

Synthesis and antimicrobial evaluation of novel heterocyclic compounds containing thiosemicarbazone

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Abstract

Herein, six novel heterocyclic compounds containing thiosemicarbazone were obtained by the condensation reaction of thiazole with thiosemicarbazide and benzaldehyde derivatives. The structures of newly obtained thiosemicarbazone-based heterocyclic compounds were investigated by spectroscopic methods (element analysis, infrared spectra (IR), proton nuclear magnetic resonance (¹H-NMR), high resolution mass spectrometry (HRMS), scanning electron microscopy and energy dispersive X-ray (SEM-EDX). The antimicrobial efficiency of the obtained thiosemicarbazone-based heterocyclic compounds was screened *in vitro* against some pathogenic bacteria and yeast as potential medicinal agents. New heterocyclic compounds containing thiosemicarbazone were determined to be effective in varying degrees at inhibiting the activity of the tested disease-causing pathogenic strains. The heterocyclic compounds were found to show high or moderate antimicrobial activity. It was found that the synthesized heterocyclic compounds showed high or moderate antimicrobial activity.

Keywords

heterocyclic compounds, thiosemicarbazide, condensation reaction, antimicrobial activity

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Introduction

Schiff bases are obtained by condensation reaction from primary amines with aldehydes or ketones derivatives and also are called imine or azomethine. Schiff bases and metal complexes are extensively researched owing to their multidirectional applications in coordination chemistry, pharmaceutical chemistry, biochemistry, analytical chemistry, supramolecular chemistry, organic chemistry, bioinorganic chemistry, medicine, catalysis, metallurgy, dye industry, material science, photography, agriculture.^{1–5}

Thiosemicarbazones (RNH-CS-NH-N=CR'R'') are an important and interesting class of Schiff bases.⁶ Thiosemicarbazone compounds possess a range of potential applications such as luminescence property, catalytic activity, magnetic property, disperse dyes property.^{7,8} Thiosemicarbazones also have anticorrosion, antifouling, and plant growth-promoting activities.^{6,9} Additionally, thiosemicarbazones act in the inhibition of RNR (ribonucleotide reductase) enzyme, which is significant in cell replication.¹⁰ Especially, thiosemicarbazones containing sulphur and small hydrophobic moieties are highly effective in inhibiting the RNR enzyme.¹¹ Thiosemicarbazones are widely investigated owing to their biological, chemical, pharmacological

and medical features. Such heterocycles have a wide range of activities such as antimicrobial, anticancer, antimalarial, antioxidant, antibacterial, antiplatelet, antitumor, anti-inflammatory, antiparasitic, hypoglycemic, antitubercular, anticonvulsant, analgesic, anti-HIV, antiviral, herbicidal, antiproliferative, haemolytic, antiamebic activity and cytotoxic activities.^{12–21} Heterocyclic compounds can be used as catalysts and dyes.^{22–23} Thiazoles are cyclic organic compounds and possess a broad of applications such as sensors, agrochemicals, liquid crystals, and pharmacological activities.²⁴

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Especially thiosemicarbazones containing thiazole are of great importance compounds because of their therapeutic, biological and pharmacological activities. These compounds containing azomethine nitrogen and thiocarbonyl sulphur donor atoms form metal complexes and show various biological activities.^{25–27} Heterocyclic thiosemicarbazone complexes have various antifungal and antibacterial, biological, and cytotoxic activities.^{28–30}

In the present study, new heterocyclic compounds containing thiosemicarbazone were prepared by condensations between benzaldehyde derivations and thiosemicarbazone-based heterocyclic compounds to evaluate them as potential antibacterial and antifungal agents. The structural significance and difference of the newly synthesized heterocyclic thiosemicarbazone compounds is that they have the potential to exhibit superior biological activity due to the presence of two azomethine groups.

Experimental

Chemicals and devices

All materials were supplied from Sigma-Aldrich or Merck. Elemental analyses were taken with a Thermo Scientific Flash 2000 model elemental analyzer. IR was recorded using a Shimadzu IR Prestige-21 model spectrophotometer at 400 to 4000 cm^{-1} . ^1H -NMR spectra were performed on a Bruker Biospin brand Avance III 400 MHz model device. HRMS analyzes were obtained using a Waters brand SYNAPT G1 MS model device. SEM-EDX images were performed with a Quanta FEG 250 device.

Common method for the synthesis of heterocyclic compounds containing thiosemicarbazone

All heterocyclic compounds containing thiosemicarbazone (MTSC-Br, MTSC-Cl, MTSC-CH₃, FTSC-Br, FTSC-Cl, and FTSC-CH₃) were obtained by condensations by the same common method as shown in Figure 1. Novel thiosemicarbazone-based heterocyclic compounds were obtained by adding of 4-methyl-3-thiosemicarbazide or 4-phenylthiosemicarbazide (4 mmol) to a stirred mixture of 2-aminothiazole-5-carboxaldehyde (4 mmol) in ethyl alcohol (50 mL) and heated at 90 °C for 4 h. The pH of the solution was adjusted to 5–5.5 by adding 1 mL of acetic acid. 5-chlorosalicylaldehyde or 5-methylsalicylaldehyde or 5-bromosalicylaldehyde (4 mmol) was added to the mixture, and then was stirred under reflux for another 2 h at 90 °C. The solution was cooled to room temperature, and purified with ethyl alcohol, filtered, and the colored product was obtained.

The composition of all heterocyclic compounds containing thiosemicarbazone was determined by SEM-EDX analysis, HRMS spectrum, elemental analysis, FT-IR, and ^1H -NMR spectra.

MTSC-Br. Yield, 57%; Dark red solid; m.p. 218–220 °C; IR (KBr, ν , cm^{-1}): 3347 (OH), 3030 (CH)_{aro.}, 1622 ($\text{CH}=\text{N}$), 1516 ($\text{CH}=\text{N}$)_{tyz.}, 1454 ($\text{C}=\text{C}$), 1207, 828 ($\text{C}=\text{S}$), 760 ($\text{C}-\text{S}-\text{C}$), 1026 (N-N), 3280 (N-H); ^1H -NMR (400 MHz, DMSO-d₆, ppm): 11.68 (1H, s, N-NH), 11.24 (1H, s, Me-NH), 10.21 (1H, s, Ar-OH), 9.61, 9.27 (1H, s, $\text{CH}=\text{N}$), 6.81–8.59 (5H, m, Ar-H), 1.91 (3H, s, HN-CH₃); HRMS ES⁺ (m/z): 399.97 [$\text{M}+2\text{H}$]⁺; Elemental analysis (calcd. (found), C₁₃H₁₂N₅S₂OBr): C: 39.20 (42.02), H: 3.02 (4.13), N: 17.59 (15.54), S: 16.08 (17.76). (+) ESI-HRMS m/z: calculated for [C₁₃H₁₂N₅S₂OBr + 2H]⁺ 400.00, observed 399.97.

MTSC-Cl. Yield, 62%; Dark brown solid; m.p. 209–211 °C; IR (KBr, ν , cm^{-1}): 3348 (OH), 2994 (CH)_{aro.}, 1598 ($\text{CH}=\text{N}$), 1547 ($\text{CH}=\text{N}$)_{tyz.}, 1481 ($\text{C}=\text{C}$), 1202, 829 ($\text{C}=\text{S}$), 763 ($\text{C}-\text{S}-\text{C}$), 1034 (N-N), 3138 (N-H); ^1H -NMR (400 MHz, DMSO-d₆, ppm): 11.50 (1H, s, N-NH), 11.23 (1H, s, Me-NH), 10.23 (1H, s, Ar-OH), 9.61, 9.28 (1H, s, $\text{CH}=\text{N}$), 6.86–8.60 (5H, m, Ar-H), 1.91 (3H, s, HN-CH₃); HRMS ES⁺ (m/z): 352.01 ([$\text{M}-2\text{H}$])⁺; Elemental analysis (calcd. (found), C₁₃H₁₂N₅S₂OCl): C: 44.07 (42.01), H: 3.39 (4.97), N: 19.77 (18.54), S: 18.08 (21.27). (+) ESI-HRMS m/z: calculated for [C₁₃H₁₂N₅S₂OCl-2H]⁺ 352.00, observed 352.01.

MTSC-CH₃. Yield, 50%; Dark brown solid; m.p. 207–209 °C; IR (KBr, ν , cm^{-1}): 3354 (OH), 2999 (CH)_{aro.}, 1595 ($\text{CH}=\text{N}$), 1548 ($\text{CH}=\text{N}$)_{tyz.}, 1522 ($\text{C}=\text{C}$), 1203, 840 ($\text{C}=\text{S}$), 799 ($\text{C}-\text{S}-\text{C}$), 1030 (N-N), 3142 (N-H); ^1H -NMR (400 MHz, DMSO-d₆, ppm): 11.40 (1H, s, N-NH), 11.23 (1H, s, Me-NH), 10.21 (1H, s, Ar-OH), 9.68, 9.27 (1H, s, $\text{CH}=\text{N}$), 6.79–8.33 (5H, m, Ar-H), 1.91 (3H, s, HN-CH₃), 1.06 (3H, s, Ar-CH₃); HRMS ES⁺ (m/z): 332.07 ([$\text{M}-\text{H}$])⁺; Elemental analysis (calcd. (found), C₁₄H₁₅N₅S₂O): C: 50.45 (47.18), H: 4.50 (3.02), N: 21.02 (19.18), S: 19.22 (22.17). (+)ESI-HRMS m/z: calculated for [C₁₄H₁₅N₅S₂O-H]⁺ 332.00, observed 332.07.

FTSC-Br. Yield, 71%; Metallic bronze solid; m.p. 225–227 °C; IR (KBr, ν , cm^{-1}): 3300 (OH), 2980 (CH)_{aro.}, 1593 ($\text{CH}=\text{N}$), 1550 ($\text{CH}=\text{N}$)_{tyz.}, 1495 ($\text{C}=\text{C}$), 1251, 872 ($\text{C}=\text{S}$), 794 ($\text{C}-\text{S}-\text{C}$), 1082 (N-N), 3150 (N-H); ^1H -NMR (400 MHz, DMSO-d₆, ppm): 11.63 (1H, s, N-NH), 11.03 (1H, s, Ph-NH), 10.21 (1H, s, Ar-OH), 9.59, 8.18 (1H, s, $\text{CH}=\text{N}$), 6.98–7.72 (5H, m, Ar-H); HRMS ES⁺ (m/z): 457.97 [M]⁺; Elemental analysis (calcd. (found), C₁₈H₁₄N₅S₂OBr): C: 46.96 (43.91), H: 3.04 (4.57), N: 15.22 (13.29), S: 13.92 (16.04). (+)ESI-HRMS m/z: calculated for [C₁₈H₁₄N₅S₂OBr-3H]⁺ 457.00, observed 457.97.

FTSC-Cl. Yield, 66%; Mustard colour solid; m.p. 212–214 °C; IR (KBr, ν , cm^{-1}): 3333 (OH), 2970 (CH)_{aro.}, 1593 ($\text{CH}=\text{N}$), 1548 ($\text{CH}=\text{N}$)_{tyz.}, 1508 ($\text{C}=\text{C}$), 1271, 853

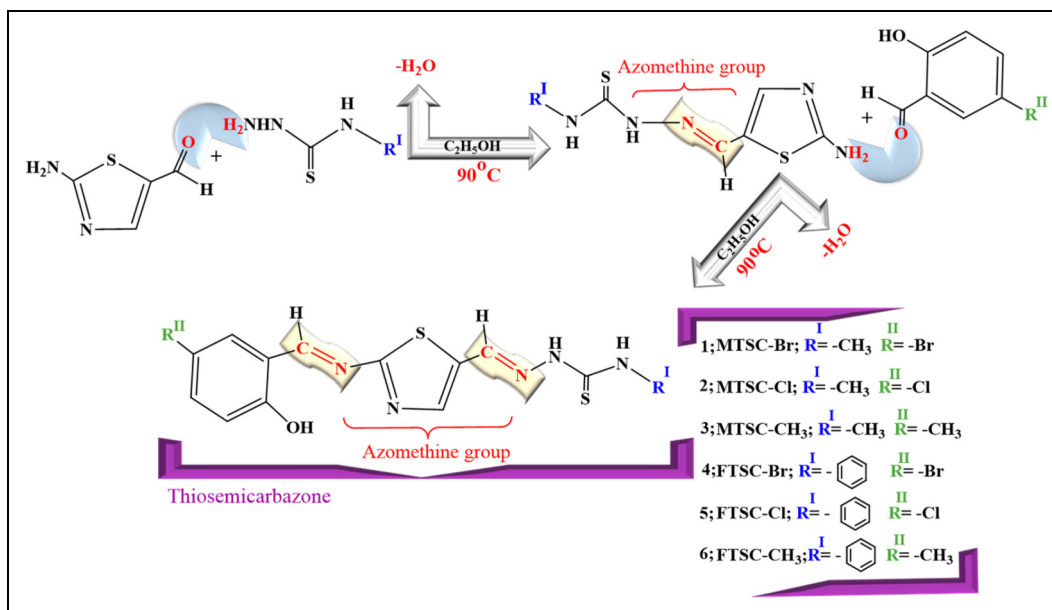


Figure 1. Synthesis reaction of heterocyclic compounds (1; MTSC-Br, 2; MTSC-Cl, 3; MTSC-CH₃, 4; FTSC-Br, 5; FTSC-Cl, 6; FTSC-CH₃).

(C = S), 748 (C-S-C), 1088 (N-N), 3127 (N-H); ¹H-NMR (400 MHz, DMSO-d₆, ppm): 11.63 (1H, s, N-NH), 11.01 (1H, s, Ph-NH), 10.23 (1H, s, Ar-OH), 9.58, 8.18 (1H, s, CH = N), 7.02–7.66 (5H, m, Ar-H); HRMS ES⁺ (m/z): 414.03 ([M]⁺; Elemental analysis (calcd. (found), C₁₈H₁₄N₅S₂OCl): C: 51.92 (49.42), H: 3.37 (4.87), N: 16.83 (14.61), S: 15.38 (17.98). (+)ESI-HRMS m/z: calculated for [C₁₈H₁₄N₅S₂OCl-2H]⁺ 414.00, observed 414.03.

FTSC-CH₃. Yield, 83%; Dark mustard solid; m.p.202–204° C; IR (KBr, ν, cm⁻¹): 3396 (OH), 2932 (CH)_{aro.}, 1593 (CH = N), 1550 (CH = N)_{lyz.}, 1497 (C = C), 1265, 824 (C = S), 748 (C-S-C), 1074 (N-N), 3130 (N-H); ¹H-NMR (400 MHz, DMSO-d₆, ppm): 11.63 (1H, s, N-NH), 11.51 (1H, s, Ph-NH), 10.22 (1H, s, Ar-OH), 9.59, 8.19 (1H, s, CH = N), 6.89–7.66 (5H, m, Ar-H), 1.91 (3H, s, HN-CH₃), 1.06 (3H, s, Ar-CH₃), 2.24 (3H, s, Ar-CH₃); HRMS ES⁺ (m/z): 394.09 ([M-H]⁺; Elemental analysis (calcd. (found), C₁₉H₁₇N₅S₂O): C: 57.72 (59.04), H:4.30 (3.17), N: 17.72 (19.84), S: 16.20 (18.66). (+)ESI-HRMS m/z: calculated for [C₁₉H₁₇N₅S₂O-H]⁺ 394.00, observed 394.09.

Antimicrobial assay

The antimicrobial efficiencies of the heterocyclic compounds containing thiosemicarbazone were assessed against some pathogenic Gram-positive bacteria (*Micrococcus luteus* ATCC9341, *Listeria monocytogenes* ATCC19115, *Bacillus cereus* RSKK863, *Staphylococcus epidermidis* ATCC12228, *Staphylococcus aureus* ATCC25923), and some pathogenic Gram-negative bacteria (*Klebsiella pneumonia* ATCC27853,

Salmonella typhi H NCTC9018394, *Pseudomonas aeruginosa* ATCC2785, *Proteus vulgaris* RSKK96026, *Listeria monocytogenes* ATCC19115) and yeast (*Candida albicans* Y-1200-NIH) by the well-diffusion technique.³¹ Dimethylformamide (DMF) was used as solvent control in this technique and was found to have no antibacterial and antifungal efficiency against any of the organisms tested. All thiosemicarbazone-based heterocyclic compounds were solved (3.5 µg/mL) in DMF. Pathogens were incubated in Nutrient Broth agar (10⁶ CFU/mL) for 24 h at 37 °C. After that, these cultures were homogenized by adding them to Mueller-Hinton Agar (MHA), cooled to 45 °C, and cooled by pouring them into sterile petri dishes. Then, 6 mm diameter wells were opened in these agars, and the thiosemicarbazone-based heterocyclic compounds were added. The plates were incubated in an oven at 37°C for 24 h, and the inhibition zone of each compound was then measured, and the average of two replicate activity values was taken.

Additionally, standard antibiotics were used: kanamycin (K30), sulphamethoxazole (SXT25), amoxicillin (AMC30), ampicillin (AMP10) and nystatin (NYS100). Pathogenic bacteria were compared to K30, SXT25, AMC30, AMP10 antibiotics, and yeast were compared to NYS100.

Results and discussion

Characterization of heterocyclic compounds containing thiosemicarbazone

Some analytical data of all heterocyclic compounds are given in Table 1. It was found that the chemical formulas

Table 1. Elemental analyses and some analytical data of heterocyclic compounds.

Compound	Chemical Formula	Colour / Yield (%)	Elemental analysis (calc.) %			
			C	H	N	S
MTSC-Br	C ₁₃ H ₁₂ N ₅ S ₂ OBr (398)	Dark red / 57%	39.20 (42.02)	3.02 (4.13)	17.59 (15.54)	16.08 (17.76)
MTSC-Cl	C ₁₃ H ₁₂ N ₅ S ₂ OCl (354)	Dark brown / 62%	44.07 (42.01)	3.39 (4.97)	19.77 (18.54)	18.08 (21.27)
MTSC-CH ₃	C ₁₄ H ₁₅ N ₅ S ₂ O (333)	Dark brown / 50%	50.45 (47.18)	4.50 (3.02)	21.02 (19.18)	19.22 (22.17)
FTSC-Br	C ₁₈ H ₁₄ N ₅ S ₂ OBr (460)	Metallic bronze / 71%	46.96 (43.91)	3.04 (4.57)	15.22 (13.29)	13.92 (16.04)
FTSC-Cl	C ₁₈ H ₁₄ N ₅ S ₂ OCl (416)	Mustard colour / 66%	51.92 (49.42)	3.37 (4.87)	16.83 (14.61)	15.38 (17.98)
FTSC-CH ₃	C ₁₉ H ₁₇ N ₅ S ₂ O (395)	Dark / 83%	57.72 (59.04)	4.30 (3.17)	17.72 (19.84)	16.20 (18.66)

Table 2. IR vibration frequencies (cm⁻¹) of heterocyclic compounds.

Compound	$\nu(\text{OH})$	$\nu(\text{CH})_{\text{aro.}}$	$\nu(\text{CH}=\text{N})/ \nu(\text{CH}=\text{N})_{\text{tyz.}}$	$\nu(\text{C}=\text{C})$	$\nu(\text{C}=\text{S})$	$\nu(\text{C}-\text{S}-\text{C})$	$\nu(\text{N}-\text{N}) / \nu(\text{N}-\text{H})$
MTSC-Br	3347	3030	1622 1516	1454	1207 828	760	1026 3280
MTSC-Cl	3348	2994	1598 1547	1481	1202 829	763	1034 3138
MTSC-CH ₃	3354	2999	1595 1548	1522	1203 840	799	1030 3142
FTSC-Br	3300	2980	1593 1550	1495	1251 872	794	1082 3150
FTSC-Cl	3333	2970	1593 1548	1508	1271 853	748	1088 3127
FTSC-CH ₃	3396	2932	1593 1550	1497	1265 824	748	1074 3130

of the compounds were compatible with the of elemental analysis results.

IR spectra data for heterocyclic compounds containing thiosemicarbazone are given in Table 2 and are demonstrated in Figure S-1. $\nu(\text{CH}=\text{N})$ stretching vibrations of azomethine groups obtained by the reaction of amines with aldehydes, were determined in the 1593–1622 cm⁻¹ and 1516–1550 cm⁻¹ regions, respectively. The stretching vibrations of $\nu(\text{C}-\text{S}-\text{C})$ belonging to the thiazole groups appeared in the ranges 748–799 cm⁻¹. The stretching vibrations of $\nu(\text{OH})$, $\nu(\text{CH})$, $\nu(\text{C}=\text{C})$ aromatic ring, $\nu(\text{N}-\text{H})$ and $\nu(\text{N}-\text{N})$ were determined in the 3300–3396 cm⁻¹, 2932–3030 cm⁻¹, 1454–1522 cm⁻¹, 1026–1088 cm⁻¹ and 3127–3280 cm⁻¹, ranges, respectively. In addition, $\nu(\text{C}=\text{S})$ absorption bands were observed in the 828–872 cm⁻¹ and 1202–1271 cm⁻¹ regions, respectively. In addition, $\nu(\text{C}=\text{S})$ vibrations were determined in the 828–872 cm⁻¹ and 1202–1271 cm⁻¹ regions, respectively.^{32,33}

Characteristic ¹H-NMR spectrum data for heterocyclic compounds containing thiosemicarbazone are given in Table 3 and are demonstrated in Figure S-2. The peaks of unsymmetrical azomethines (CH=N) achieved by the condensation reaction of amines and aldehydes, were observed in the 8.18–9.28 ppm and 9.58–9.68 ppm ranges, respectively. Because of the dissimilar chemical environment of NH protons (N-NH and Me-NH), in the ¹H-NMR spectra of MTSC-Br, MTSC-Cl, and MTSC-CH₃ were observed

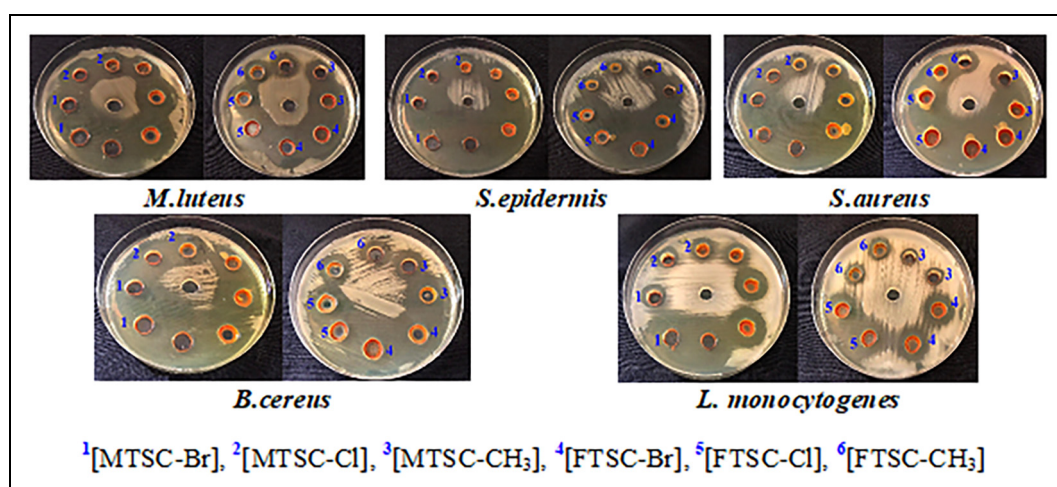
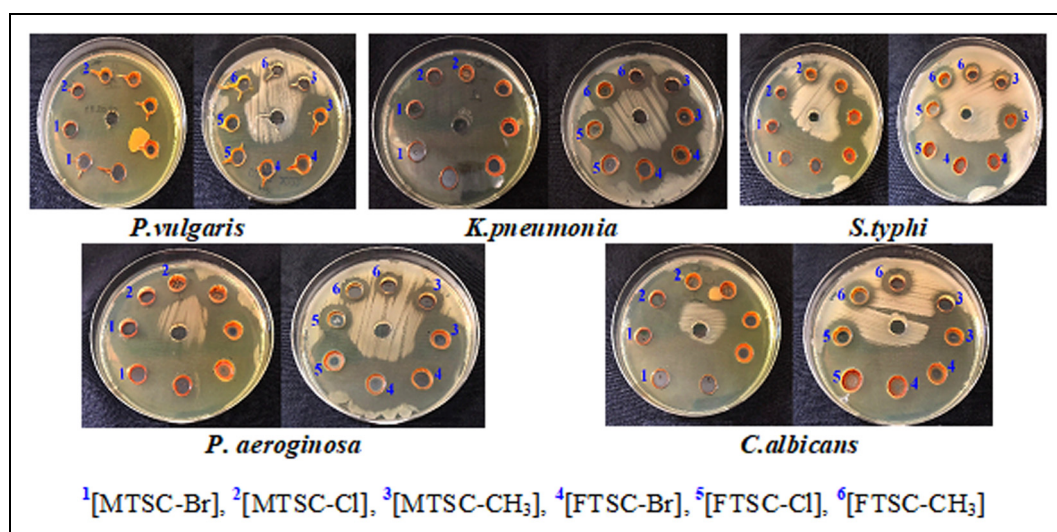
two signals in the 11.40–11.68 ppm and 11.23–11.24 ppm ranges, respectively. For FTSC-Br, FTSC-Cl, and FTSC-CH₃, (N-NH) and (Ph-NH) signals were determined in the 11.63–11.63 ppm and 10.51–11.03 ppm regions, respectively. The aromatic (Ar-H) and phenolic (Ar-OH) protons were revealed in the ranges 10.21–10.23 ppm and 6.79–8.60 ppm, respectively. In addition, the peaks attributable to methyl protons (HN-CH₃) in MTSC-Br, MTSC-Cl, and MTSC-CH₃ were observed at 1.91 ppm. The methyl proton (Ar-CH₃) in MTSC-CH₃ and FTSC-CH₃ were also observed at 1.06 ppm and 2.20 ppm, respectively.^{34–35}

SEM-EDX analyzes of heterocyclic compounds containing thiosemicarbazone are given in Figure S-3. According to the SEM images, which provide information about the morphology, it was seen that the thiosemicarbazone-based heterocyclic compounds had a crystal structure (layer or cloud or rock salt-shaped) in small particles. Also, EDX analyzes confirmed the chemical composition of the thiosemicarbazone-based heterocyclic compounds, including C, O, S, N, Cl, Br, *etc.* atoms.

The photographs of inhibition regions and the graphical representation of pathogenic bacteria for antimicrobial efficiency of heterocyclic compounds containing thiosemicarbazone are demonstrated in Figures 2, 3, and in Figures 4, 5, respectively. The obtained thiosemicarbazone compounds were investigated *in vitro* for antibacterial and antifungal efficiencies against selected disease-causing

Table 3. $^1\text{H-NMR}$ chemical shift (ppm) of heterocyclic compounds.

Compound	N-NH	Me-NH	Ph-NH	Ar-OH	CH = N	Ar-H	HN-CH ₃ /Ar-CH ₃
MTSC-Br	11.68	11.24	-	10.21	9.61, 9.27	6.81–8.59	1.91 /-
MTSC-Cl	11.50	11.23	-	10.23	9.61, 9.28	6.86–8.60	1.91 /-
MTSC-CH ₃	11.40	11.23	-	10.21	9.68, 9.27	6.79–8.33	1.91 / 1.06
FTSC-Br	11.63	-	11.03	10.21	9.59, 8.18	6.98–7.72	- /-
FTSC-Cl	11.63	-	11.01	10.23	9.58, 8.18	7.02–7.66	- /-
FTSC-CH ₃	11.63	-	10.51	10.22	9.59, 8.19	6.89–7.66	- / 2.24

**Figure 2.** Photographs of inhibition zones (mm) of some Gram (+) bacteria.**Figure 3.** Photographs of inhibition zones (mm) of some Gram (-) bacteria and yeast.

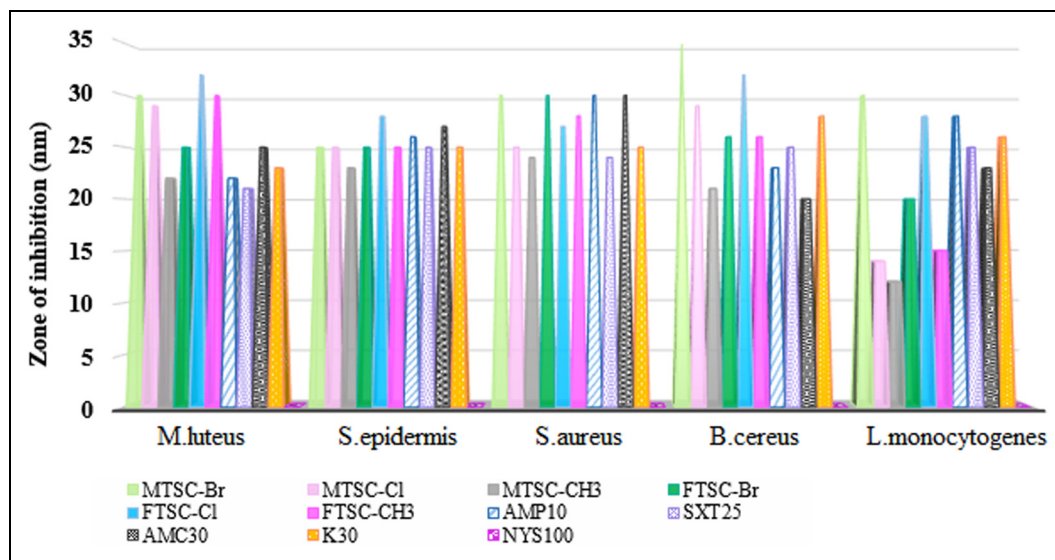


Figure 4. Graphical illustration of Gram (+) pathogenic bacteria and standard antibiotics.

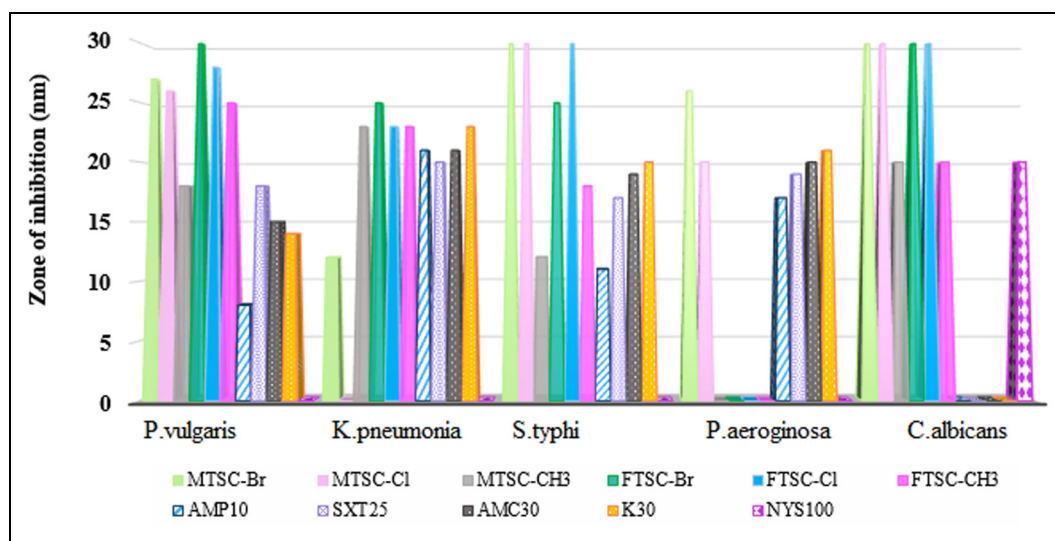


Figure 5. Graphical illustration of Gram (-) pathogenic bacteria and standard antibiotics.

pathogenic bacteria and yeast. According to the results of the antimicrobial investigation, the thiosemicarbazone-based heterocyclic compounds were determined to inhibit the tested pathogens to different degrees. *S. epidermidis*, *M. luteus*, *B. cereus*, *L. monocytogenes*, and *S. aureus* were used as Gram-positive bacteria. MTSC-Br showed the highest antibacterial efficiency against *B. cereus* (35 mm). MTSC-Br also showed higher activity against *M. luteus* (30 mm), *L. monocytogenes* (30 mm), and *S. aureus* (30 mm). *B. cereus* is an opportunist and contaminating pathogen that causes food poisoning.³⁶ MTSC-Cl exhibited the most inhibitory effect against *B. cereus*

(29 mm) and *M. luteus* (29 mm). *M. luteus* is a pathogen that causes various infections, such as septic shock, endocarditis, meningitis, and septic arthritis.³⁷ MTSC-CH₃ and FTSC-Br demonstrated the highest efficiency against *S. aureus* (24 mm / 30 mm). *S. aureus* pathogen causes various diseases such as skin soft tissue.³⁸ FTSC-Cl showed the highest antibacterial effect against *M. luteus* (32 mm) and *B. cereus* (32 mm). FTSC-CH₃ exhibited the most inhibitory effect against *M. luteus* (30 mm) in Gram-positive bacteria. *K. pneumonia*, *S. typhi* H, *P. vulgaris*, and *P. aeruginosa* were used as Gram-negative bacteria. MTSC-Br, MTSC-Cl, and

FTSC-Cl demonstrated the highest antibacterial efficiency against *S. typhi* H (34 mm). *S. typhi* H is a bacteria responsible for typhoid and paratyphoid diseases.³⁹ MTSC-CH₃ showed the highest activity against *K. pneumonia* (23 mm). It is an opportunistic pathogen that infects via medical devices such as catheters and causes urinary infections, osteomyelitis, and bacteremia.⁴⁰ FTSC-Br and FTSC-CH₃ exhibited the most inhibitory effect against *P. vulgaris* (30 mm / 25 mm). *P. vulgaris* is a bacteria that causes wound infections, nosocomial infections, and urinary tract infections such as cystitis, and prostatitis.⁴¹ MSTSC-CH₃, FTSC-Br, FTSC-Cl, and FTSC-CH₃ did not show inhibition efficiency against *K. pneumonia* among Gram-negative bacteria, while MTSC-Cl did not show activity against *P. aeruginosa*. The effects of thiosemicarbazone-based heterocyclic compounds against the yeast *C. albicans* were examined in comparison with the standard antibiotic nystatin. MTSC-Br (38 mm), MTSC-Cl (35 mm), FTSC-Br (31 mm), FTSC-Cl (35 mm) were more effective than nystatin. MTSC-CH₃ (20 mm) and FTSC-CH₃ (20 mm) were effective as nystatin. It was observed that the antifungal efficiencies of thiosemicarbazone-based heterocyclic compounds, including the electron-withdrawing group (Br / Cl) were more effective than the thiosemicarbazone-based heterocyclic compounds, including the electron donating group (CH₃). MTSC-Br showed quite higher (about twice) antifungal activity than *C. albicans*. It is a fungus that causes infections such as the oral cavity, vagina, gastrointestinal tract, and blood stream.⁴²

According to the results, heterocyclic compounds containing thiosemicarbazone exhibited high or moderate antimicrobial efficiency in comparison to standard antibiotics. It was observed that different functional groups increased or decreased the antimicrobial activity of thiazole-based thiosemicarbazones. All thiosemicarbazone-based heterocycles were determined to be more effective against gram-positive than gram-negative bacteria. It was determined that MTSC-Br showed the highest activity against Gram (+) bacteria (*B. cereus*), Gram (-) bacteria (*S. typhi* H), and yeast (*C. albicans*). As a result, it can be said that all thiosemicarbazone-based heterocyclic compounds are biologically active compounds and it can be predicted that they can be used as potential antibacterial and antifungal agents.

Conclusion

Heterocyclic thiosemicarbazones, which are an important class of Schiff bases and contain groups such as azomethine and sulphur, have very diverse biological efficiencies. Therefore, it is important to synthesize new heterocyclic thiosemicarbazones as potential antimicrobial agents. Herein, novel heterocyclic compounds containing thiosemicarbazone were synthesized by condensation reaction and

characterized by some spectral techniques. Antibacterial and antifungal effects of novel thiosemicarbazone-based heterocycles were evaluated *in vitro* against selected pathogens causing disease. It was observed that electron-withdrawing/-donating groups in heterocyclic compounds affected the antimicrobial activity against the tested pathogens. Antimicrobial activity results demonstrated that the synthesized thiosemicarbazone-based heterocyclic compounds were highly/moderately effective against selected pathogenic bacteria and yeast. In conclusion, novel heterocyclic compounds containing thiosemicarbazone can be recommended as potent antibacterial and antifungal agents for use in some applications such as biology, medicine, and pharmacy.

Highlights

Novel heterocyclic compounds containing thiosemicarbazone (MTSC-Br, MTSC-Cl, MTSC-CH₃, FTSC-Br, FTSC-Cl and FTSC-CH₃) were synthesized by the condensation reaction.

The heterocyclic compounds were characterized by means of spectral measurements. (element analysis, infrared spectra, proton nuclear magnetic resonance, high resolution mass spectrometry, scanning electron microscopy and energy dispersive X-ray).

The antibacterial and antifungal activities of the heterocyclic compounds were evaluated against some disease-causing pathogenic bacteria and yeast as potential medicinal agents.

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Supplemental material

Supplemental material for this article is available online.

References

1. Ghosh P, Dey SK, Ara H, et al. A review on synthesis and Versatile applications of some selected Schiff bases with their transition metal complexes. *Egypt J Chem* 2019; 62: 523–547.

2. Kumar S, Dhar DN and Saxena PN. Applications of metal complexes of Schiff bases-A review. *J Sci Ind Res* 2009; 68: 181–187.
3. Karmaz E, Özkan EH, Yetim NK, et al. New nanospheres to use in the determination of Imidan Phosmet and Vantex Pesticides. *J Inorg Organomet Polym* 2021; 31: 2915–2924.
4. Kurnaz NY, Özkan EH, Özcan C, et al. Preparation of AChE immobilized microspheres containing thiophene and furan for the determination of pesticides by the HPLC-DAD method. *J Mol Struct* 2020; 1222: 128931. 1–11.
5. Uddin MN, Ahmed SS and Rahatul ASM. Review: biomedical applications of schiff base metal complexes. *J Coord Chem* 2020; 73: 3109–3149.
6. Khalid M, Jawaria R, Khan MU, et al. An efficient synthesis, spectroscopic characterization, and optical nonlinearity response of novel salicylaldehyde thiosemicarbazone derivatives. *ACS Omega* 2021; 6: 16058–16065.
7. Laverick RJ, Carter AB, Klein HA, et al. Synthesis and characterisation of Fe(III) and Co(III) complexes of thiazole-containing thiosemicarbazone ligands. *Inorganica Chim Acta* 2017; 463: –8.
8. Gaffer HE and Khalifa ME. Eco-friendly synthesis of some thiosemicarbazones and their applications as intermediates for 5-arylthiazole disperse dyes. *Molecules* 2015; 20: 21982–21991.
9. Basak P, Gangopadhyay S, De S, et al. Cobalt(III) complexes of some aromatic thiohydrazides-synthesis, characterization and structure. *Inorganica Chim Acta* 2010; 363: 1495–1499.
10. Carroll WR, Gardner DM, Melton ER, et al. ¹H, ¹³C, and ¹⁵N NMR conformational characterization of a series of 2-acetylthiazolethiosemicarbazone compounds. *J Mol Struct* 2018; 1157: 8–13.
11. Ertas M, Sahin Z, Bulbul EF, et al. Potent ribonucleotide reductase inhibitors: thiazolecontaining thiosemicarbazone derivatives. *Arch Pharm Chem Life Sci* 2019; 352: 1900033. 1–13.
12. Fayed EA, Ragab A, Eldin RRE, et al. In vivo screening and toxicity studies of indolinone incorporated thiosemicarbazone, thiazole and piperidinosulfonyl moieties as anticonvulsant agents. *Bioorg Chem* 2021; 116: 105300.
13. Santiago EF, Oliveira SA, Filho GBO, et al. Evaluation of the anti-schistosoma Mansonii activity of thiosemicarbazones and thiazoles. *Antimicrob Agents Chemother* 2014; 58: 352–363.
14. Sudo RT, Calasans-Maia JA, Galdino SL, et al. Interaction of morphine with a new Alpha2-adrenoceptor agonist in mice. *J Pain* 2010; 11: 71–78.
15. Sanemitsu Y, Kawamura S, Satoh J, et al. Synthesis and herbicidal activity of 2-acylimino-3-phenyl-1,3-thiazolines-A new family of bleaching herbicides. *J Pestic* 2006; 31: 305–310.
16. Braga SFP, Fonseca NC, Ramos JP, et al. Synthesis and cytotoxicity evaluation of thiosemicarbazones and their Thiazole derivatives. *Braz J Pharm Sci* 2016; 52: –4.
17. Gaikwad ND, Patil SV and Bobade VD. Synthesis and antimicrobial activity of novel thiazole substituted pyrazole derivatives. *J Heterocycl Chem* 2013; 50: 519–527.
18. Queiroz CM, de Oliveira FGB, Espíndola JWP, et al. Thiosemicarbazone and thiazole: in vitro evaluation of leishmanicidal and ultrastructural activity on *Leishmania Infantum*. *Med Chem Res* 2020; 29: 1–16.
19. Kovacevic Z, Chikhani S, Lui GYL, et al. The iron-regulated metastasis suppressor NDRG1 targets NEDD4L, PTEN, and SMAD4 and inhibits the PI3K and ras signaling pathways. *ARS* 2013; 18: 874–887.
20. Mishra V, Pandeya SN, Clercq ED, et al. Synthesis of aryl semicarbazone of 4-aminoacetophenone and their anti-HIV activity. *Pharm Acta Helv* 1998; 73: 215–218.
21. Moustafa AMY. In vitro anti leukemia cancer activity of some novel pyrazole derivatives and pyrazoles containing thiazole moiety. *Am J Org Chem* 2019; 5: 55–70.
22. Jonsson T, Emteborg M and Irgum K. Heterocyclic compounds as catalysts in the peroxyoxalate chemiluminescence reaction of bis(2,4,6-trichlorophenyl)oxalate. *Anal Chim Acta* 1998; 361: 205–215.
23. Emanuele L and D'Auria M. The use of heterocyclic azo dyes on different Textile materials: a review. *Organics* 2024; 5: 277–289.
24. Prajapati NP, Patel KD, Vekariya RH, et al. Thiazole fused thiosemicarbazones: microwave-assisted synthesis, biological evaluation and molecular docking study. *J Mol Struct* 2019; 1179: 401–410.
25. Arafa WAA and Badry MG. Facile synthesis of bis-thiosemicarbazone derivatives as key precursors for the preparation of functionalised bis-thiazoles. *J Chem Res* 2016; 40: 385–392.
26. Yallur BC, Krishna PM and Challa M. Bivalent Ni(II), Co(II) and Cu(II) complexes of [(E)-[(2-methyl-1,3-thiazol-5-yl)methylidene]amino] thiourea: synthesis, spectral characterization, DNA and in-vitro ANti-bacterial studies. *Heliyon* 2021; 7: e06838.
27. Faizul A, Satendra S, Lal KS, et al. Synthesis of Schiff bases of naphtha[1,2-d]thiazol-2-amine and metal complexes of 2-(2'-hydroxy)benzylideneaminonaphthothiazole as potential antimicrobial agents. *J Zhejiang Univ Sci B* 2007; 8: 446–452.
28. Nartop D, Özkan EH and Özdemir I. Novel α-N-heterocyclic thiosemicarbazone complexes: synthesis, characterization, and antimicrobial of properties investigation. *RSC Adv* 2024; 14: 29308–29318.
29. Kasuga NC, Sekino K, Kuomo C, et al. Synthesis, structural characterization and antimicrobial activities of 4- and 6-coordinate nickel (II) complexes with three thiosemicarbazones and semicarbazone ligands. *J Inorg Biochem* 2001; 84: 55–65.
30. Alshater H, Al-Sulami AI, Aly SA, et al. Antitumor and antibacterial activity of Ni(II), Cu(II), Ag(I), and Hg(II) complexes with ligand derived from thiosemicarbazones: characterization and theoretical studies. *Mol* 2023; 28: 1–18.
31. Ülke E, Özkan EH, Nartop D, et al. New antimicrobial polymeric microspheres containing azomethine. *J Inorg Organomet Polym* 2022; 32: 3971–3982.

32. Obasi LN, Ukoha PO, Chah KF, et al. Synthesis, spectroscopic characterization and antibacterial screening of novel N-(benzothiazol-2-yl)ethanamides. *Ecl Quím* 2011; 36: 7–17.
33. Wiles DAI, Gingkasa BA and Suprluchuk XDT. The C=S stretching vibration in the infrared Spectra of some thiosemicarbazones. *Can J Chem* 1967; 45: 469–473.
34. Güveli S. *The investigation of the reactions of dichlorobis-triphenylphosphine-Ni(II) Complex with some thiosemicarbazone derivatives*. PhD Thesis, İstanbul University, 2012. 1–164.
35. Silverstein RM and Webster FX. *Spectrometric identification of organic compounds*. 6th ed. New York, USA: John Wiley & Sons, 1998.
36. Nartop D and Ögütçü H. Novel unsymmetric diimines: synthesis and biological evaluation against pathogenic microorganisms. *J Med Chem Sci* 2020; 3: 219–227.
37. Nartop D and Ögütçü H. Synthesis of new unsymmetrical Schiff bases as potential antimicrobial agents. *Sinop Uni. J Nat Sci* 2020; 5: 13–25.
38. Çiçek İ, Tunç T, Oğutcu H, et al. Synthesis and antibacterial activity of new chiral aminoalcohol and benzimidazole hybrids. *Bioorg Chem* 2020; 5: 4650–4654.
39. Nartop D, Tokmak E, Özkan EH, et al. Synthesis of novel polymers containing Schiff base as potential antimutagenic and antimicrobial agents. *J Med Chem Sci* 2020; 3: 363–372.
40. Vuotto C, Longo F, Balice MP, et al. Antibiotic resistance related to biofilm formation in *Klebsiella Pneumoniae*. *Pathogens* 2014; 3: 743–758.
41. Drzewiecka D. Significance and roles of *Proteus spp.* Bacteria in natural environments. *Microb Ecol* 2016; 72: 741–758.
42. Carolus H, Dyck KV and Dijk PV. *Candida Albicans* and *Staphylococcus* Species: a threatening twosome. *Front Microbiol* 2019; 10: 2162. 1–8.