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## Novel hydrazones bearing thiazole scaffold: synthesis, characterization, antimicrobial activities and ADME profile investigation

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### ABSTRACT

A novel series of acyl hydrazone derivatives was synthesized by condensing acyl hydrazide of 2-(4-hydroxyphenyl)-4-methylthiazole-5-carboxylic acid with various substituted aldehydes under reflux, in the presence of a catalytic amount of mineral acid. The reaction progress and purity of the synthesized compounds were monitored by TLC, and their melting points were recorded. Structural characterization was carried out using HRMS, FT-IR, and <sup>1</sup>H and <sup>13</sup>C NMR, confirming the successful formation of the target compounds. The synthesized compounds were further evaluated for their ADME profiles to assess drug-likeness and pharmacokinetic behavior. Antimicrobial activities were screened against selected bacterial strains, including gram-positive (*Staphylococcus aureus*, *Bacillus cereus*) and gram-negative (*Salmonella typhimurium*, *Escherichia coli*) organisms, using Tetracycline as a reference standard. The results demonstrated that several compounds exhibited notable antimicrobial properties. Among the tested derivatives, HAS-01 and HAS-03 showed the most promising activity, with significant inhibition against both gram-positive and gram-negative bacteria. These compounds also displayed favorable ADME characteristics, suggesting their potential as lead candidates for further development. The study highlights the importance of the thiazole-based acyl hydrazone scaffold in designing new antimicrobial agents and provides a strong foundation for further optimization and structure–activity relationship studies.

**Keywords:** Acyl Hydrazone, Thiazole, Antimicrobial Activity, ADME

## 1. INTRODUCTION

Fischer first introduced the term acyl hydrazone/hydrazone in 1888 to characterize a functional group resulting from the condensation of hydrazine with an aldehyde or a ketone [1]. The typical structure of acyl hydrazones consists of a carbonyl group (C=O) attached to a hydrazine moiety (-NH-NH<sub>2</sub>), forming a distinct linkage that plays a critical role in defining their chemical and biological properties [2, 3]. Acyl hydrazones are commonly synthesized through the condensation reaction between an acyl derivative, such as an aldehyde or ketone, and hydrazine or its substituted forms [4]. This process results in the formation of a hydrazone bond, accompanied by the release of water as a byproduct [5, 6]. This moiety serves a fascinating class of compounds that bridge multiple disciplines [7]. They find applications across multiple disciplines, such as medicinal chemistry [8], organic synthesis [9] and materials science [10], owing to their versatile chemical characteristics and significant biological activities resembling other heterocyclic moieties [11, 12].

They exhibit a range of applications, particularly in the development of pharmaceuticals [13, 14]. They have been recognized as potential inhibitors in several biochemical pathways and have demonstrated significant activity against a range of diseases, including cancer [15] and various infectious disorders [16]. Additionally, their capability to form stable complexes with metal ions makes them valuable in coordination chemistry and as important precursors for the synthesis of complex molecular structures [17, 18]. Moreover, they are relevant in the context of material science, where they are utilized in the development of polymers and other advanced materials [19].

Their unique properties, including thermal stability and sensitivity to environmental stimuli, make them well-suited for use in sensors and drug delivery systems [20]. The synthesis, characterization, and diverse applications of acyl hydrazones continue to be areas of significant research, fostering advancements not only in scientific knowledge but also in their practical utilization across various fields [21].

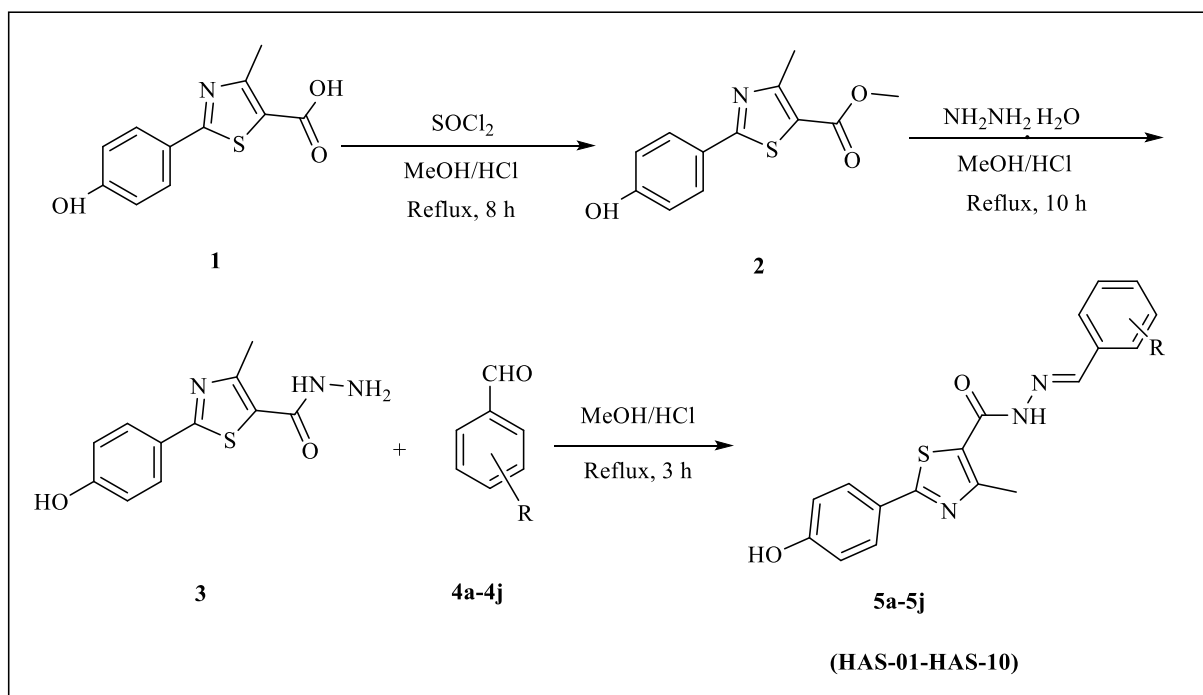
Thiazole, a prominent member of the pentatomic heterocyclic family, is widely recognized as an essential scaffold in medicinal chemistry [22]. Composed of sulphur and nitrogen atoms, thiazole displays significant electron-donating and electron-withdrawing properties, which contribute to its strong influence on biological activity [23]. In drug development, the incorporation of multiple pharmacophores into a single molecular framework can produce compounds with superior biological efficacy [24]. Thus, the combination of thiazole and hydrazone structures has the potential to generate innovative, highly active drug candidates effective against multidrug-resistant microbes and capable of mitigating oxidative processes [25]. These derivatives have shown considerable promise as antimicrobial [26], anticancer [27], antiviral [28], antimalarial [29], anticonvulsant [30], anti-inflammatory [31] and antidiabetic agents [32]. Based on the accumulated data, we propose the design and synthesis of novel hybrid molecules incorporating both pharmacophores, followed by a comprehensive evaluation of their antimicrobial efficacy.

In the present study, the synthesis of a series of novel acyl hydrazone derivatives (**HAS-01 to HAS-10**) (Scheme 1) was successfully reported, with a focus on obtaining high yields and purity. The optimized molecular geometries of the compounds were determined through computational methods, while their structural features were further elucidated by examining the IR vibrational frequencies, which provided insights into functional group interactions. Additionally, the <sup>1</sup>H and <sup>13</sup>C NMR chemical shifts of compounds (**HAS-01 to HAS-10**) were

carefully analyzed to assess their molecular environment, offering a detailed understanding of the electronic and spatial characteristics of each derivative.

## 2. MATERIALS AND METHODS

Thin-layer chromatography was accomplished on 0.2 mm precoated plates of silica gel G60 F<sub>254</sub> (Merck). Visualization was made with UV light (254 and 365 nm) or with an iodine vapor. IR spectra were recorded on FTIR Shimadzu. <sup>1</sup>H NMR (400 MHz), and <sup>13</sup>C NMR (100 MHz) NMR spectra were recorded on a Bruker ADVANCE II spectrometer in DMSO-d<sub>6</sub>. Chemical shifts are expressed in  $\delta$  ppm downfield from TMS as an internal standard. Mass spectra were determined using direct inlet probe on an LCMS-QDa 6 mass spectrometer. Solvents were evaporated with a BUCHI rotary evaporator. Melting points were measured in open capillaries and were uncorrected.



**Scheme 1.** Synthetic Route of Thiazole based Acyl Hydrazone Derivatives.

## 3. EXPERIMENT

### 3. 1. Synthetic Protocols

#### 3. 1. 1. Synthesis of ethyl-2-(4-hydroxyphenyl)-4-methylthiazole-5-carboxylate:

2-(4-hydroxyphenyl)-4-methylthiazole-5-carboxylic acid (**1**) (2.35g, 0.01M) was made soluble in methanol in a round bottom flask. The reaction was put forward by the addition of thionyl chloride (1.18g, 0.01M) at 0-5 °C temperature. The reaction was put back to room temperature and was refluxed for 8 h. The reaction was traced using TLC. On completion of

the reaction, ethyl 2-(4-hydroxyphenyl)-4-methylthiazole-5-carboxylate (**2**) was precipitated, filtered, dried and re-crystallized using ethyl acetate. Ethyl 2-(4-hydroxyphenyl)-4-methylthiazole-5-carboxylate was synthesized according to the procedure given in the literature and melting point is corrected [33].

### 3. 1. 2. Synthesis of 2-(4-hydroxyphenyl)-4-methylthiazole-5-carbohydrazide:

Ethyl 2-(4-hydroxyphenyl)-4-methylthiazole-5-carboxylate (**2**) (2.63g, 0.01M) and hydrazine hydrate (2.24 ml, 0.07M) was mixed in methanol in a round bottom flask. The reaction is refluxed for 10 hrs to synthesize 2-(4-hydroxyphenyl)-4-methylthiazole-5-carbohydrazide (**3**). The reaction was traced using TLC. On completion of the reaction was precipitated, filtered, dried and re-crystallized using dimethyl formamide [34].

### 3. 1. 3. General procedure for synthesis of N'-arylidene-2-(4-hydroxyphenyl)-4-methylthiazole-5-carbohydrazide:

2-(4-hydroxyphenyl)-4-methylthiazole-5-carbohydrazide (**3**) (2.49 gm, 0.01M) and substituted benzaldehyde (4a-j) (0.01M) were mixed in methanol in a round bottom flask. The reaction was refluxed for 03 hrs to synthesize N'-arylidene-2-(4-hydroxyphenyl)-4-methylthiazole-5-carbohydrazide (**HAS-01 to HAS-10**) as shown in Scheme 1. The reaction was traced using TLC. On completion of the reaction was precipitated, filtered, dried and re-crystallized using methanol and dimethyl formamide adduct [35, 36].

**Table 1.** Physical properties of novel acyl hydrazones.

Compound Code	-R	Molecular Formula	M.P. (°C)	MW	% Yield
HAS-01	2-Nitrobenzaldehyde	C <sub>18</sub> H <sub>14</sub> N <sub>4</sub> O <sub>4</sub> S	265	382	88%
HAS-02	3,4-Dimethoxybenzaldehyde	C <sub>20</sub> H <sub>19</sub> N <sub>3</sub> O <sub>4</sub> S	240	397	92%
HAS-03	Anisaldehyde	C <sub>19</sub> H <sub>17</sub> N <sub>3</sub> O <sub>3</sub> S	247	367	90%
HAS-04	4-Chlorobenzaldehyde	C <sub>18</sub> H <sub>14</sub> ClN <sub>3</sub> O <sub>2</sub> S	235	371	77%
HAS-05	4-Hydroxybenzaldehyde	C <sub>18</sub> H <sub>15</sub> N <sub>3</sub> O <sub>3</sub> S	254	353	87%
HAS-06	4-Methyl benzaldehyde	C <sub>19</sub> H <sub>17</sub> N <sub>3</sub> O <sub>2</sub> S	233	351	72%
HAS-07	4-hydroxy 3,5-dimethoxybenzaldehyde	C <sub>20</sub> H <sub>19</sub> N <sub>3</sub> O <sub>5</sub> S	244	413	80%
HAS-08	Salicylaldehyde	C <sub>18</sub> H <sub>15</sub> N <sub>3</sub> O <sub>3</sub> S	243	353	85%
HAS-09	Thiophene 2-aldehyde	C <sub>16</sub> H <sub>13</sub> N <sub>3</sub> O <sub>2</sub> S <sub>2</sub>	245	343	85%
HAS-10	p-dimethylaminobenzaldehyde	C <sub>20</sub> H <sub>20</sub> N <sub>4</sub> O <sub>2</sub> S	223	380	68%

### 3. 2. ADME properties:

The ADME properties profile of our created compounds was studied by the Swiss ADME server to detect the safer and potential drug candidate(s) to filter out the compounds that are most likely to fail in the subsequent stages of drug development due to unfavourable ADME properties [37. 38]. We assessed all synthesized compounds' ADME method. Also, we measured the Topological Polar Surface Area (TPSA), as this is another important property related to the bioavailability of drugs. Thus, passively absorbed molecules with a TPSA > 140 Å are thought to have low oral bioavailability [39].

Compounds **HAS-01, HAS-07, and HAS-09** have shown higher values of TPSA showing poor absorption. Whereas, the compounds **HAS-02, HAS-03, HAS-04, HAS-05, HAS-06, HAS-08 and HAS-10** tend to have fair absorption. The GI absorption score is a measure of the extent of absorption of a molecule from the intestine following oral administration [40]. The absorption could be excellent if the result were high. In this study, the GI absorption of most of the compounds was high predicting them to be well absorbed from the intestine. Compounds (**HAS-01 – HAS-10**) fulfilled the Lipinski rule. The ADME properties profiles for the created compounds are shown in Table 2.

**Table 2.** ADME properties profile of the synthesized compounds.

Compounds	H-bond Acceptors	H-bond Donors	MR	TPSA	GI Absorption	BBB Permeant	Lipinski Violations
<b>HAS-01</b>	6	2	104.53	148.64	Low	No	0
<b>HAS-02</b>	6	2	108.69	121.28	High	No	0
<b>HAS-03</b>	5	2	102.2	112.05	High	No	0
<b>HAS-04</b>	4	2	100.72	102.82	High	No	0
<b>HAS-05</b>	5	3	97.73	123.05	High	No	0
<b>HAS-06</b>	4	2	100.67	102.82	High	No	0
<b>HAS-07</b>	7	3	110.71	141.51	Low	No	0
<b>HAS-08</b>	5	3	97.73	123.05	High	No	0
<b>HAS-09</b>	4	2	93.58	131.06	Low	No	0
<b>HAS-10</b>	4	2	109.91	106.06	High	No	0

### 3. 3. Determination of antimicrobial activity

The antibacterial activity of compounds (**HAS-01 – HAS-10**) and standard antibiotic (Tetracycline) was determined against two gram-positive bacteria (*Staphylococcus aureus* ATCC25923, *Bacillus cereus* ATCC11778) and two gram-negative bacteria (*Salmonella*

*typhimurium* ATCC23564, *Escherichia coli* NCIM2931), by agar well diffusion method [41]. The microorganisms were maintained at 4 °C. Molten Mueller Hinton agar (40-42 °C) was seeded with 200 µl of inoculums ( $1 \times 10^8$  cfu/ml) and poured into Petri dishes. 100 µl of 20 mg/ml drug in 100% DMSO was added in well. The plates were incubated at 37 °C for 24 hr. DMSO was used as a negative control. Antimicrobial activity was assayed by measuring the diameter of the zone of inhibition formed around the well and the diameter was measured in millimeters.

**Table 3.** Antimicrobial Activities of Synthesized Compounds and Standard Drug (Tetracycline).

	<i>Staphylococcus aureus</i>	<i>Bacillus cereus</i>	<i>Salmonella Typhimurium</i>	<i>Escherichia coli</i>
<b>Tetracycline</b>	16	25	13	15
<b>HAS-01</b>	24	0	18	13
<b>HAS-02</b>	15	0	0	0
<b>HAS-03</b>	17	0	20	10
<b>HAS-04</b>	20	0	0	11
<b>HAS-05</b>	0	0	14	0
<b>HAS-06</b>	0	0	20	0
<b>HAS-07</b>	0	0	23	0
<b>HAS-08</b>	0	0	19	10
<b>HAS-09</b>	0	10	0	0
<b>HAS-10</b>	0	12	0	0

The antimicrobial activity of synthesized compounds (**HAS-01 to HAS-10**) was evaluated with 20 mg/ml concentration against two gram-positive bacteria and two gram-negative bacteria as shown in Table 3. The compounds (**HAS-01 to HAS-05**) show inhibition against *S. aureus* while (**HAS-09 and HAS-10**) show inhibition against *B. cereus*. Whereas (**HAS-01, HAS-03, HAS-05 to HAS-08**) showing inhibition against *S. typhimurium*, and (**HAS-01, HAS-03, HAS-04 and HAS-08**) showing inhibition against *E. coli*. Overall gram-negative bacteria were more sensitive towards the synthesized compounds than the gram-positive bacteria, which may be because of the variation in the composition of the cell wall of the gram-positive bacteria and gram-negative bacteria. In certain cases, compounds show better inhibition than standard antibiotic tetracycline. Overall, remarkable antimicrobial activity was exhibited by (**HAS-01 and HAS-03**) than the other compounds in Table 3.

#### 4. RESULTS AND DISCUSSION

In the current study, 2-(4-hydroxyphenyl)-4-methylthiazole-5-carboxylic acid (**1**) acts as the precursor for the synthesis of acyl hydrazone derivatives (**HAS-01 to HAS-10**). To synthesize ethyl 2-(4-hydroxyphenyl)-4-methylthiazole-5-carboxylate (**2**), (**1**) was reacted with thionyl chloride and methanol. 2-(4-hydroxyphenyl)-4-methylthiazole-5-carbohydrazide (**3**) was obtained by adding hydrazine hydrate to (**2**). (**3**) was reacted with differing aldehydes to synthesize Acyl hydrazone derivatives (**HAS-01 to HAS-10**). The compounds were synthesized according to the procedure in the literature. The chemical structure of compounds was identified by, HRMS, FT-IR and <sup>1</sup>H-NMR spectra.

#### 5. SPECTRAL DATA OF SYNTHESIZED COMPOUNDS

##### **2-(4-hydroxyphenyl)-4-methyl-N'-(2-nitrobenzylidene)thiazole-5-carbohydrazide (HAS-01):**

The yield of the pale-yellow product (HAS-01) was 89%, (m.p. 265 °C), FT-IR (KBr, cm<sup>-1</sup>) 3650 (O-H), 3550 (N-H), 2937 (C-H), 1649 (C=O), 1510 (C=C) 1595 (C=N), 1354 (NO<sub>2</sub> str.) 661 (C-S); MS (m/z): 381 (M-H); <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>) δ(ppm) 12.03 (s, 1H), 10.12 (s, 1H), 8.50 (s, 1H), 8.12 (s, 1H), 8.11 – 7.94 (m, 1H), 7.91 – 7.77 (m, 2H), 7.74 – 7.48 (m, 1H), 7.02 – 6.70 (m, 2H), 2.67 (s, 3H); <sup>13</sup>C NMR (100 MHz, DMSO- d<sub>6</sub>) δ (ppm) 116 (C-2), 124.25 (C-14 C-3), 125.38 (C-10, C-11), 128.64 (C-12, C-13), 128.71 (C-4), 128.76 (C-9, C-8), 131.16 (C-15), 134.50 (C-1), 148.74 (C-6), 160.82 (C-5); Anal. Calcd. for C<sub>18</sub>H<sub>14</sub>N<sub>4</sub>O<sub>4</sub>S; C, 56.54; H, 3.69; N, 14.65; O, 16.74; S, 8.38; Found: C, 56.59; H, 3.73; N, 14.62; O, 16.75; S, 8.31.

##### **N'-(3,4-dimethoxybenzylidene)-2-(4-hydroxyphenyl)-4-methylthiazole-5-carbohydrazide (HAS-02):**

The yield of the pale-yellow product (HAS-02) was 92%, (m.p. 240 °C). FT-IR (KBr, cm<sup>-1</sup>) 3630 (O-H), 3515 (N-H), 2937 (C-H), 1685 (C=C), 1647 (C=O), 1577 (C=N), 1139 (C-O-C), 1111 (C-O-C), 700 (C-S); MS (m/z): 398 (M+H); <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>) δ 11.71 (s, 1H), 10.14 (s, 1H), 8.02 (s, 1H), 7.19-7.84 (m, 4H) 6.08 – 7.06 (m, 3H), 3.86 (m, 6H), 2.51 (s, 3H); <sup>13</sup>C NMR (400 MHz, DMSO-d<sub>6</sub>): δ (ppm) 19.37 (C-7), 55.53 (C-17), 56.06 (C-16), 108.57 (C-15, C-12), 112.02 (C-02), 116.50 (C-11), 117.62 (C-3), 112.50 (C-10), 124.35 (C-4), 127.31 (C-8), 128.47 (C-9), 143.73 (C-13), 149.56 (C-1), 151.08 (C-08), 160.66 (C-5); Anal. Calcd. for C<sub>20</sub>H<sub>19</sub>N<sub>3</sub>O<sub>4</sub>S; C, 60.44; H, 4.82; N, 10.57; O, 16.10; S, 8.07; Found: C, 60.59; H, 4.80; N, 10.45; O, 16.06; S, 8.10.

##### **2-(4-hydroxyphenyl)-n'-(4-methoxybenzylidene)-4-methylthiazole-5-carbohydrazide (HAS-03):**

The yield of the pale-yellow product (HAS-03) was 90%, (m.p. 247 °C). FT-IR (KBr, cm<sup>-1</sup>) 3530 (O-H), 3470 (N-H), 2927 (C-H), 1653 (C=O), 1608 (C=C), 1517 (C=N), 1170 (C-O-C), 702 (C-S); MS (m/z): 366 (M-H); <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>) δ <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>) δ 11.62 (s, 1H), 10.10 (s, 1H), 8.09 – 7.66 (m, 4H), 7.04 (d, J = 8.4 Hz, 3H), 6.96 – 6.67 (m, 2H), 2.92 – 2.19 (m, 6H).; <sup>13</sup>C NMR (400 MHz, DMSO-d<sub>6</sub>) δ (ppm) 19.39 (C-7), 55.86 (C-13), 115.11 (C-11) 116.60 (C-2), 124.45 (C-10), 127.18 (C3), 128.70 (C-4), 129.36



(C-8), 143.95 (C-9) 160.67(C-1), 161.70 (C-12), 162.60 (C-5); Anal. Calcd. for  $C_{19}H_{17}N_3O_3S$ ; C, 62.11; H, 4.66; N, 11.44; O, 13.06; S, 8.73; Found: C, 62.40; H, 4.52; N, 11.03; O, 13.45; S, 8.60

**N'-(4-chlorobenzylidene)-2-(4-hydroxyphenyl)-4-methylthiazole-5-carbohydrazide (HAS-04):**

The yield of the pale-yellow product (HAS-04) was 77%, (m.p. 235 °C). FT-IR (KBr,  $cm^{-1}$ ) 3420 (O-H), 3250 (N-H), 2930 (C-H), 1678 (C=C), 1604 (C=O), 1566 (C=N), 785 (C-Cl), 729 (C-S); MS (m/z): 372 (M+H);  $^1H$  NMR (400 MHz, DMSO- $d_6$ ) 11.92 (s, 1H), 9.99 (s, 1H), 8.06 (s, 1H), 7.81 (d,  $J = 7.6$  Hz, 3H), 7.67 (d,  $J = 7.3$  Hz, 1H), 7.58 – 7.32 (m, 2H), 7.24 – 6.38 (m, 2H), 2.69 (s, 3H);  $^{13}C$  NMR (400 MHz, DMSO- $d_6$ )  $\delta$  (ppm) 17.2 (C-7), 116.65 (C-2) 123.99 (C-3, C-12), 126.41 (C-11), 127.10 (C-10), 128.68 (C-4), 130.08 (C8), 131.47 (C-9), 134.22 (C-1), 136.89 (C-6) 161.07(C-5); Found: C, 61.36; H, 4.32; N, 11.60; O, 13.62; S, 9.10.

**N'-(4-hydroxybenzylidene)-2-(4-hydroxyphenyl)-4-methylthiazole-5-carbohydrazide (HAS-05):**

The yield of the pale-yellow product (HAS-05) was 87%, (m.p. 254 °C); FT-IR (KBr,  $cm^{-1}$ ) 3629 (O-H), 3650 (O-H), 3543 (N-H), 2931 (C-H), 1673 (C=C), 1660 (C=O), 1640 (C=N), 702 (C-S); MS (m/z): 353; Anal. Calcd. for  $C_{18}H_{15}N_3O_3S$ : Elemental Analysis: C, 61.18; H, 4.28; N, 11.89; O, 13.58; S, 9.07; Found: C, 61.21; H, 4.29; N, 11.85; O, 13.51; S, 9.14.

**2-(4-hydroxyphenyl)-4-methyl-n'-(4-methylbenzylidene)thiazole-5-carbohydrazide (HAS-06):**

The yield of the pale-yellow product (HAS-06) was 72%, (m.p. 233 °C); FT-IR (KBr,  $cm^{-1}$ ) 3424 (O-H), 3502 (N-H), 2940 (C-H), 2937 (C-H), 1653 (C=C), 1680 (C=O), 1551 (C=N), 719 (C-S); MS (m/z): 351; Anal. Calcd. for  $C_{19}H_{17}N_3O_2S$ : C, 64.94; H, 4.88; N, 11.96; O, 9.11; S, 9.12; Found: C, 64.86; H, 4.91; N, 11.84; O, 9.19; S, 9.20.

**N'-(4-hydroxy-3,5-dimethoxybenzylidene)-2-(4-hydroxyphenyl)-4-methylthiazole-5-carbohydrazide (HAS-07):**

The yield of the pale-yellow product (HAS-07) was 80%, (m.p. 244 °C).; FT-IR (KBr,  $cm^{-1}$ ) 3627 (O-H) 3651 (O-H), 3505 (N-H), 2915 (C-H), 1622 (C=C), 1653 (C=O), 1557 (C=N), 1119 (C-O-C), 1137 (C-O-C), 705 (C-S); 413; Anal. Calcd. for  $C_{20}H_{19}N_3O_5S$ : C, 58.10; H, 4.63; N, 10.16; O, 19.35; S, 7.75; Found: C, 58.45; H, 4.49; N, 10.27; O, 19.12; S, 7.67.

**N'-(2-hydroxybenzylidene)-2-(4-hydroxyphenyl)-4-methylthiazole-5-carbohydrazide (HAS-08):**

The yield of the pale-yellow product (HAS-08) was 85%, (m.p. 243 °C); FT-IR (KBr,  $cm^{-1}$ ) 3620 (O-H), 3613 (O-H), 3520 (N-H), 2941 (C-H), 1673 (C=C), 1660 (C=O), 1570 (C=N), 711 (C-S); 353; Anal. Calcd. for  $C_{18}H_{15}N_3O_3S$ : C, 61.18; H, 4.28; N, 11.89; O, 13.58; S, 9.07; Found: C, 61.22; H, 4.39; N, 11.76; O, 13.44; S, 9.19.

**2-(4-hydroxyphenyl)-4-methyl-n'-(thiophen-2-ylmethylene)thiazole-5-carbohydrazide (HAS-09):**

The yield of the pale-yellow product (HAS-09) was 85%, (m.p. 245 °C); FT-IR (KBr,  $cm^{-1}$ ) 3636 (O-H), 3500 (N-H), 2910 (C-H), 1653 (C=C), 1623 (C=O), 1507 (C=N), 702 (C-S),



709 (C-S); MS (m/z): 343; Anal. Calcd. for  $C_{16}H_{13}N_3O_2S_2$ : C, 55.96; H, 3.82; N, 12.24; O, 9.32; S, 18.67; Found: C, 55.88; H, 3.76; N, 12.19; O, 9.76; S, 18.41.

**N'-(4-(dimethylamino)benzylidene)-2-(4-hydroxyphenyl)-4-methylthiazole-5-carbohydrazide (HAS-10):**

The yield of the pale-yellow product (HAS-10) was 68%, (m.p. 223 °C); FT-IR (KBr,  $cm^{-1}$ ) 3621 (O-H), 3523 (N-H), 2930 (C-H), 2914 (C-H), 1612 (C=C), 1622 (C=O), 1523 (C=N), 704 (C-S); MS (m/z): 380; Anal. Calcd. for  $C_{20}H_{20}N_4O_2S$ : C, 63.14; H, 5.30; N, 14.73; O, 8.41; S, 8.43; Found: C:63.22; H, 5.32; N, 14.46; O, 8.71; S, 8.29.

## 8. CONCLUSION

The overall aim of the present work was to synthesize, characterize, and evaluate the antimicrobial activity of new acyl hydrazone derivatives. We found that the reaction of various aldehydes and hydrazide afforded a good yield of a series of acyl hydrazones (**HAS-01 to HAS-10**) in the presence of hydrochloric acid as a catalyst and methanol as a solvent. Among the antimicrobial analysis, gram-negative bacteria were more sensitive towards the synthesized compounds than the gram-positive. Because of the excellent biological activity of components of hybrid compounds, easy purification step and high yields, the investigation of acyl hydrazones will be the subject of our future investigations.

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