.06)	184

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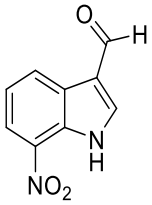
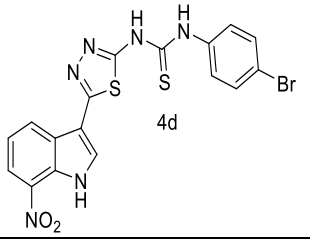
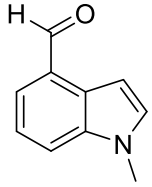
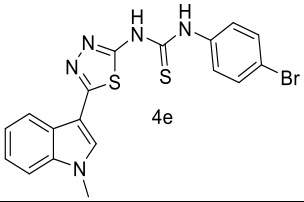
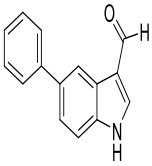
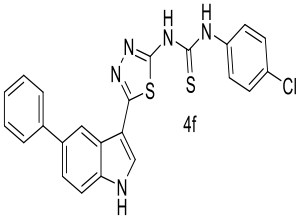
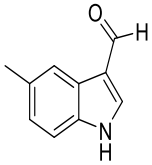
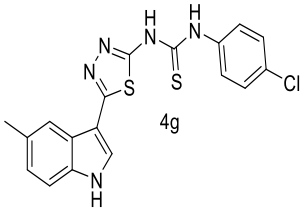
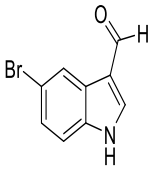
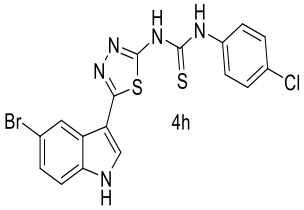
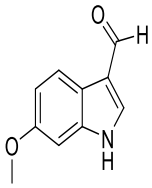
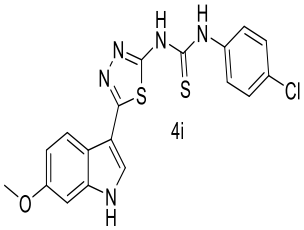
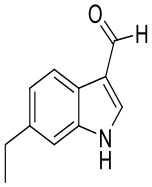
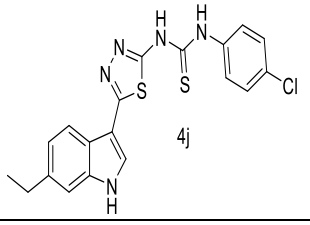
04		4-BrC$_6$H$_4$	 4d	75	42.96 (42.95)	2.33 (2.32)	17.68 (17.67)	187
05		4-BrC$_6$H$_4$	 4e	80	48.65 (48.64)	3.18 (3.17)	15.76 (15.75)	182
06		4-ClC$_6$H$_4$	 4f	90	59.80 (59.79)	3.49 (3.48)	15.16 (15.15)	180
07		4-ClC$_6$H$_4$	 4g	85	54.06 (54.05)	3.53 (3.52)	17.51 (17.50)	181
08		4-ClC$_6$H$_4$	 4h	80	43.93 (43.92)	2.39 (2.38)	15.07 (15.06)	182
09		4-ClC$_6$H$_4$	 4i	78	51.98 (51.97)	3.39 (3.38)	16.84 (16.83)	185
10		4-ClC$_6$H$_4$	 4j	77	55.13 (55.12)	3.90 (3.89)	16.92 (16.91)	184

Spectral data of Synthesised Compounds

Compound 4a

^{1}H NMR: δ 6.98-7.13 (2H, 7.05 (d, *J* = 7.7 Hz), 7.06 (d, *J* = 8.1 Hz)), 7.36 (2H, d, *J* = 8.4, Hz), 7.56-7.74 (3H, 7.62 (d, *J* = 8.4 Hz), 7.68 (t, *J* = 8.1Hz)), 7.88 (1H, t, *J* = 7.8Hz), 8.25 (1H, t, *J* = 0.5 Hz).

^{13}C NMR: δ 110.5 (1C, s), 111.3 (1C, s), 118.7 (1C, s), 121.9 (2C, s), 122.3 (1C, s), 124.1 (1C, s), 124.8 (1C, s),

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128.2 (1C, s), 128.4 (1C, s), 131.7 (2C, s), 136.4 (1C, s), 139.0 (1C, s), 160.7 (1C, s), 165.1 (1C, s), 178.2 (1C, s).
Mass (m/z):430
IR (KBr, Cm^{-1}): 3090-3277(-NH-), 1626(C=N), 1509(C=C), 2957(-CH aromatic), 823(CS-Cstretching)

Compound 4b

^{1}H NMR: δ 1.69-2.11 (8H, 1.78 (d, *J* = 13.1, Hz), 1.81 (d, *J* = 13.1, Hz), 1.89 (d, *J* = 13.4Hz), 2.01 (d, *J* = 13.4, Hz)), 4.91 (1H, d, *J* = 8.1, Hz), 6.93-7.20 (3H), 6.99 (t, *J* = 8.0, 1.2, Hz), 7.05 (d, *J* = 7.7, Hz), 7.13 (d, *J* = 8.0Hz)), 7.36 (2H, d, *J* = 8.4Hz), 7.62 (2H, d, *J* = 8.4Hz), 7.92 (1H, t, *J* = 7.8Hz), 8.35 (1H, t, *J* = 0.5 Hz).

^{13}C NMR: δ 23.1 (2C, s), 32.8 (2C, s), 55.2 (1C, s), 110.5 (1C, s), 112.0 (1C, s), 118.7 (1C, s), 121.9 (2C, s), 122.3 (1C, s), 125.1 (1C, s), 127.3 (1C, s), 128.2 (1C, s), 128.4 (1C, s), 131.7 (2C, s), 135.7 (1C, s), 139.0 (1C, s), 160.7 (1C, s), 165.1 (1C, s), 178.2 (1C, s).
Mass (m/z):498
IR (KBr, Cm^{-1}): 3089-3270(-NH-), 1620(C=N), 1515(C=C), 2960(-CH aromatic), 830(CS-Cstretching)

Compound 4c as sown in fiure 1, 2, 3, and 4

^{1}H NMR: δ 7.30-7.47 (3H, 7.36 (d, *J* = 8.4Hz), 7.40 (d, *J* = 8.3Hz)), 7.54-7.68 (3H), 7.60 (t, *J* = 8.3Hz), 7.62 (d, *J* = 8.4Hz)), 7.81 (1H, t, *J* = 1.6Hz), 8.25 (1H, t, *J* = 0.5 Hz).
^{13}C NMR: δ 110.5 (1C, s), 112.9 (1C, s), 118.1 (1C, s), 121.9 (2C, s), 122.3 (1C, s), 124.8 (1C, s), 127.3 (1C, s), 128.9 (1C, s), 130.4 (1C, s), 131.7 (2C, s), 136.4 (1C, s), 139.0 (1C, s), 160.7 (1C, s), 165.1 (1C, s), 178.2 (1C, s).
Mass (m/z):464
IR (KBr, Cm^{-1}): 3085-3265(-NH-), 1625(C=N), 1518(C=C), 2970(-CH aromatic), 820(CS-Cstretching)

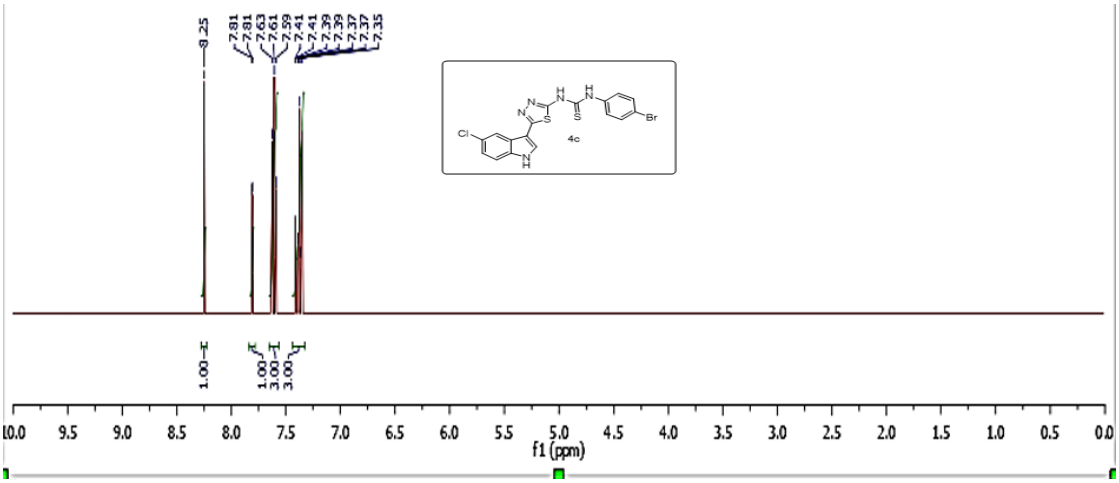

Figure 1: 1HNMR spectra of Compound 4c

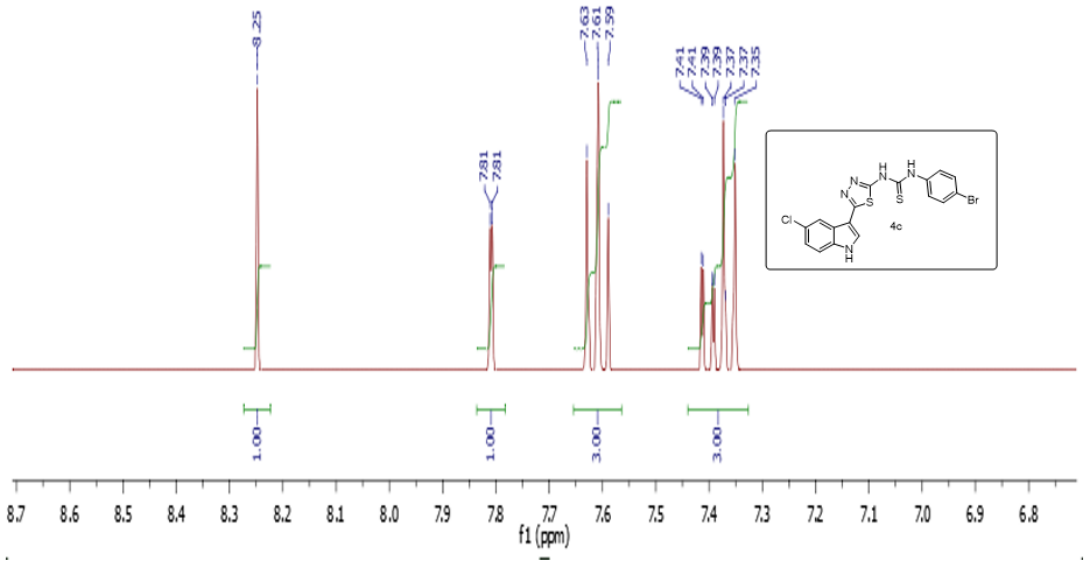

Figure 2: Expandable 1HNMR spectra of Compound 4c

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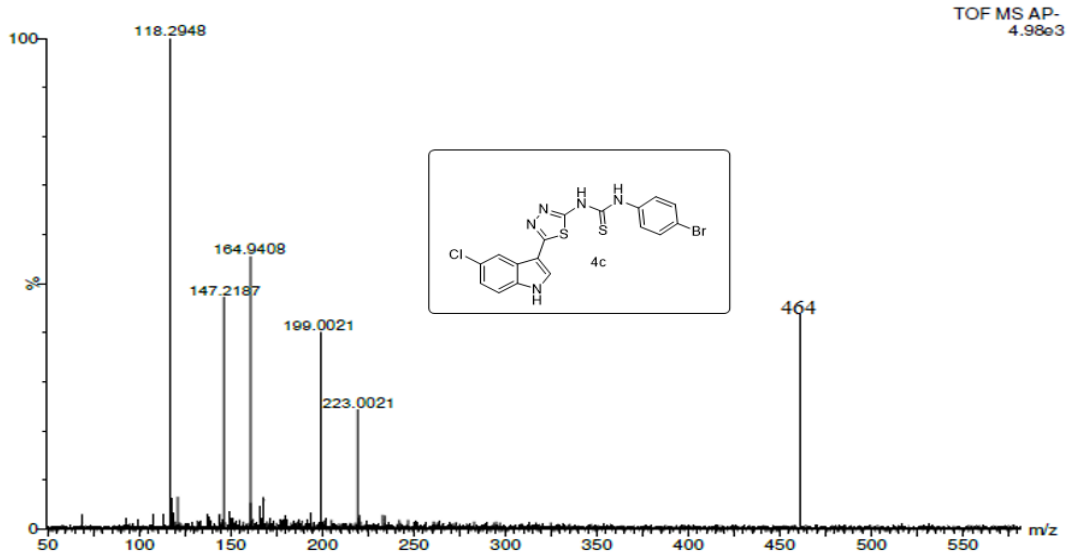

Figure 3: Mass Spectra of Compound 4c

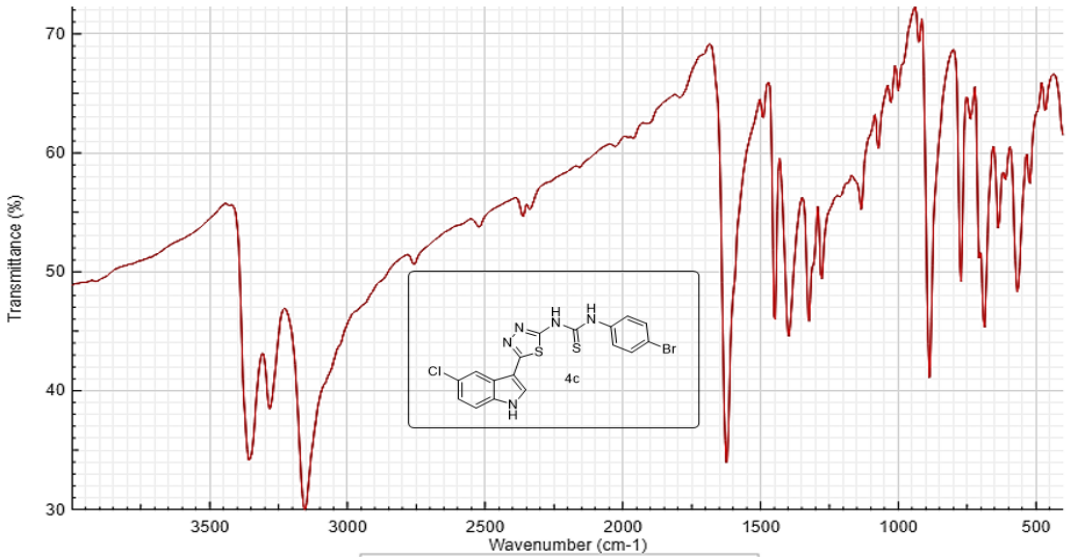

Figure 4: IR Spectra of Compound 4c

Compound 4d

^{1}H NMR: δ 7.01-7.22 (2H, 7.07 (d, *J* = 8.5Hz), 7.15 (d, *J* = 8.5Hz)), 7.36 (2H, d, *J* = 8.4Hz), 7.53-7.68 (3H), 7.60 (d, *J* = 7.8, Hz), 7.62 (d, *J* = 8.4, Hz)), 8.26 (1H, d, *J* = 0.4 Hz)

^{13}C NMR: δ 110.5 (1C, s), 117.7 (1C, s), 118.7 (1C, s), 121.9 (2C, s), 122.3 (1C, s), 124.8 (1C, s), 127.3 (1C, s), 129.0 (1C, s), 131.7 (2C, s), 139.0 (1C, s), 139.4-139.6 (2C, 139.5 (s), 139.5 (s)), 160.7 (1C, s), 165.1 (1C, s), 178.2 (1C, s).

Mass (m/z):475

IR (KBr, Cm^{-1}): 3050-3260(-NH-), 1615(C=N), 1515(C=C), 2980(-CH aromatic), 815(CS-Cstretching)

Compound 4e as shown in figure 5, 6,7, 8 and 9

^{1}H NMR: δ 3.62 (3H, s), 6.98-7.29 (3H, 7.04 (td, *J* = 7.7, 1.3 Hz), 7.12 (d, *J* = 8.0, Hz), 7.23 (t, *J* = 8.0, Hz)), 7.36 (2H, d, *J* = 8.4, Hz), 7.62 (2H, d, *J* = 8.4, Hz), 7.91 (1H, t, *J* = 7.8, Hz), 8.34 (1H, t, *J* = 0.5 Hz).

^{13}C NMR: δ 32.8 (1C, s), 110.5 (1C, s), 112.0 (1C, s), 118.7 (1C, s), 121.9 (2C, s), 122.3 (1C, s), 125.1 (1C, s), 127.3 (1C, s), 128.2 (1C, s), 128.4 (1C, s), 131.7 (2C, s), 137.2 (1C, s), 139.0 (1C, s), 160.7 (1C, s), 165.1 (1C, s), 178.2 (1C, s).

Mass (m/z):444

IR (KBr,Cm^{-1}): 3050-3260(-NH-), 1615(C=N), 1515(C=C), 2980(-CH aromatic), 815(CS-Cstretching)

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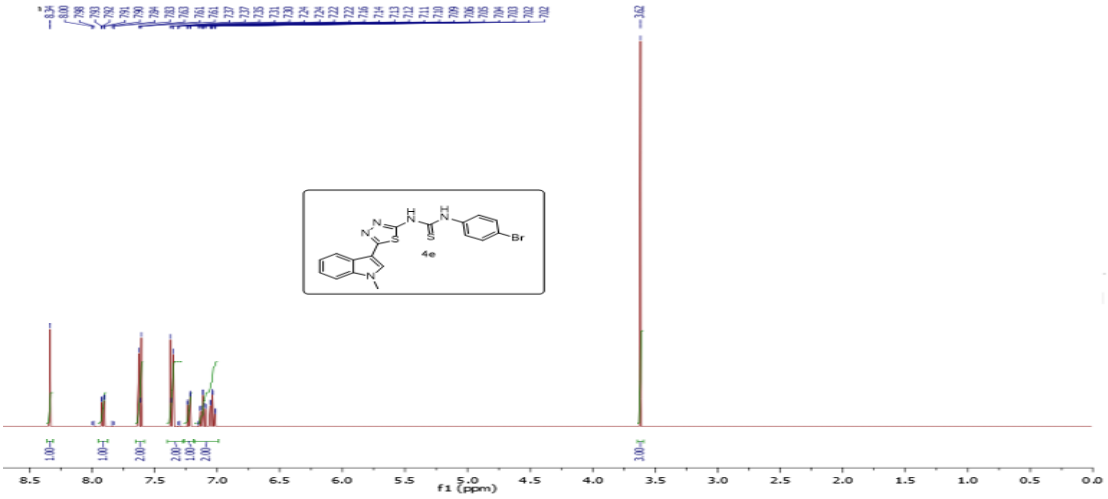

Figure 5: 1HNMR spectra of Compound 4e

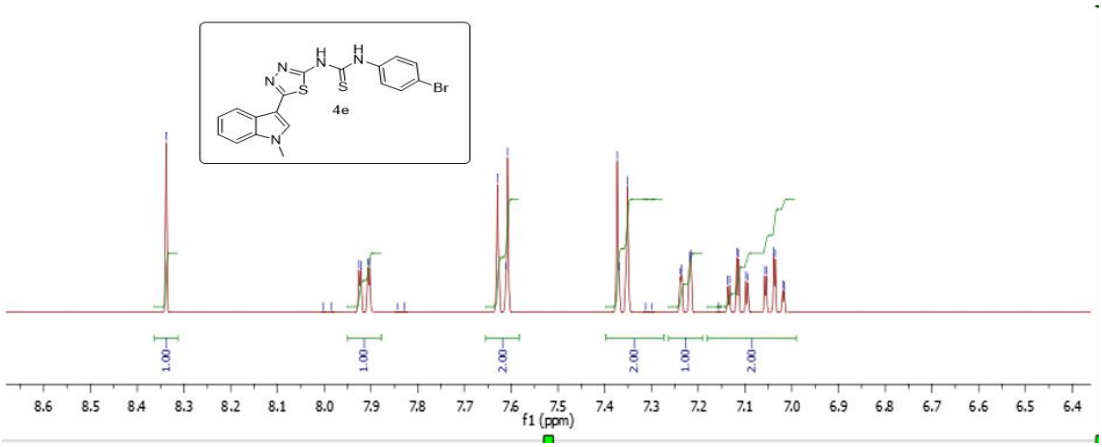

Figure 6: Expandable 1HNMR spectra of Compound 4e

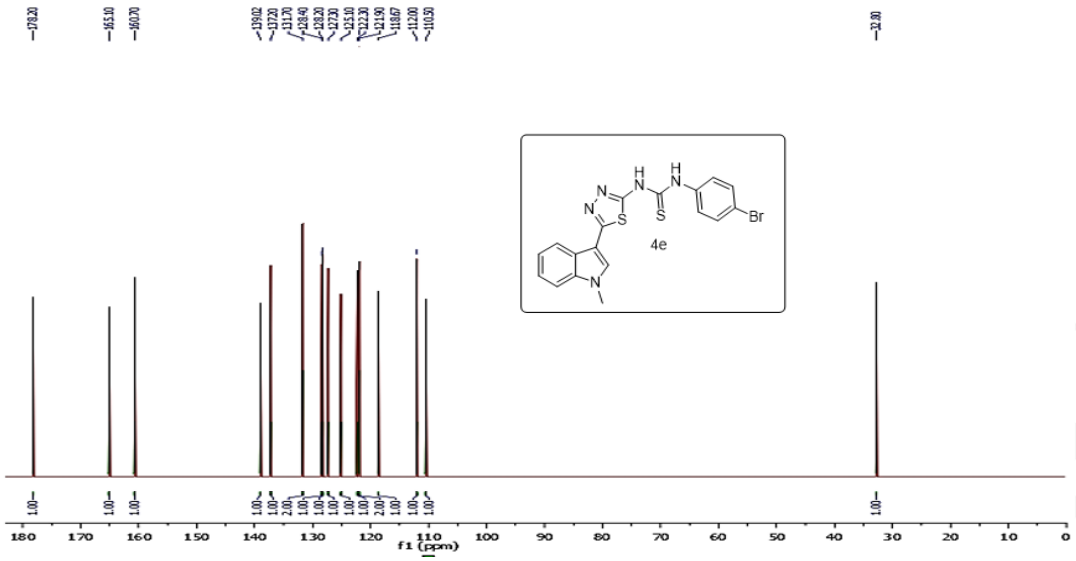

Figure 7: C13 NMR spectra of Compound 4e

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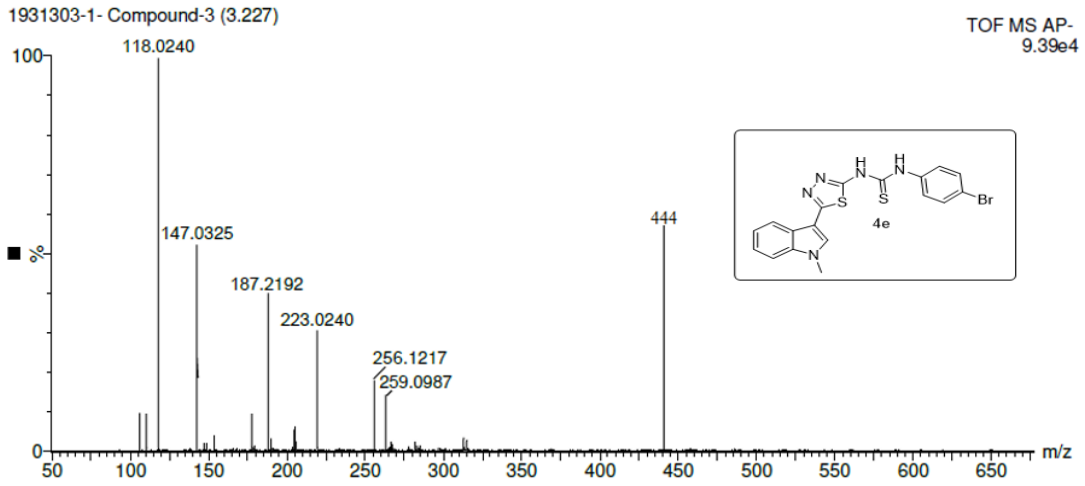

Figure 8: Mass spectra of Compound 4e

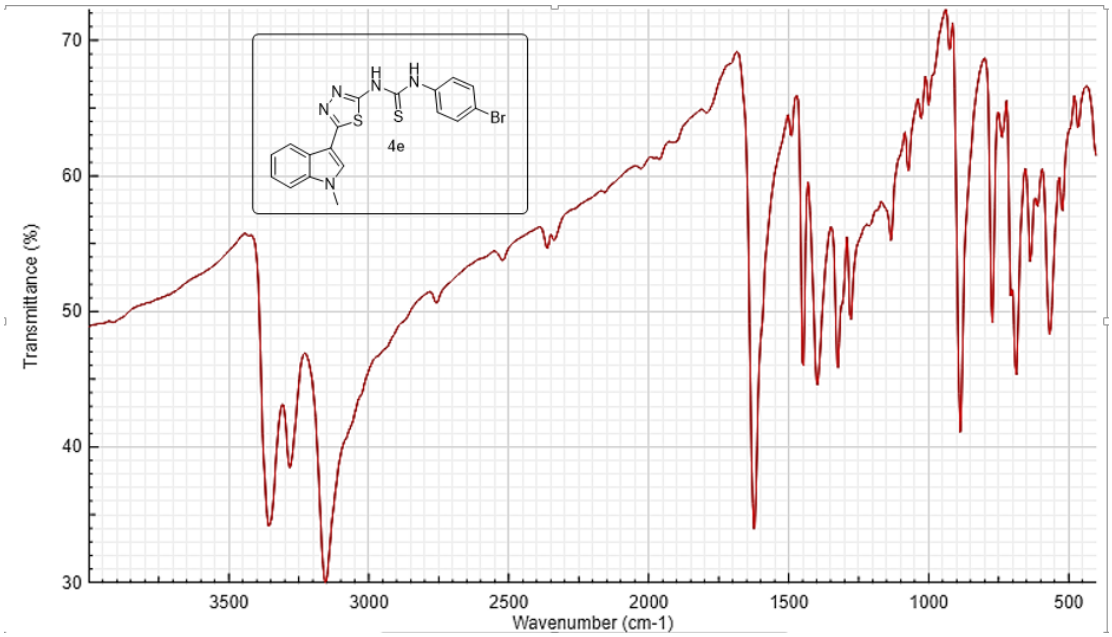

Figure 9: IR spectra of Compound 4e

Compound 4f

^{1}H NMR: δ 7.35-7.67 (10H, 7.41 (d, *J* = 8.1, Hz), 7.43 (t, *J* = 6.3, Hz), 7.49 (d, *J* = 8.1, Hz), 7.51 (d, *J* = 7.9, Hz), 7.54 (d, *J* = 8.7, Hz), 7.61 (d, *J* = 7.9, Hz)), 7.98 (1H, t, *J* = 8.7, Hz), 8.23 (1H, t, *J* = 2.6, Hz), 8.67 (1H, t, *J* = 0.4 Hz).

^{13}C NMR: δ 110.5 (1C, s), 111.4 (1C, s), 118.4 (1C, s), 120.5 (2C, s), 124.8 (1C, s), 127.1 (1C, s), 127.3 (1C, s), 127.7-127.8 (3C, 127.7 (s), 127.8 (s)), 128.4 (2C, s), 128.9 (2C, s), 133.7 (1C, s), 134.2 (1C, s), 136.4 (1C, s), 138.9-139.1 (2C, 138.9 (s), 139.0 (s)), 160.7 (1C, s), 165.1 (1C, s), 178.2 (1C, s).

Mass (m/z):461

IR (KBr, Cm^{-1}): 3049-3260(-NH-), 1610(C=N), 1509(C=C), 2970(-CH aromatic), 810(CS-Cstretching)

Compound 4g

^{1}H NMR: δ 2.20 (3H, s), 6.96 (1H, d, *J* = 8.2, Hz), 7.35-7.62 (6H, 7.41 (d, *J* = 8.1, Hz), 7.49 (d, *J* = 8.1, Hz), 7.49 (t, *J* = 8.2, 0.5 Hz), 7.57 (t, *J* = 1.8, 0.5 Hz)), 8.20 (1H, t, *J* = 0.5 Hz).

^{13}C NMR: δ 21.3 (1C, s), 110.5 (1C, s), 111.4 (1C, s), 119.9 (1C, s), 120.5 (2C, s), 124.8 (1C, s), 127.3 (1C, s), 128.9 (2C, s), 129.6 (1C, s), 133.7 (1C, s), 134.8 (1C, s), 136.4 (1C, s), 139.0 (1C, s), 160.7 (1C, s), 165.1 (1C, s), 178.2 (1C, s).

Mass (m/z):399

IR (KBr, Cm^{-1}): 3049-3260(-NH-), 1610(C=N), 1509(C=C), 2970(-CH aromatic), 810(CS-Cstretching)

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Compound 4h
^{1}H NMR: δ 7.17 (1H, d, *J* = 8.3Hz), 7.35-7.74 (6H, 7.41 (d, *J* = 8.1Hz), 7.49 (d, *J* = 8.1, Hz), 7.58 (t, *J* = 8.3, Hz), 7.69 (t, *J* = 1.7, 0.5 Hz)), 8.25 (1H, t, *J* = 0.5 Hz).
^{13}C NMR: δ 110.5 (1C, s), 112.8 (1C, s), 118.4 (1C, s), 120.5 (2C, s), 121.1 (1C, s), 124.8 (1C, s), 127.3 (1C, s), 128.9 (2C, s), 131.7 (1C, s), 133.7 (1C, s), 136.4 (1C, s), 139.0 (1C, s), 160.7 (1C, s), 165.1 (1C, s), 178.2 (1C, s).
Mass (m/z):464
IR (KBr, Cm^{-1}): 3039-3260(-NH-), 1619(C=N), 1508 (C=C), 2975(-CH aromatic), 815(CS-Cstretching)

Compound 4i
^{1}H NMR: δ 3.62 (3H, s), 6.85 (1H, d, *J* = 8.5, Hz), 7.30-7.65 (6H, 7.35 (t, *J* = 1.6, Hz), 7.41 (d, *J* = 8.1, Hz), 7.49 (d, *J* = 8.1Hz), 7.58 (t, *J* = 8.5, 0.5 Hz)), 8.33 (1H, t, *J* = 0.5 Hz).
^{13}C NMR: δ 56.0 (1C, s), 101.9 (1C, s), 110.5 (1C, s), 112.1 (1C, s), 114.5 (1C, s), 120.5 (2C, s), 124.8 (1C, s), 127.3 (1C, s), 128.9 (2C, s), 133.7 (1C, s), 136.4 (1C, s), 139.0 (1C, s), 158.8 (1C, s), 160.7 (1C, s), 165.1 (1C, s), 178.2 (1C, s)

Mass (m/z):415
IR (KBr, Cm^{-1}): 3039-3260(-NH-), 1619(C=N), 1508 (C=C), 2975(-CH aromatic), 815(CS-Cstretching)

Compound 4j
^{1}H NMR: δ 1.16 (3H, t, *J* = 7.3 Hz), 2.40 (2H, q, *J* = 7.3 Hz), 6.96 (1H, d, *J* = 8.2, 1.8 Hz), 7.35-7.61 (6H, 7.41 (d, *J* = 8.1, Hz), 7.49 (d, *J* = 8.1, Hz), 7.49 (t, *J* = 8.2, 0.5 Hz), 7.55 (t, *J* = 1.8, 0.5 Hz)), 8.21 (1H, d, *J* = 0.5, 0.4 Hz)
^{13}C NMR: δ 14.6 (1C, s), 28.7 (1C, s), 110.5 (1C, s), 111.4 (1C, s), 120.5 (2C, s), 121.2 (1C, s), 124.8 (1C, s), 127.3 (1C, s), 128.9 (2C, s), 129.9 (1C, s), 133.7 (1C, s), 136.4 (1C, s), 136.9 (1C, s), 139.0 (1C, s), 160.7 (1C, s), 165.1 (1C, s), 178.2 (1C, s).

Mass (m/z):413
IR (KBr, Cm^{-1}): 3039-3260(-NH-), 1619(C=N), 1508 (C=C), 2975(-CH aromatic), 815(CS-Stretching)

Pharmacological Activity
Antimicrobial Activity
For bacterial growth nutrient agar media was used having a composition of beef extract, 3g; bacteriological peptones, 5g; agar, 20g, the pH was adjusted to 6.2 + 0.2 at 25 (+2) °C and for fungal growth malt extract agar (MEA) was used composed of malt extract, 20 g; bacteriological peptone, 5g; agar, 20g, the pH was adjusted to 5.4 + 0.2 at 25 (+2) °C. Media was prepared by dissolving the all ingredients in 1L distilled water and heated up to 60-70°C and was sterilized in an autoclave at 121°C for 15-20 mins. Against the several species, the antibacterial and antifungal activity was expressed by the measurement of the zone of inhibition by diffusion agar method. At equal distance, four holes were made in the sterile agar plates with the help of sterile cork borer in both media i.e. in nutrient agar and in malt extract agar. The synthesized compounds were dissolved in DMSO and 100µg/ml concentration of each compound was filled in the holes. Controlled holes were filled with DMSO solvent. For bacterial isolates plates were placed in a BOD at 37°C ± 2°C and on the other hand fungal isolates were incubated at 28°C ± 2°C for 24-48 hrs. Zone of inhibition created by active compounds were measured after 24-48 hrs. Ciprofloxacin was used as standard antibacterial agent while Miconazole was used as a standard antifungal agent.

Table 2: Antimicrobial results of the synthesized and tested compounds

Compound	**Concentration (µg/ml)**	**Zone of inhibition (in mm)**					
		Gram positive		**Gram negative**		**Fungal strain**	
		B. subtilis	***S.aureus***	***P. aeruginosa***	***E.coli***	***C. albicans***	***A.niger***
4a	100	23	27	19	26	18	18
4b	100	22	26	18	26	19	16
4c	**100**	**28**	**29**	23	29	22	21
4d	100	21	25	20	24	20	15
4e	**100**	**27**	**28**	22	28	21	20
4f	100	26	27	21	26	18	18
4g	100	25	24	18	24	17	17
4h	100	24	23	17	25	16	14
4i	100	23	22	15	23	15	13
4j	100	21	23	14	22	14	12
Ciprofloxacin	**50**	**25**	**28**	**22**	**27**	-	-
Miconazole	**50**	-	-	-	-	**20**	**19**

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RESULTS

The antimicrobial activity of the synthesized compounds were assayed using cup plate technique in the nutrient agar at 100 µg/ml concentration is shown in [Table 2]. Ciprofloxacin standards were active at 50 µg/ml on all the Gram (+ve) bacteria with a zone of inhibition for Bacillus subtilis, Staphylococcus aureus, and Gram (-ve) bacteria Pseudomonas aeruginosa, Escherichia coli. From the antibacterial screening, it was concluded that compounds 4c and 4e showed a larger zone of inhibition as compared to standard drugs Ciprofloxacin and Miconazole.

CONCLUSION

All the newly synthesized 1,3,4-thiadiazole derivatives were screened for their antimicrobial activity. For antibacterial studies, microorganisms employed were Gram-positive species Bacillus subtilis, Staphylococcus aureus and Gram negative species Pseudomonas aeruginosa and for antifungal Candida albicans, A. niger species were used as organisms. The compounds with substituted rings have more activity as compared to unsubstituted rings. Compounds 4c, 4e exhibited the maximum activity because in these di substituted halogen chlorine and Bromine was substituted by electron withdrawing groups. The second reason for higher activity of 5c, 5e is another substitution by electron withdrawing groups are present.

REFERENCES

1. R. Kharb, P. Kaur, P.C. Sharma, M.S. Yar, Int. J. Res. Pharm. Bio. Sci., 2011, 2(4), 1520-1540.
2. R. Kharb, K. Bansal, A.K. Sharma, Der Pharma Chemica., 2012, 4(6), 2470-2488.
3. H. Bhuva, D. Sahu, B.N. Shah, D.C. Modi, M.B. Patel, Pharmacologyonline, 2011, 1, 528-543.
4. A. Semwal, B. Chaudhary, R. Singh, A. Bagchi, Int. J. Recent Advances Pharm. Res., 2013, 3(1), 1-13.
5. Y. Iizawa, K. Okonogi, R. Hayashi, T. Iwahi, T. Yamazaki, A. Imada, Agen.Chemother 1993, 37(1), 100.
6. S.N. Swamy, Basappa, P.S. Priya, B. Prabhuswamy, B.H. Doreswamy, J.S. Prasad, Eur. J. Med. Chem., 2006, 41, 531-538.
7. G. Mishra, A.K. Singh, K. Jyoti, Int. J. Chem. Tech. Res.,2011, 3(3),1380-1393.
8. Q.S. Chun, Z.W Nian, T.J. Hai, L.S. Yun, Z. Min, Z. Jun, Chemical Letters, 2004, 15(4), 404-407.
9. S. Waghamale, P. Piste, Int. J. Pharma. Bio Sci., 2013, 4(3), 310-332.
10. N.S. Mahajan, S.R. Pattan, R.L. Jadhav, N.V. Pimpodkar, A.M. Manikrao, Int. J. Chem. Sci., 2008, 6(2), 800- 806.
11. K.M. Basavaraja, B. Somasekhar, S. Appalaraju, Indian. J. Heterocycl. Chem.,2008,18, 69-72.
12. Kempegowda, G.P.S Kumar, D. Prakash, T.T Mani, Der Pharma Chemica., 2011, 3 (2), 330-341.
13. E. Doaa, A. Rahman, K.O Mohamed, Der Pharma Chemica., 2014, 6(1), 323-335
14. A.A. Chowki, C.S. Magdum, P.L. Ladda, S.K. Mohite, Int. J. Chem. Sci., 2008, 6(3), 1600-1605.
15. K.P. Bhusari, P.B. Khedekar, S.N. Umathe, R.H. Bahekar, R.R. Rao, Indian J. Hetero.Chem.2009, 275-278.
16. R. Basawaraj, M. Suresh, S.S. Sangapure, Indian J. Heterocycl. Chem., 2005,15, 153-156.
17. P. Mullick, S.A. Khan, S. Verma, O. Alam, Bull. Korean Chem. Soc., 2011, 32(3), 1011-1016.
18. N. Siddiqui, P. Ahuja, W. Ahsan, S.N. Pandeya, M.S. Alam, J. Chem. Pharma. Res., 2009, 1(1), 19-30.
19. J.K. Gupta, R.K. Yadav, R. Dudhe, P.K. Sharma, Int. J. Pharm. Tech. Res., 2010, 2(2): 1493-1507.
20. P. Chaturvedi, P. Valentina, P. Kamaria, Der Pharmacia Lettre, 2013, 5(4), 344-350.
21. M.M. Raj, H.V. Patel, L.M. Raj, N.K. Patel, Int. J. Pharm. Chem. Bio. Sci., 2013, 3(3), 814-819.
22. V. Rao V, R.P Yejella, A. Akula, G, S. Guntuku, B.R. Doddi, V.R Vutla, Bioorg Med Chem. LettI., 2012, 21, 430-37