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Novel Structural Hybrids of Pyrrole and Thiazole Moieties: Synthesis and Evaluation of Antibacterial and Antifungal Activities

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Abstract

One of the best ways to design new biocidal agents is synthesizing hybrid molecules by combining two or more bioactive moieties in a single molecular scaffold. So, new series of pyrroles bearing a thiazole moiety were synthesized using 1-methyl-1*H*-pyrrole-2-carbaldehyde thiosemicarbazones **1a–c**. Cyclization of thiosemicarbazone derivatives **1a–c** with ethyl chloroacetate, ethyl 2-chloropropanoate, chloroacetone and phenacyl bromide afforded the corresponding thiazolidin-4-ones **2a–c**, 5-methylthiazolidin-4-ones **3a–c**, 4-methyl-2,3-dihydrothiazoles **4a–c**, and 4-phenyl-2,3-dihydrothiazoles **5a–c**, respectively. The antimicrobial activity of the new thiazole derivatives was evaluated.

Keywords: Pyrroles; Thiosemicarbazones; Thiazoles; Antibacterial activity; Antifungal activity

1. Introduction

One of the most serious future challenges to health care professionals is the emergence of multi-drug resistance pathogenic bacteria that rapidly develop resistance to currently used antibiotics. These medical problems can be reduced by the discovery of novel antibacterial and antifungal agents.[1–10]

Pyrrole is widely known as a biologically active scaffold which possesses a diverse nature of activities.[11,12] The combination of different pharmacophores in a pyrrole ring system has led to the formation of more active compounds.[12] The marketed drugs containing a pyrrole ring system are known to have many biological properties such as antipsychotic, β-adrenergic antagonist, anxiolytic, anticancer (leukemia, lymphoma and myelofibrosis etc.), antibacterial, antifungal, antiprotozoal, antimalarial and many more.[13–15] Pyrrolomycins and *N*-alkylated derivatives of pyrrolomycin are natural antibiotics and contain nitropyrrole nucleus which is stable and chemically reactive for antifungal activity.[16] Verrucarine E and fenpiclonil are therapeutically useful antibacterial compounds. A naturally occurring pyoluteorin was found to posses antibacterial activity. Sortase A is a transpeptidase responsible for covalently anchoring many surface proteins in Gram-positive peptidoglycan, thus encouraging adhesion and biofilm formation. The inhibition of SrtA is related to the at-

tenuation of virulence in *Staphylococcus aureus* and also in other important Gram-positive pathogens, such as *Listeria monocytogenes*, *S. pneumoniae*, and *S. smutans.*[17,18]

Thiazole moiety frequently appears in the structure of many natural products as well as biologically active compounds. Thiazole moiety displayed crucial role in the medicinal chemistry research, where they have therapeutic effects against several diseases. Thiazoles showed the broad variety of biological activities, such as anti-inflammatory,[19] analgesic,[20] allergies,[21] hypertension,[22] hypnotics,[23] schizophrenia,[24] anti-cancer,[25] antibacterial, antifungal[1] and anti-HIV[26] activities. Thiazole moiety represented the integral scaffold of the all penicillin derivatives. Penicillins are the first effective antibiotics used to treat microbes that played critical roles in the therapy of the bacterial diseases.[27] Abafungin is a broad-spectrum antifungal agent. Thiabendazole is a fungicide and parasiticide where it represented a new bacterial DNA gyrase B inhibitors.[28] Furthermore, most of fused thiazoles are attractive scaffolds for obtaining high potential drug candidates.[29,30] Fused thiazoles, such as purine and their analogs possess significant biological activities.[31]

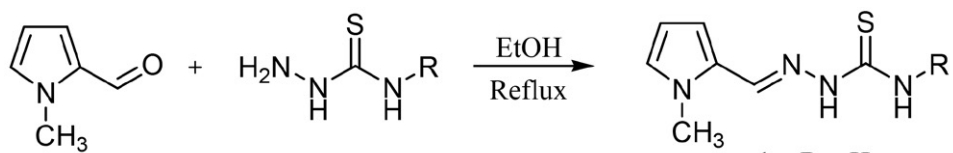
The synthesized compounds design was based on three points. First point is the many reports validation of pyrrole as antimicrobial agents. Second point, thiazole moiety has been already reported for its antimicrobial activity, thiazoles have occupied a prominent role in the design of biologically active agents. Thirdly, one of the main strategies for the discovery of new drugs is to modify the structure of a known drug or to unite two or more pharmacophoric moieties that being combined in one molecular scaffold to obtain the synergistic effect or developing newly affordable antibacterial activity having a new mode of action. To assemble novel biologically active compounds with potent antimicrobial effect, it is aimed to synthesize and evaluate the antimicrobial activity of series of 2-substituted pyrroles containing thiazole nucleus separated by a hydrophobic linker.

2. Results and Discussion

The starting 1-methyl-1*H*-pyrrole-2-carbaldehyde thiosemicarbazones **1a**–**c** were synthesized through the condensation reaction between 1-methyl-1*H*-pyrrole-2-carbaldehyde and thiosemicarbazide derivatives in ethanol under reflux (Scheme 1). ^{1}H NMR spectrum of **1b** indicated doublet and singlet signals at δ 3.01 and 3.80 ppm for NH-$\underline{CH_3}$ and NCH_3 protons, two signals at δ 7.88 and 11.14 ppm assignable for two NH protons, in addition to three multiplet signals at δ 6.08, 6.51 and 6.94 ppm for pyrrole protons with singlet signal at δ 8.04 ppm corresponding to CH=N proton. Also, ^{13}C NMR indicated signals at δ 31.3 (CH_3), 36.51 (CH_3), 108.73, 114.85, 127.34, 128.28, 136.32 (CH=N) and 177.49 (C=S) ppm.

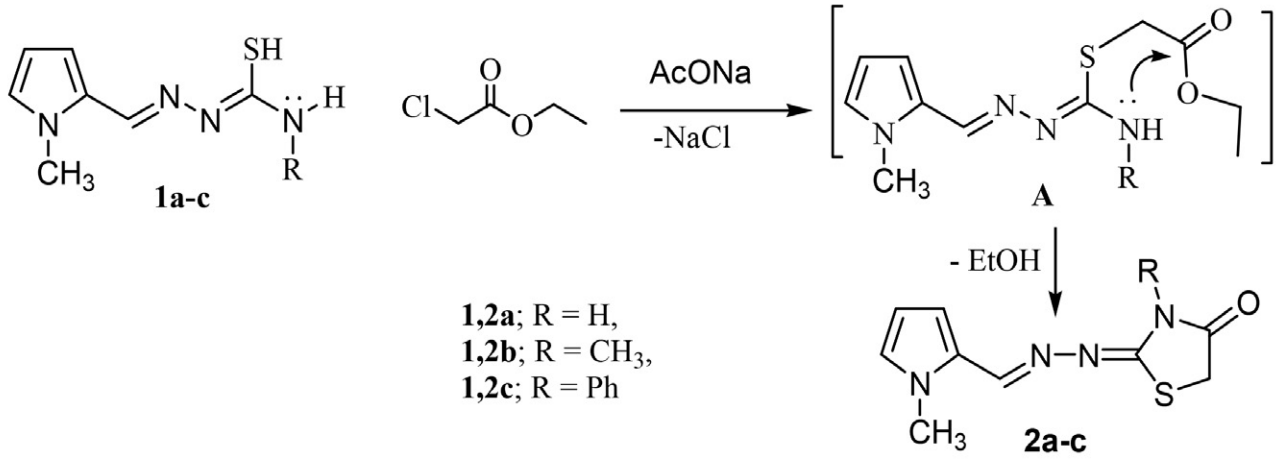
Thiosemicarbazones **1a**–**c** were subjected to cycloalkylation with different halogenated compounds in the hope of obtaining biologically activity thiazoles. Thus, when thiosemicarbazones **1a**–**c** were left to react with ethyl chloroacetate in refluxing ethanol containing a catalytic amount of fused sodium acetate resulted in the formation of the corresponding thiazolidines **2a**–**c** that were obtained in good yields. Evidence for assigned structures is provided by analytical and spectroscopic data. For example, ^{1}H NMR spectrum of **2a**, as an example, exhibited two singlet signals at δ 3.86 and 3.87 ppm assignable to CH_3 and CH_2 protons. The three protons of pyrrole ring were displayed at δ 6.12, 6.56 and 7.01 ppm as multiplet, singlet and singlet signals, respectively. A singlet signal at δ 8.25 ppm appeared for azomethine proton and a broad signal at δ 11.84 ppm due to imino proton. The formation of thiazolidone **2** may be assumed to proceed through initial alkylation for thiosemicarbazones **1** to afford the non-isolable intermediate **A** followed by intramolecular cyclization with elimination of ethanol (Scheme 2).

Similarly, 5-methyl-thiazolidin-4-one derivatives **3a**–**c** were obtained *via* cycloalkylation of thiosemicarbazones **1a**–**c** with ethyl 2-chloropropanoate in ethanol in the presence of sodium acetate under reflux condition. ^{1}H NMR spectrum of **3a** showed three diagnostic aliphatic signals for $\underline{CH_3}$–CH, NCH_3 and $\underline{CH}$-CH_3 protons at δ 1.49 (doublet), 3.87 (singlet) and 4.17 (quartet) ppm, respectively. The protons of pyrrole were displayed at δ 6.12, 6.55 and 7.10 ppm. Beside the last aromatic protons, ^{1}H NMR spectrum displayed signals for azomethine at δ 8.25 ppm together with NH broad signals at δ 11.80 ppm. In addition, under the same reaction conditions, cyclocondensation of thiosemicarbazones **1a**–**c** with chloroacetone furnished the corresponding 4-methyl-2,3-dihydrothiazole derivatives **4a**–**c**. ^{1}H NMR spectrum of **4a** exhibited two characteristic singlet signals for two methyl protons at δ 2.14 and 3.83 ppm. The H-5 of thiazole appaered at δ 6.06



1a; R = H,
1b; R = CH_3,
1c; R = Ph

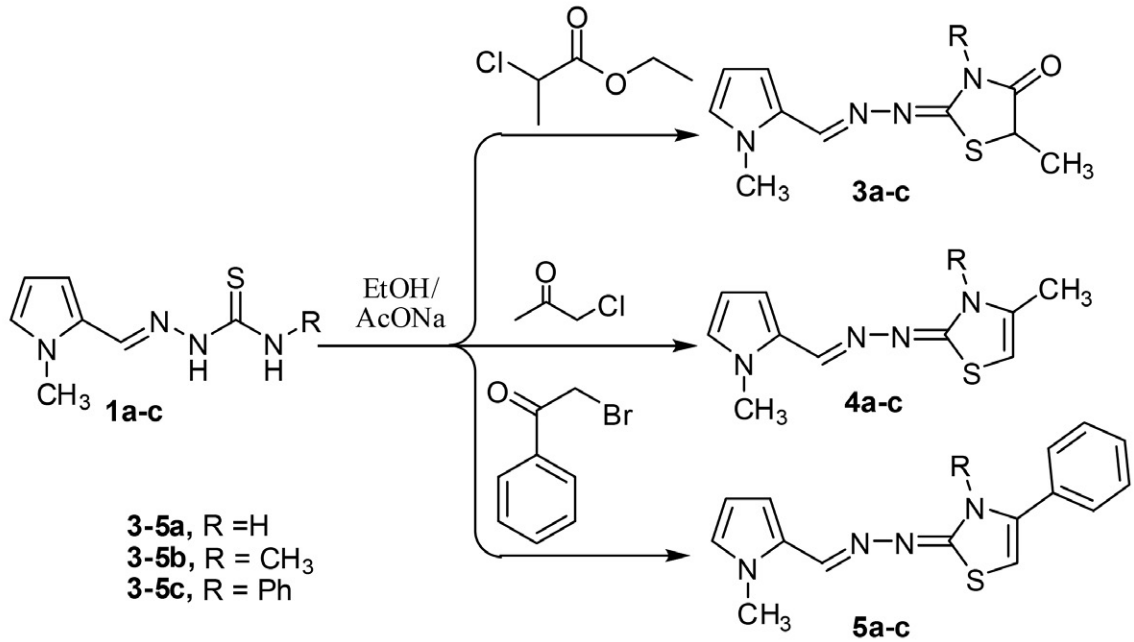
Scheme 1: Synthesis of 1-methyl-1*H*-pyrrole-2-carbaldehyde thiosemicarbazones **1a**–**c**



Scheme 2: Synthesis of thiazolidines **2a**–**c**

ppm. The pyrrole protons were displayed at δ 6.28, 6.37 and 6.90 ppm, azomethine at δ 7.94 ppm. A broad signal at δ 11.39 ppm appeared for NH proton. Moreover, cyclocondensation of thiosemicarbazones **1a**–**c** with phenacyl bromide furnished the corresponding 4-phenyl-2,3-dihydrothiazole derivatives **5a**–**c**. ^{1}H NMR spectrum of **5a** showed singlet signal at δ 3.87 ppm assignable to NCH_3. The protons of phenyl group were displayed at δ 6.08, 7.40 and 7.85 ppm as triplet (one proton), triplet (two protons), and doublet (two protons), respectively. The protons of pyrrole were displayed at δ 6.93, 7.25 and 7.30 ppm. Signals at 6.41 and 7.98 ppm were characteristics for CH-thiazole and CH=N, respectively and a broad signal at δ 11.77 ppm due to NH proton (Scheme 3).

The newly synthesized compounds were screened for their expected antifungal and antibacterial activities. Three different microbial groups were used. Group 1: Gram-positive bacteria: *Bacillus subtilis* (RCMB 015 (1) NRRL B-543) and *Staphylococcus aureus (*ATCC 25923). Group 2: Gram-negative bacteria: *Proteus vulgaris* (RCMB 004 (1) ATCC 13315) and *Escherichia coli* (ATCC 25922). Group 3: Fungi: *Candida albicans* (RCMB 005003 (1) ATCC 10231) and *Aspergillus fumigatus* (RCMB 002008). For the screening of antibacterial activity, diffusion agar technique[1] was applied at 10 mg/mL concentration, well diameter 6.0 mm (100 μL was tested). For comparison, Gentamycin and Ketoconazole were used as antibacterial and antifungal agents, respectively. The inhibition zone diameters are depicted in Table 1. Regarding the antimicrobial activity of thiazole derivatives, they displayed good effects towards *P. vulgaris* only. Few compounds displayed weak effects towards some of the tested organisms. The



Scheme 3: Synthesis of thiazole derivatives **3a**–**c**, **4a**–**c** and **5a**–**c**.

Table 1: The mean results of inhibition zone in mm produced on a range of pathogenic microorganisms

Compd. No.	Gram positive bacteria		Gram negative bacteria		Fungi	
	B. subtilis	*S. aureus*	*P. vulgaris*	*E. coli*	*C. albicans*	*A. fumigatus*
2a	NA	NA	21	10	NA	NA
2b	NA	NA	23	9	NA	NA
2c	NA	NA	10	NA	NA	NA
3a	NA	NA	16	NA	NA	NA
3b	9	NA	15	10	8	NA
3c	8	8	16	9	NA	9
4a	12	NA	13	NA	9	8
4b	NA	NA	24	12	NA	NA
4c	8	9	18	10	8	8
5a	9	NA	15	13	NA	NA
5b	NA	NA	18	8	NA	NA
5c	9	NA	17	9	9	8
Gentamycin	26	24	25	30	—	—
Ketoconazole	—	—	—	—	20	17

major compounds displayed no effects towards most of the tested organisms.

3. Conclusion

New series of pyrroles bearing a thiazole moiety were synthesized through cyclization of 1-methyl-1*H*-pyrrole-2-carbaldehyde thiosemicarbazone derivatives with ethyl chloroacetate, ethyl 2-chloropropanoate, chloroacetone and phenacyl bromide. The thiazole derivatives displayed good effects towards *P. vulgaris* only. Few compounds displayed weak effects towards some of the tested organisms. The major compounds displayed no effects towards most of the tested organisms.

3. 1. Experimental Section

Nuclear magnetic resonance spectra were carried out in deuterated dimethylsulfoxide (DMSO-d_6) by using Bruker spectrometers (^{1}H NMR 400 MHz; ^{13}C NMR 101 MHz) with chemical shift in δ from internal TMS. Mass spectra were recorded on GC/MS Finnigan SSQ 7000 spectrophotometer and GC Ms-QP 1000 EX mass spectrometer at 70 eV. Elemental analyses were carried out on a EuroVector instrument C, H, N analyzer EA3000 Series.

Synthesis of *N*-Substituted-2-((1-methyl-1*H*-pyrrol-2-yl)methylene)hydrazinecarbothioamides 1a–c[32]

The mixture of 0.01 mol of 1-methyl-1*H*-pyrrole-2-carbaldehyde and 0.01 mol of the selected thiosemicarbazides (thiosemicarbazide, *N*-methylthiosemicarbazide, *N*-phenylthiosemicarbazide) was heated in 50 mL ethanol under reflux for 0.5 h., left to cool, the resultant solid product was collected by filtration. The solid products were crystallized from ethanol.

***N*-Methyl-2-((1-methyl-1*H*-pyrrol-2-yl)methylene)hydrazinecarbothioamide (1b).** Yield 1.76 g (90%); m.p. 180–182 °C; ^{1}H NMR δ 3.01 (d, 3H, *J* = 4.6 Hz, $NHCH_3$), 3.80 (s, 3H, NCH_3), 6.08 (m, 1H, pyrrole-H), 6.51 (m, 1H, pyrrole-H), 6.94 (m, 1H, pyrrole-H), 7.88 (br, 1H, NH), 8.04 (s, 1H, CH=N), 11.14 (s, 1H, NH); ^{13}C NMR: δ 31.3 (CH_3), 36.51 (CH_3), 108.73, 114.85, 127.34, 128.28, 136.32 (CH=N), 177.49 (C=S); MS *m/z* (%): 196 (M^+; 67.4). Anal. Calcd. for $C_8H_{12}N_4S$ (196.27): C, 48.96; H, 6.16; N, 28.55. Found: C, 48.87; H, 6.14; N, 28.47%.

***N*-Methyl-2-((1-methyl-1*H*-pyrrol-2-yl)methylene)hydrazinecarbothioamide (1c).** Yield 2.45 g (95%); m.p. 140–142 °C; ^{1}H NMR: δ 3.86 (s, 3H, NCH_3), 6.12 (m, 1H, pyrrole-H), 6.64 (m, 1H, pyrrole-H), 6.99 (m, 1H, pyrrole-H), 7.18 (t, 1H, *J* = 7.4 Hz, Ph-H), 7.35 (t, 2H, *J* = 7.8 Hz, Ph-H), 7.64 (d, 2H, *J* = 7.7 Hz, Ph-H), 8.15 (s, 1H, CH=N), 9.55 (s, 1H, NH), 11.55 (s, 1H, NH); MS *m/z* (%): 258 (M^+; 46.0). Anal. Calcd. for $C_{13}H_{14}N4S$ (258.34): C, 60.44; H, 5.46; N, 21.69. Found: C, 60.38; H, 5.45; N, 21.73%.

Synthesis of Thiazolidin-4-one Derivatives 2a–c

The mixture of 0.01 mol of the thiosemicarbazide derivatives **1a–c**, 0.01 mol of ethyl chloroacetate and 0.02 mol of fused sodium acetate was dissolved 50 mL ethanol. The solution was heated under reflux for 3 hours, then left to cool. The obtained products were collected by filtration. The solid products were recrystallized from ethanol.

2-(((1-Methyl-1*H*-pyrrol-2-yl)methylene)hydrazono)thiazolidin-4-one (2a). Yield 1.89 g (85%); m.p. 248–250 °C; ^{1}H NMR: δ 3.86, 3.87 (2s, 5H, CH_2 and CH_3), 6.12 (m, 1H, pyrrole-H), 6.56 (s, 1H, pyrrole-H), 7.01 (s, 1H, pyrrole-H), 8.25 (s, 1H, CH=N), 11.84 (s, 1H, NH); MS *m/z* (%): 222 (M^+; 33.8). Anal. Calcd. for $C_9H_{10}N_4OS$ (222.27): C, 48.63; H, 4.53; N, 25.21. Found: C, 48.57; H, 4.55; N, 25.17%.

3-Methyl-2-(((1-methyl-1*H*-pyrrol-2-yl)methylene)hydrazono)thiazolidin-4-one (2b). Yield 1.88 g (80%); m.p. 183–184 °C; ^{1}H NMR: δ 3.16 (s, 3H, CH_3), 3.88 (s, 3H, CH_3), 3.92 (s, 2H, CH_2-thiazole), 6.13 (s, 1H, pyrrole-H), 6.59 (s, 1H, pyrrole-H), 7.03 (s, 1H, pyrrole-H), 8.35 (s, 1H, CH=N); ^{13}C NMR: δ 29.77 (CH_3), 32.54 (CH_3), 37.02 (CH_2), 109.00, 117.49, 127.55, 129.74, 150.00 (CH=N), 162.69 (CH=N), 172.61 (C=O); MS *m/z* (%): 236 (M^+; 62.2). Anal. Calcd. for $C_{10}H_{12}N_4OS$ (236.29): C, 50.83; H, 5.12; N, 23.71. Found: C, 50.86; H, 5.10; N, 23.67%.

2-(((1-Methyl-1*H*-pyrrol-2-yl)methylene)hydrazono)-3-phenylthiazolidin-4-one (2c). Yield 2.53 g (85%); m.p. 256–258 °C; ^{1}H NMR: δ 3.88 (s, 3H, CH_3), 4.07 (s, 2H, CH_2-thiazole), 6.10 (m, 1H, pyrrole-H), 6.53 (m, 1H, pyrrole-H), 7.02 (s, 1H, pyrrole-H), 7.38 (d, 2H, *J* = 7.2 Hz, Ph-H), 7.46 (d, 1H, *J* = 7.3 Hz, Ph-H), 7.52 (t, 2H, *J* = 7.4 Hz, Ph-H), 8.15 (s, 1H, CH=N); MS *m/z* (%): 298 (M^+; 22.3). Anal. Calcd. for $C_{15}H_{14}N_4OS$ (298.36): C, 60.38; H, 4.73; N, 18.78. Found: C, 60.43; H, 4.75; N, 18.82%.

Synthesis of 5-Methyl-thiazolidin-4-one Derivatives 3a–c

The mixture of 0.01 mol of the thiosemicarbazide derivatives **1a-c**, 0.01 mol of ethyl 2-chloropropanoate and 0.02 mol of fused sodium acetate was dissolved 50 mL ethanol. The solution was heated under reflux for 5 hours. After cooling, precipitated solid were obtained which were collected by filtration and recrystallized from ethanol.

5-Methyl-2-(((1-methyl-1*H*-pyrrol-2-yl)methylene)hydrazono)thiazolidin-4-one (3a). Yield 1.65 g (70%); m.p. 210–212 °C; ^{1}H NMR: δ 1.49 (d, 3H, *J* = 7.2 Hz, CH_3), 3.87 (s, 3H, NCH_3), 4.17 (q, 1H, *J* = 7.2 Hz, thiazole-H), 6.12 (m, 1H, pyrrole-H), 6.55 (m, 1H, pyrrole-H), 7.10 (s, 1H, pyrrole-H), 8.25 (s, 1H, CH=N), 11.80 (br, 1H, NH); MS *m/z* (%): 236 (M^+; 49.0). Anal. Calcd. for $C_{10}H_{12}N_4OS$ (236.29): C, 50.83; H, 5.12; N, 23.71. Found: : C, 50.86; H, 5.11; N, 23.67%.

3,5-Dimethyl-2-(((1-methyl-1*H*-pyrrol-2-yl)methylene)hydrazono)thiazolidin-4-one (3b). Yield 1.68 g (67%); ^{1}H NMR: δ 1.50 (d, 3H, *J* = 7.2 Hz, CH_3), 3.27 (s, 3H, CH_3), 3.89 (s, 3H, CH_3), 4.20 (m, 1H, thiazole-H), 6.14 (m, 1H, pyrrole-H), 6.55 (m, 1H, pyrrole-H), 7.13 (s, 1H, pyrrole-H), 8.25 (s, 1H, CH=N); MS *m/z* (%): 250 (M^+; 18.7). Anal. Calcd. for $C_{11}H_{14}N_4OS$ (250.32): C, 52.78; H, 5.64; N, 22.38. Found: C, 52.73; H, 5.61; N, 22.42%.

5-Methyl-2-(((1-methyl-1*H*-pyrrol-2-yl)methylene)hydrazono)-3-phenylthiazolidin-4-one (3c). Yield 2.34 g (75%); ^{1}H NMR: δ 1.51 (d, 3H, *J* = 7.2 Hz, CH_3), 3.86 (s, 3H, NCH_3), 4.22 (m, 1H, thiazole-H), 6.10–7.10 (m, 8H, Ph-H and pyrrole-H), 8.32 (s, 1H, CH=N); MS *m/z* (%): 312 (M^+; 27.0). Anal. Calcd. for $C_{16}H_{16}N_4OS$ (312.39): C, 61.52; H, 5.16; N, 17.93. Found: C, 61.48; H, 5.14; N, 17.96%.

Synthesis of 4-Methyl-2,3-dihydrothiazole Derivatives 4a–c

The mixture of 0.01 mol of the thiosemicarbazide derivatives **1a–c**, 0.01 mol of chloroacetone and 0.02 mol of fused sodium acetate was dissolved 50 mL ethanol. The solution was heated under reflux for 6 h and left to cool. The obtained product was collected by filtration. The solid products were recrystallized from ethanol.

4-Methyl-2-(((1-methyl-1*H*-pyrrol-2-yl)methylene)hydrazono)-2,3-dihydrothiazole (4a). Yield 1.65 g (75%); m.p. 177–179 °C; ^{1}H NMR: δ 2.14 (s, 3H, CH_3), 3.83 (s, 3H, NCH_3), 6.06 (m, 1H, pyrrole-H), 6.28 (s, 1H, thiazole-H), 6.37 (m, 1H, pyrrole-H), 6.90 (s, 1H, pyrrole-H), 7.94 (s, 1H, CH=N), 11.39 (s, 1H, NH); MS *m/z* (%): 220 (M^+; 46.6). Anal. Calcd. for $C_{10}H_{12}N_4S$ (220.29): C, 54.52; H, 5.49; N, 25.43. Found: C, 54.48; H, 5.50; N, 25.38%.

3,4-Dimethyl-2-(((1-methyl-1*H*-pyrrol-2-yl)methylene)hydrazono)-2,3-dihydro-thiazole (4b). Yield 1.64 g (70%); m.p. 196–198 °C; ^{1}H NMR: δ 2.12 (s, 3H, CH_3), 3.31 (s, 3H, NCH_3), 3.86 (s, 3H, NCH_3), 5.95 (m, 1H, Ar-H), 6.06 (m, 1H, Ar-H), 6.39 (m, 1H, thiazole-H), 6.89 (s, 1H, Ar-H), 8.17 (s, 1H, CH=N); ^{13}C NMR: δ 14.21 (CH_3), 31.48 (CH_3), 36.86 (CH_3), 95.69, 108.40, 114.34, 127.78, 128.77, 136.52, 143.22, 168.37 (CH=N); MS *m/z* (%):234 (M^+; 45.7). Anal. Calcd. for $C_{11}H_{14}N_4S$ (234.32): C, 56.38; H, 6.02; N, 23.91; N, 17.34. Found: C, 56.34; H, 6.04; N, 23.87%.

4-Methyl-2-(((1-methyl-1*H*-pyrrol-2-yl)methylene)hydrazono)-3-phenyl-2,3-dihydrothiazole (4c). Yield 2.22 g (75%); ^{1}H NMR: δ 2.15 (s, 3H, CH_3), 3.85 (s, 3H, NCH_3), 5.95 (m, 1H, Ar-H), 6.10–6.90 (m, 8H, pyrrole-H and Ph-H), 8.26 (s, 1H, CH=N); MS *m/z* (%): 296 (M^+; 24.8). Anal. Calcd. for $C_{16}H_{16}N_4S$ (296.39): C, 64.84; H, 5.44; N, 18.90. Found: C, 64.86; H, 5.42; N, 18.86%.

Synthesis of 4-Phenyl-2,3-dihydrothiazole Derivatives 5a–c

The mixture of 0.01 mol of the thiosemicarbazide derivatives **1a–c**, 0.01 mol of phenacyl bromide and 0.02 mol of fused sodium acetate was dissolved 50 mL ethanol. The solution was heated under reflux for 6 h and left to cool. The obtained product was collected by filtration. The solid products were recrystallized from ethanol.

2-(((1-Methyl-1*H*-pyrrol-2-yl)methylene)hydrazono)-4-phenyl-2,3-dihydrothiazole (5a).[33] Yield 2.40 g (85%); m.p. 180–182 °C; ^{1}H NMR: δ 3.87 (s, 3H, CH_3), 6.08 (m, 1H, pyrrole-H), 6.41 (m, 1H, pyrrole-H), 6.93 (s, 1H, pyrrole-H), 7.25 (s, 1H, thiazole-H), 7.30 (d, 1H, *J* = 7.3 Hz, Ph-H), 7.40 (t, 2H, *J* = 7.6 Hz, Ph-H), 7.85 (d, 2H, *J* = 7.4 Hz, Ph-H), 7.98 (s, 1H, CH=N); 11.77 (br, 1H, NH); MS *m/z* (%): 282 (M^+; 43.1). Anal. Calcd. for $C_{15}H_{14}N_4S$ (282.36): C, 63.80; H, 5.00; N, 19.84. Found: C, 63.77; H, 4.98; N, 19.78%.

3-Methyl-2-(((1-methyl-1*H*-pyrrol-2-yl)methylene)hydrazono)-4-phenyl-2,3-dihydrothiazole (5b). Yield 2.37 g (80%); m.p. 127–128 °C; ^{1}H NMR: δ 3.27 (s, 3H, CH_3), 3.89 (s, 3H, CH_3), 6.06 (m, 1H, pyrrole-H), 6.32 (s, 1H, thiazole-H), 6.43 (m, 1H,pyrrole-H), 6.93 (s, 1H, pyrrole-H), 7.50 (m, 5H, Ar-H), 8.23 (s, 1H, CH=N); MS *m/z* (%): 296 (M^+; 23.2). Anal. Calcd. for $C_{16}H_{16}N_4S$ (296.39): C, 64.84; H, 5.44; N, 18.90. Found: C, 64.79; H, 5.46; N, 18.87%.

2-(((1-Methyl-1*H*-pyrrol-2-yl)methylene)hydrazono)-3,4-diphenyl-2,3-dihydro-thiazole (5c). Yield 3.04 g (85%); ^{1}H NMR: δ 3.92 (s, 3H, CH_3), 6.06 (m, 14H, thiazole-H, pyrrole-H, 2Ph-H), 8.34 (s, 1H, CH=N); MS *m/z* (%): 358 (M^+; 49.0). Anal. Calcd. for $C_{21}H_{18}N_4S$ (358.46): C, 70.36; H, 5.06; N, 15.63. Found: C, 70.41; H, 5.08; N, 15.57%.

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Povzetek

Eden izmed najboljših načinov za načrtovanje novih biocidnih spojin je sinteza hibridnih molekul, do katerih pridemo s povezavo dveh ali več bioaktivnih fragmentov v eno samo molekulsko ogrodje. Tako smo iz serije 1-metil-1*H*-pirol-2-karbaldehid tiosemikarbazonov **1a**–**c** pripravili nov set pirolov, ki so vsebovali tiazolni fragment. Ciklizacija tiosemikarbazonskih derivatov **1a**–**c** z etil kloroacetatom, etil 2-kloropropanoatom, kloroacetonom ali fenacil bromidom je vodila do ustreznih tiazolidin-4-onov **2a**–**c**, 5-metiltiazolidin-4-onov **3a**–**c**, 4-metil-2,3-dihidrotiazolov **4a**–**c** in 4-fenil-2,3-dihidrotiazolov **5a**–**c**. Določili smo tudi antimikrobne aktivnosti novih tiazolskih derivatov.