



A Convenient and Efficient One-Pot Three Component Synthesis of 1,3-Bis (2-Substituted Aryl)-4,5-Diphenyl Oxazol-3(2H-Yl) Thiourea as Potential Antimicrobial Agents

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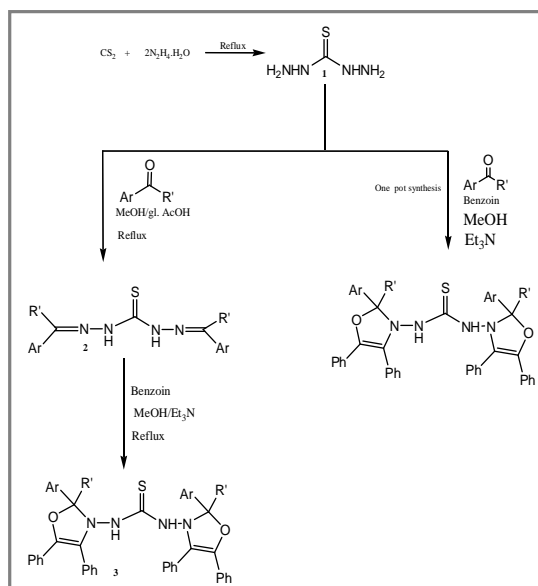
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ABSTRACT

A series of 1,3-bis (2-substituted aryl)-4,5-diphenyl oxazol-3(2H-yl) thioureas (**3**) were synthesized in a single step with a three-component protocol, using dihydraziniumthiocarbazinate, substituted araldehyde / ketone and benzoin in methanol. The structure of these compounds based on spectral (IR, ¹HNMR) as well as elemental analysis. These compounds have been screened for their antibacterial and antifungal activities. Some of them showed promising antimicrobial activity.

Graphical Abstract



Schematic diagram indicating the synthesis of compounds

Keywords: Dihydraziniumthiocarbazinate, 4, 5-diphenyl oxazol, Schiff's base, Thiourea, Pesticidal activity

INTRODUCTION

Antibiotics are among the most prescribed drugs in the world today. Several bacterial infections such as diarrhoea, food poisoning, rheumatic salmonellosis, extra intestinal and intestinal wall infections are caused by gram-positive and gram-negative pathogens [1, 2]. This resistance of pathogens bacteria towards available antibiotics is rapidly becoming a major threat world-wide to human health. In addition, the primary opportunities fungal infections continue to increase dramatically because of growing number of immune compromised patients like AIDS victims or those undergoing anticancer chemotherapy and transplantation [3-5]. Not only this, they also easily gained resistance, which is the main problem encountered in developing safe and efficient antifungal agents. Therefore, design of new antibacterial compounds in structural classes to deal with these problems is of prime interest.

Oxazoles are a class of compounds that are believed to occur in nature from post-translational modification of serine and threonine residues in peptides. They are the key building blocks of natural products, pharmaceuticals and synthetic intermediates. Oxazoles have not only attracted great interest due to their appearance as subunit of various biologically active natural products but also because of their appearance as subunit of valuable precursors in many useful synthetic transformations. Among the numerous heterocyclic moieties of biological and pharmacological interests, the oxazole ring is endowed with a vital role in the manufacture of various active drugs as brain-derived neurotropic factor induced [6], analgesic [7], trypanocidal activity [8], antimetabolic agents with pro-apoptotic activity, antifungal activity [9], anti-inflammatory [10], antidepressant [11], anticancer [12], antimicrobial and antiobesity [13].

Thiourea and its derivatives have found extensive applications in the field of medicine, agriculture and analytical chemistry. They are known to exhibit a wide variety of biological activities such as antiviral, antibacterial, antifungal [14], antitubercular, herbicidal, insecticidal [15] and act as chelating agents [16], in catalysis [17], in anion recognition [18] and to play a role in some epoxy resin curing agents [14].

The union of heterocyclic ring with thiourea linkage often results in compounds with enhanced biological performance [19]. In light of these observations and in continuation of our ongoing work on novel heterocycles with biological interest, we consider it of interest to combine oxazole nucleus with thiourea linkage to see their additive effect towards biological activities of titled compounds. Several groups have been substituted at position-2 in oxazole ring to investigate the influence of such structural variation on anticipated biological activity.

MATERIALS AND METHODS

Instrumentation: All chemicals were purchased from Aldrich Chemical Company (USA). They were used without further purification. All melting points that were measured with a capillary apparatus are uncorrected. All the compounds were checked by IR, ¹HNMR and elemental analysis. IR spectra were recorded in KBr on a Perkin-Elmer model 400 FTIR spectrometer. ¹HNMR spectra were recorded in DMSO at ambient temperature using a Bruker Avance II 400 NMR spectrometer. The following abbreviations were used to indicate the peak multiplicity s-singlet, d-doublet, t-triplet, m-multiplet. Column chromatography was performed on silica gel (Merck).

General procedure

Synthesis of sym-(substituted benzylideneamino) thioureas (2c): A mixture of dihydrazinium thiocarbazine (1.06 g, 0.01 M) and 4-hydroxy benzaldehyde (2.12 g, 0.02 M) was dissolved in methanol (30 mL) with two drops of glacial acetic acid. The reaction mixture was refluxed for 3h and then poured over crushed ice. The solid mass thus obtained was filtered, washed with excess water

and then recrystallized from aqueous ethanol; m.p. 122°C, yield 88%, IR (KBr) (cm^{-1}) 3240 (-NH), 1630 ($>\text{C}=\text{N}$), 1350 ($>\text{C}=\text{S}$), 1170 (-C-N), 1250 (C-O-C), 1600,1500,1450 cm^{-1} aromatic ring, ^1H NMR (DMSO- d_6) δ 3.75 (m, 2H, NH), 2.0(s, 2H 4.90, -OH), 4.8 (s, 1H, N=CH), 7.2 (d, 8H, aromatic).

Synthesis of bis-(substituted acetophenonehydrazono) thiocarbazine (2j): A mixture of dihydrazinium thiocarbazine (1.06 g, 0.01 M) and 4-methoxy acetophenone (3.0 g, 0.02 M) in methanol (30 mL) with two drops of glacial acetic acid. The reaction mixture was refluxed for 3h and then poured over crushed ice. The solid mass thus obtained was filtered, washed with excess of water and then recrystallized from aq. ethanol; m.p. 175°C yield 77% IR (KBr) (cm^{-1}) 3240 (-NH), 1630 ($>\text{C}=\text{N}$), 1350 ($>\text{C}=\text{S}$), 1170 (-C-N), 1250 (C-O-C), 1600,1500,1450 cm^{-1} aromatic ring, ^1H NMR (DMSO- d_6) δ 3.75 (m, 1H, NH), 2.0(s, 3H, $-\text{OCH}_3$), 4.8 (s, 1H, N=CH), 7.2 (d, 8H, aromatic).

Synthesis of 1, 3-bis (2-substituted aryl-4, 5-diphenyl oxazol-3(2H)-yl) thiourea (3c): It was prepared by refluxing a mixture of sym-(4-hydroxy benzylideneimino) thiourea (1M) with benzoin (1M) and triethyl amine (1M) in methanol 50 mL for 4h. Excess solvent was removed and then poured in to water, the solid mass thus obtained was filtered, washed with excess of water and then recrystallized from aq. ethanol; m.p. 122 °C yield 88% IR (KBr) (cm^{-1}) 3240 (-NH), 1350 (C=S), 1630 (C=N), 1170 (C-N), 1250 (C-O-C), 1600, 1500 and 1460 aromatic rings, 1670 (C=C) conjugated alkene, 3550-3500 (O-H free). ^1H NMR (DMSO- d_6) 5.95 (2H s) 7.45 (8H d) 7.30 (dd 8H) 7.15 (dd 4H) 7.0 (d, 4H), 6.70 (4H d), 2.1 (2H s NH- D₂O exchangeable) 4.90 (2H s Ar-OH).

Synthesis of 1, 3-bis (2-methyl-2-substituted phenyl-4, 5-diphenyl oxazol-3(2H)-yl) thiourea (3j): It was prepared by refluxing a mixture of bis-(4- methoxyacetophenonehydrazono) thiourea (1M) with benzoin (1M) and triethyl amine (1M) in methanol 40 mL for 4h. Excess solvent was removed and then poured in to water, the solid mass thus obtained was filtered, washed with excess of water and then recrystallized from aq. ethanol m.p. 93°C yield 80% IR (KBr) (cm^{-1}) 3240 (-NH), 2870 (- CH_3),1350 (C=S), 1630 (C=N), 1170 (C-N), 1250 (C-O-C), 1600, 1500 and 1460 aromatic rings, 1670 (C=C) conjugated alkene. ^1H NMR (DMSO- d_6) 1.7 (s 6H), 3.7 (s 6H), 7.45 (8H d), 7.30 (dd 8H), 7.15 (dd 4H), 7.0 (d, 4H), 6.70 (4H d) 2.1 (2H s, NH-).

Synthesis of 1, 3-bis (2-substituted aryl-4, 5-diphenyl oxazol-3(2H)-yl) thiourea via One-pot three component reaction: The same compound was also prepared by simple pot reaction. Thus dihydraziniumthiocarbazine (0.01M), appropriate substituted aldehyde/ substituted ketones (0.01M), Benzoin (0.01M) and triethyl amine (0.01M) taken in methanol was refluxed for 4h. Excess solvent was removed and then poured in to water, the solid mass thus obtained was filtered, washed with excess of water and then recrystallized from aq. Ethanol. The yield of the product by this method was better than two pot reaction method.

Other such compounds were also prepared in a similar way and their characterization data are given as

[3a]: 1, 3-bis(2,4,5-triphenyloxazol-3(2H)-yl) thiourea: m.p. 77°C yield 85%. IR (KBr);(cm^{-1}) 3240 (-NH), 1350 (C=S), 1630 (C=N), 1170 (C-N), 1250 (C-O-C), 1600, 1500, and 1450 aromatic rings, 1670 (C=C) conjugated alkene); ^1H NMR (DMSO- d_6) 5.95 (2H s) 7.45 (8H d) 7.30(dd 8H) 7.15 (dd 4H) 7.20 (10H m) 2.1(2H s NH-).

[3b]: 1,3-bis(2-(2-hydroxyphenyl)-4,5-diphenyloxazol-3(2H)-yl)thiourea: m.p.112°C yield 88% IR (KBr) (cm^{-1}) 3240 (-NH), 1350 (C=S), 1630 (C=N), 1170 (C-N), 1250 (C-O-C), 1600, 1500 and 1450 aromatic rings, 1670 (C=C) conjugated alkene, 3550-3500 (O-H free); ^1H NMR (DMSO- d_6) 5.95 (2H s) 7.45 (8H d) 7.30 (dd 8H) 7.15 (dd 4H) 7.0 (d, dd 4H), 6.70 (4H d,dd) 2.1 (2H s NH- D₂O exchangeable) 4.90 (2H s).

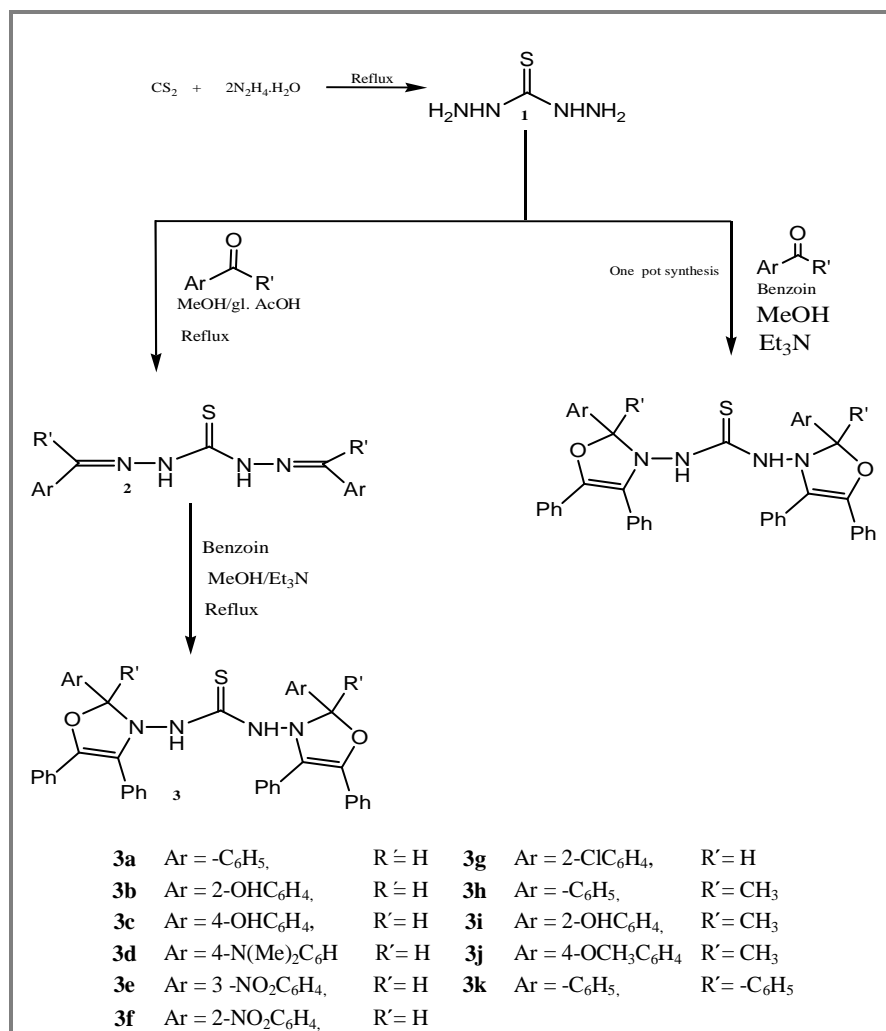


Figure 1. Schematic diagram indicating the synthesis of compounds 3a-3k

[3c]: 1,3-bis(2-(4-hydroxyphenyl)-4,5-diphenyloxazol-3(2H)-yl)thiourea: m.p. 122°C yield 88% IR (KBr) (cm⁻¹) 3240 (-NH), 1350 (C=S), 1630 (C=N), 1170 (C-N), 1250 (C-O-C), 1600, 1500, and 1450 aromatic rings, 1670 (C=C) conjugated alkene, 3550-3500 (O-H free); ¹HNMR (DMSO-d₆) 5.95 (2H s) 7.45 (8H d) 7.30 (dd 8H) 7.15 (dd 4H) 7.0 (d, 4H), 6.70 (4H d), 2.1 (2H s NH-D₂O exchangeable) 4.90 (2H s).

[3d]: 1,3-bis(2-(4-(dimethylamino)phenyl)-4,5-diphenyloxazol-3(2H)-yl)thiourea: m.p. 130°C yield 80% IR (KBr) (cm⁻¹) 3240 (-NH), 1350 (C=S), 1630 (C=N), 1170 (C-N), 1250 (C-O-C), 1600, 1500, and 1450 aromatic rings, 2940 (N-Me₃) 1670 (C=C) conjugated alkene; ¹HNMR (DMSO-d₆) 5.95 (2H s) 7.45 (8H d) 7.30 (dd 8H) 7.15 (dd 4H) 7.1 (d, 4H), 6.50 (4H d), 2.1 (2H s NH-) 2.80 (s 12 H N-Me).

[3e]: 1,3-bis(2-(3-nitrophenyl)-4,5-diphenyloxazol-3(2H)-yl)thiourea: m.p. 112°C yield 87% IR (KBr) (cm⁻¹) 3240 (-NH), 1350 (C=S), 1630 (C=N), 1170 (C-N), 1250 (C-O-C), 1600, 1500 and 1450 aromatic rings, 1560 (-N=O) 1670 (C=C) conjugated alkene; ¹HNMR (DMSO-d₆) 5.95 (2H s) 7.45 (8H d) 7.30 (dd 8H) 7.15 (dd 4H) 8.10 (s,d 4H), 7.40 (dd 2H) 7.60 (d 2H) 2.1 (2H s NH-).

[3f]: 1,3-bis(2-(2-nitrophenyl)-4,5-diphenyloxazol-3(2H)-yl)thiourea: m.p. 105°C yield 91% IR (KBr) (cm⁻¹) 3240 (-NH), 1350 (C=S), 1630 (C=N), 1170 (C-N), 1250 (C-O-C), 1600, 1500 and 1450

aromatic rings, 1560 (-N=O) 1670 (C=C) conjugated alkene; ¹HNMR (DMSO-d₆) 5.95 (2H s) 7.45 (8H d) 7.30 (dd 8H) 7.15 (dd 4H) 8.10 (d 2H), 7.40(d 4H) 7.60 (m 2H) 2.1 (2H s NH-).

[3g]: 1,3-bis(2-(2-chlorophenyl)-4,5-diphenyloxazol-3(2H)-yl)thiourea: m.p. 88°C yield 86% IR (KBr) (cm⁻¹) 3240 (-NH), 1350 (C=S), 1630 (C=N), 1170 (C-N), 710 (C-Cl), 1250 (C-O-C), 1600, 1500 and 1450 aromatic rings, 1670 (C=C) conjugated alkene; ¹HNMR (DMSO-d₆) 5.95 (2H s) 7.45 (8H d) 7.30 (dd 8H) 7.15 (dd 4H), 7.20 (d 2H) 7.1 (d, dd 4H), 7.0 (dd 2H), 2.1 (2H s NH-).

[3h]: 1,3-bis(2-methyl-2,4,5-triphenyloxazol-3(2H)-yl)thiourea: m.p. 116°C yield 93% IR (KBr) (cm⁻¹) 3240 (-NH), 1350 (C=S), 1630 (C=N), 1170 (C-N), 2870 (CH₃), 1250 (C-O-C), 160, 1500 and 1450 aromatic rings, 1670 (C=C) conjugated alkene; ¹HNMR (DMSO-d₆) 1.7 (s 6H) 7.45 (8H d) 7.30 (dd 8H) 7.15 (dd 4H), 7.20 (m 10H), 2.1 (2H s NH-).

[3i]: 1,3-bis(2-(2-hydroxyphenyl)-2-methyl-4,5-diphenyloxazol-3(2H)-yl)thiourea: m.p. 98°C yield 90% IR (KBr) (cm⁻¹) 3240 (-NH), 1350 (C=S), 1630 (C=N), 1170 (C-N), 1250 (C-O-C), 1600, 1500, and 1450 aromatic rings, 1670 (C=C) conjugated alkene, 3550-3500 (O-H free); ¹HNMR (DMSO-d₆) 1.7 (s 6H), 7.45 (8H d) 7.30 (dd 8H) 7.15 (dd 4H) 7.0 (d, dd 4H), 6.70 (4H d, dd) 2.1 (2Hs NH-) 4.90 (2H s).

[3j]: 1,3-bis(2-(4-methoxyphenyl)-2-methyl-4,5-diphenyloxazol-3(2H)-yl)thiourea: m.p. 114°C IR (KBr) (cm⁻¹) 3240 (-NH), 2870 (-CH₃), 1350 (C=S), 1630 (C=N), 1170 (C-N), 1250 (C-O-C), 1600, 1500 and 1450 aromatic rings, 1670 (C=C) conjugated alkene; ¹HNMR (DMSO-d₆) 1.7 (s 6H), 3.7 (s 6H), 7.45 (8H d) 7.30 (dd 8H) 7.15 (dd 4H) 7.0 (d, 4H), 6.70 (4H d), 2.1(2Hs NH-).

[3k]: 1-(4-methyl-2, 2, 5-triphenyloxazol-3(2H)-yl)-3-(2,2,4,5-tetraphenyloxazol-3(2H)-yl) thiourea: m. p. 100°C yield 88% IR (KBr) (cm⁻¹) 3240 (-NH), 1350 (C=S), 1630 (C=N), 1170 (C-N), 1250 (C-O-C), 1600, 1500 and 1450 aromatic rings, 1670 (C=C) conjugated alkene); ¹HNMR (DMSO-d₆) 1.7 (s 6H), 2.1 (2H s NH-), 7.45 (8H d), 7.30 (dd 8H), 7.15 (dd 4H), 7.20 (10H m).

RESULTS AND DISCUSSION

The present study describes the synthesis and antibacterial, antifungal activity in vitro of some diphenyl oxazole thiourea derivatives (3a-3k), that were tested for in vitro antibacterial and antifungal activities of the synthesized compounds were studied by the disc-diffusion method and measured by halo zone test. The diameter of the zone of inhibition was measured in mm. It was found that all the compounds were screened for their antibacterial activity against a variety of Gram-positive and Gram-negative bacterial strains, such as *E. coli* (ATCC-25922), Methicillin-resistant *S. aureus* (MRSA +ve), *Pseudomonas aeruginosa* (ATCC-27853), *Streptococcus pyogenes* and *K. pneumoniae* bacterial strains. The assaying of antifungal activity was against *C. albicans*, *Aspergillus fumigates*, *Penicillium marneffeii* and *Trichophyton mentagrophytes*. Looking at the structural activity relationship, compounds 3c, 3d, 3e, 3f and 3j exhibit significant activities, while 3d, 3e and 3f exhibit good activity as compared to standard known antibiotic, such as Ciprofloxacin that were used for comparison purposes. On the basis of the above observations, modification will be done to improve antibacterial activity, whereas the antifungal screening data showed good to moderate activity. Among the tested compounds 3d and 3j showed more potent fungicidal activity against all fungal strains.

Assignment of selected IR bands and ¹HMR spectra (400 MHz, DMSO) provides significant indications for the formation of title compounds. It may be concluded that this study describes the general method for the synthesis of some 4, 5-diphenyl oxazole thiourea derivatives under normal conditions. These results show that compounds 3c, 3d, 3e, 3f and 3j are better antibacterial agents

whereas compounds 3d and 3j exhibits excellent antibacterial as well as antifungal activity. Thus, the accumulation of the oxazole derivatives will better antibacterial as well as antifungal agents for use.

APPLICATIONS

Pharmacology: All the synthesized compounds of bis-4, 5diphenyl oxazole thiourea derivatives were evaluated for antibacterial, antifungal activities by using disk diffusion method and the Minimum Inhibitory Concentration (MIC) are summarized in Table 2 and 4 respectively.

Antibacterial activity: The newly prepared compounds were screened for their antibacterial activity against *E. coli* (ATCC-25922), Methicillin-resistant *S. aureus* (MRSA +ve), *Pseudomonas aeruginosa* (ATCC-27853), *Streptococcus pyogenes* and *K. pneumonia* (Clinical isolate) bacterial strains by disk diffusion method [20, 21].

The investigation of antibacterial screening data revealed that all the tested compounds 3c-f and 3j showed moderate to good bacterial inhibition against *S. Pyogenes* Methicillin-resistant *S. aureus* (MRSA +ve) *P. aeruginosa* *K. pneumonia* and *E. coli* species. The structure activity study showed that antimicrobial activity depends on the nature of heterocyclic moieties.

Table 1. Antibacterial activity of compounds 3c-f and 3j having promising activity
Diameter of Zone of inhibition (mm).

Compounds	<i>S. pyogenes</i>	Gram-positive bacteria		Gram-negative bacteria	
		MRSA ^a	<i>P. aeruginosa</i>	<i>K. pneumonia</i>	<i>E. coli</i>
3c	19.5±0.3	16.1±0.5	24.4±0.2	15.3±0.2	20.1±0.3
3d	21.1±0.4	20.6±0.3	23.2±0.2	19.1±0.5	20.6±0.4
3e	20.2±0.3	19.6±0.2	22.2±0.3	19.0±0.3	19.5±0.3
3f	19.9±0.4	19.3±0.3	21.2±0.4	19.0±0.3	19.5±0.3
5j	18.5±0.2	16.4±0.4	23.4±0.3	23.4±0.3	19.4±0.3
Standard	22.0±2.0	21.0±0.2	31.0±0.3	19.0±0.2	27.0±0.2
DMSO	-	-	-	-	-

Positive control (standard); Ciprofloxacin and negative control (DMSO) measured by the halo zone test (Unit, mm) a Methicillin resistant *S. aureus* (MRSA +ve)

Table 2. MIC and MBC results of compounds 3c-f and 3j and positive control Ciprofloxacin.

Compounds	<i>S. pyogenes</i>		Gram-positive bacteria				Gram-negative bacteria			
			MRSA ^a		<i>P. aeruginosa</i>		<i>K. pneumonia</i>		<i>E. coli</i>	
	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC
3c	12.5	25	12.5	25	12.5	25	12.5	50	12.5	50
3d	25	50	25	50	25	100	25	100	25	100
3e	25	50	25	50	12.5	50	25	50	25	50
3f	25	50	25	50	25	100	25	100	25	100
3j	25	50	25	50	25	100	25	100	25	100
Standard	12.5	12.5	6.25	12.5	12.5	25	6.25	25	6.25	12.5

MIC ($\mu\text{g mL}^{-1}$) minimum inhibitory concentration, i.e., the lowest concentration of the compound to inhibit the growth of bacteria completely.
MBC ($\mu\text{g mL}^{-1}$) minimum bactericidal concentration, i.e., the lowest concentration of compound for killing the bacteria completely.

Among the tested compounds, 3d and 3j showed more potent antibacterial activity (MIC $12.5 \mu\text{g mL}^{-1}$) against all bacterial strains. A comparative study also revealed that the compound 3d and 3j is less potent antibacterial agent than the compounds 3c, 3e and 3f showed effective inhibition (MIC 12.5 - $25 \mu\text{g mL}^{-1}$) against *S. pyogenes*. The maximum inhibition was observed in 3c (MIC 12.5

$\mu\text{g mL}^{-1}$) against *S. aureas* (MRSA +ve). Except 3d and 3j, all other compounds showed good activity results against *P. aeruginosa*, *K. pneumonia* and *E. coli* bacterial strains. The minimum bactericidal concentration (MBC) of the compounds was two-, three- or Four-fold higher than the corresponding MIC results.

Antifungal activity: Antifungal activity was also done by disk diffusion method. For assaying antifungal activity, *C. albicans*, *Aspergillus fumigatus*, *Penicillium marneffei* and *Trichophyton mentagrophytes* were re-cultured in DMSO by agar diffusion method [22, 23]. The inhibitory results are presented in tables 3 and 4.

Table 3. Antifungal activity of compounds 3c-f and 3j [Diameter of Zone of inhibition (mm)].

Compounds	<i>C. albicans</i>	<i>A. fumigates</i>	<i>T. mentagrophytes</i>	<i>P. marneffi</i>
3c	18.1±0.3	15.7±1.2	18.3±0.7	12.1±0.2
3d	26.2±0.4	21.1±0.3	18.4±1.2	15.8±0.3
3e	24.1±0.5	21.3±0.3	17.8±0.5	14.2±0.9
3f	18.1±0.3	16.7±1.2	17.3±0.7	13.1±0.2
5j	27.2±0.4	22.1±0.2	19.4±0.8	14.8±0.3
Standard	30.0±0.2	27.0±0.2	19.4±0.8	13.1±0.2
DMSO	-	-	-	-

Positive control (standard); Ciprofloxacin and negative control (DMSO) measured by the halo zone test (Unit, mm) a Methicillin resistant *S. aureas* (MRSA +ve)

Table 4. MIC and MFC of compounds 3c-f and 3j.

Compounds	<i>C. albicans</i>		<i>A. fumigates</i>		<i>T. mentagrophytes</i>		<i>P. marneffi</i>	
	MIC	MFC	MIC	MFC	MIC	MFC	MIC	MFC
3c	25	100	25	50	25	50	25	100
3d	12.5	25	12.5	25	12.5	50	12.5	25
3e	12.5	50	12.5	50	25	50	25	50
3f	25	50	25	50	25	50	25	100
3j	12.5	25	12.5	25	12.5	50	12.5	25
Standard	6.25	25	12.5	12.5	6.25	25	12.5	25

MIC ($\mu\text{g mL}^{-1}$) minimum inhibitory concentration i.e., the lowest concentration of the compound to inhibit the growth of fungus completely
MFC ($\mu\text{g mL}^{-1}$) minimum fungicidal concentration, i.e., the lowest concentration of the compound for killing the fungus completely.

The antifungal screening data showed good to moderate activity. All compounds showed good fungicidal activity against *C. albicans*, *Aspergillus fumigatus*, *Penicillin marneffei* and *Trichophyton mentagrophytes* fungal strains. Among the tested compounds, 3d and 3j showed more potent fungicidal activity against all fungal strains (MIC $12.5\mu\text{g mL}^{-1}$). The compounds 3c, 3e and 3f showed maximum inhibition results against *C. albicans*, and *Aspergillus fumigatus*. The inhibition activity of the compound 3c ($12.5\mu\text{g mL}^{-1}$) against *Penicillium marneffei* and *Trichophyton mentagrophytes* is significantly higher than the other tested compounds. The compounds 3d and 3j were moderately active against most of the fungal strains. The MFC of the compounds was found to be two-, three- or Four-fold higher than the corresponding MIC results.

Thus, the nature of heterocycles and basic skeleton of molecules have significant influence on the extent of antibacterial and antifungal activities. A comparative study of the results (Tables 1, 2, 3 and 4) with standard drugs (Ciprofloxacin and Griseofulvin) revealed that none of the compounds exceed the activity of commercial drugs.

CONCLUSIONS

In the present study, the antibacterial and antifungal activities of the oxazole thiourea derivatives were investigated. The compounds (3d-3f) displayed good antibacterial activity as compared to Ciprofloxacin whereas compounds 3d and 3j also displayed good antifungal agents. Thus, the newly synthesized compounds can be used as template for future development through modification and derivatives to design more potent and selective antimicrobial as well as antifungal agents.

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