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Research Article

Synthesis of Cinnamanilide Derivatives and Their Antioxidant and Antimicrobial Activity

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The amide derivatives of cinnamic acid were synthesized and their antimicrobial and antioxidant activities were investigated. The investigation of antimicrobial potentials of the compounds demonstrated a strong activity against 21 bacterial strains comprising Gram-positive and Gram-negative bacteria. Compounds **2a**, **2b**, and **3b** showed strong antimicrobial activity against all microorganisms with the pMIC value ranging from 2.45 to 3.68. Compounds **2a**, **3a**, and **3b** demonstrated strong antioxidant activity with % inhibition of the DPPH radical of 51% (±1.14), 41% (±1.01), and 50% (±1.23), respectively. These findings indicate that the amide derivatives of the cinnamic acid possess strong antibacterial and antioxidant activities.

1. Introduction

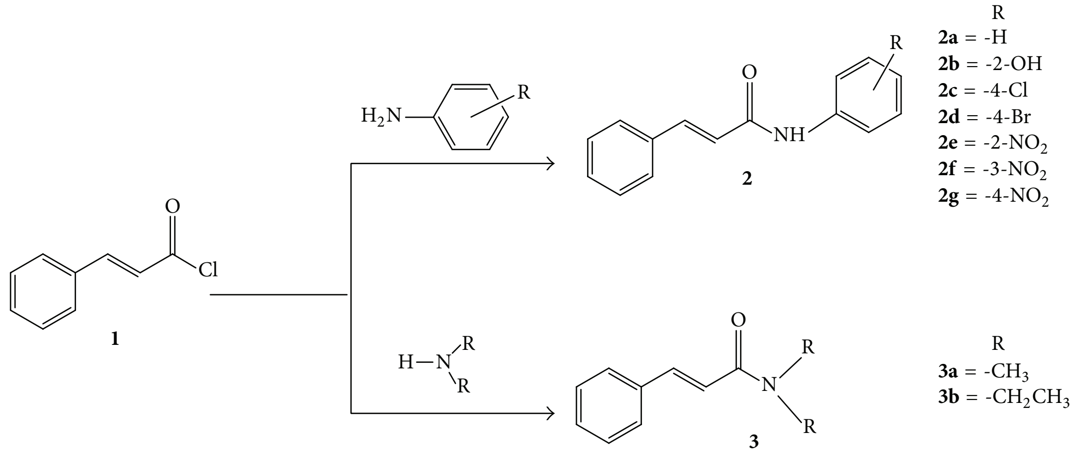
Discovery of simple organic compounds with the antimicrobial and antioxidant activities is of growing concern in the food industries for their preservative properties [1, 2]. Preservation of industrial food containing polyunsaturated fatty acids (eicosapentaenoic ($20{:}5\omega$-3) acid) has been a subject of growing interest, because of their importance in human nutrition. ω-3-Polyunsaturated fatty acids have several health benefits in cardiovascular disease, immune disorders, inflammation, allergies, and diabetes [3]. Therefore, the development of the antimicrobial compounds that can act as food preservatives by inhibiting the growth of bacteria or fungi, including mold, is very important [4].

Apart from the bacterial deterioration, the radical associated oxidation of fatty acids is one of the most important reactions leading to a degeneration of food [5, 6]. Several compounds with the antioxidant activity have been used to slow down the radical associated oxidative reactions. Antioxidants are molecules that inhibit or quench free radical reactions and delay or inhibit the cellular damage [7, 8]. The butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), and tertiary butylhydroquinone (TBHQ) have been used commonly as food antioxidants. However, some of these molecules are known to possess toxic and carcinogenic side effects in animal models [9]. Therefore, the demand has increased because of questions about the long-term safety and negative consumer perception of the commonly used synthetic antioxidants BHT and BHA. The discovery of compounds that can show both antimicrobial and antioxidant activities with no toxic effects on health is highly awaited.

Due to its common occurrence in plants and its low toxicity [10, 11], cinnamic acid has been evaluated as an antioxidant compound [12, 13]. Moreover, the cinnamic acid derivatives are reported to possess better antimicrobial activity than cinnamic acid itself [14, 15]. In the present paper the synthesis, antimicrobial, and antioxidant activities of the amide derivatives of cinnamic acid are presented.

2. Materials and Methods

All chemicals, solvents, and biochemical reagents were of analytical grade and purchased from commercial sources. 1,1-Diphenyl-2-picrylhydrazyl (DPPH) was purchased from Aldrich Chemical Co. (Milwaukee, WI, USA). UV-Vis spectra were obtained on a Perkin-Elmer 554 double beam spectrophotometer. The final products were characterized by ^{1}H



Scheme 1: Synthesis of compounds **2a**–**2g** and **3a**-**3b**.

and ^{13}C NMR (JEOL FX-90Q FT NMR, 300 MHz) and mass spectrometry (JEOL JMS 600 Mass Spectrometer).

*2.1. General Procedure for the Synthesis of Compounds **2a**–**2g** and **3a**-**3b**.* Compounds **2a**–**2d** and **3a**-**3b** (Scheme 1) were synthesized by slight modification of the typical procedure adopted for various cinnamic acid derivatives [16, 17]. To a stirred solution containing aniline derivatives or amine derivatives (25 mmol), K_2CO_3 (4.15 g, 30 mmol), and tetrahydrofuran (30 mL), the cinnamoyl chloride (4.10 g, 20 mmol) dissolved tetrahydrofuran (5 mL) was added dropwise at 0°C. The mixture was stirred at 0°C for 30 min and then at RT for 3 hours. The solution was concentrated under vacuum and then poured on ice cold water with stirring. The precipitated product was washed with water and dried in an oven at 100°C. The final compounds were then obtained by crystallization from ethanol.

For the synthesis of compounds **2e**–**2g**, to a stirred solution of respective aniline derivatives (30 mmol) in diethyl ether (30 mL), the cinnamoyl chloride (4.10 g, 20 mmol) dissolved in diethyl ether (5 mL) was added dropwise at 0°C. The mixture was stirred at 0°C for 30 min and then at RT for 3 hours. After completion of reaction the solvent was concentrated and then added to 100 mL of dichloromethane. The solution was washed 3 times with 1 N HCl and 2 times with 1 N $NaHCO_3$. The separated organic layer was dried over Mg_2SO_4 and solvent was evaporated completely to obtain a residue. The final compounds were obtained by crystallization from ethanol.

*(**2a**) N-Phenylcinnamamide.* 75.55% yield, ^{1}H NMR ($CDCl_3$, 300 MHz, 298 K) δ (ppm): 9.74 (s, 1H, -NH), 7.57 (m, 10H, Ar-H), 7.50 (d, 1H, $J = 15.6$ Hz, CH=CH), 6.72 (d, 1H, $J = 15.6$ Hz, CH=CH). ^{13}C NMR (300 MHz, $CDCl_3$): 163.66 (**C**=O), 140.32 (Ar-**C**H=CH), 139.16, 134.86, 129.42, 128.90, 128.11, 127.52, 122.31 (Ar), 121.62 (CH=**C**H-C=O). JEOL JMS 600, EI$^+$ mode: $m/z = 223.2089$ $[M]^+$, 224.2087 $[M + H]^+$.

*(**2b**) N-(2-Hydroxyphenyl)cinnamamide.* 50.76%, ^{1}H NMR (d6-DMSO, 300 MHz, 298 K) δ (ppm): 10.03 (bs, 1H, -NH), 9.52, (s, 1H, -OH), 7.96 (d, 1H, $J = 15.6$ Hz, CH=CH), 7.38–7.65 (m, 6H, Ar-H), 7.18 (d, 1H, $J = 15.6$ Hz, CH=CH), 6.90–6.96 (dt, 2H, Ar-H), 6.81 (t, 1H, Ar-H). ^{13}C NMR (d6-DMSO, 300 MHz, 298 K): 164.6 (**C**=O), 148.3 (HO-Ar$_{\text{-}\mathbf{C}}$), 140.7 (Ar-**C**H=CH), 135.5, 130.2, 129.5, 128.5, 128.3, 127.3, 125.1, 123.3, 122.5, 116.2 (Ar), 119.5 (CH=**C**H-C=O). JEOL JMS 600, EI$^+$ mode: $m/z = 239.2945$ $[M]^+$, 240.2946 $[M + H]^+$.

*(**2c**) N-(4-Chlorophenyl)cinnamamide.* 76.65% yield, ^{1}H NMR ($CDCl_3$, 300 MHz, 298 K) δ (ppm): 7.76 (d, 1H, $J = 15.6$ Hz, CH=CH), 7.62–7.60 (m, 4H, Ar-H), 7.52 (d, 2H, Ar-H), 7.41–7.39 (m, 3H, Ar-H), 7.33 (br, 1H, -NH), 6.58 (d, $J = 15.6$ Hz, 1H, CH=CH). ^{13}C NMR (300 MHz, $CDCl_3$): 164.0 (**C**=O), 142.9 (Ar-**C**H=CH), 136.6, 134.5 (Ar), 130.2 (Cl-Ar$_{\text{-}\mathbf{C}}$), 129.1, 129.04, 128.9, 121.2 (Ar-C), 120.04 (CH=**C**H-C=O). JEOL JMS 600, EI$^+$ mode: $m/z = 257.7134$ $[M]^+$, 258.7136 $[M + H]^+$.

*(**2d**) N-(4-Bromophenyl)cinnamamide.* 70.45% yield, ^{1}H NMR ($CDCl_3$, 300 MHz, 298 K) δ (ppm): 7.79 (d, 1H, $J = 15.6$ Hz, CH=CH), 7.57–7.54 (m, 4H, Ar-H), 7.49 (d, 2H, Ar-H), 7.43–7.41 (m, 3H, Ar-H), 7.34 (br, 1H, -NH) 6.55 (d, 1H, $J = 15.6$ Hz, CH=CH). ^{13}C NMR (300 MHz, $CDCl_3$): 164.1 (**C**=O), 141.0 (Ar-**C**H=CH), 138.0, 132.2, 130.1, 129.5, 129.3, 128.1 (Ar), 121.5 (Br-Ar$_{\text{-}\mathbf{C}}$), 119.7 (CH=**C**H-C=O). JEOL JMS 600, EI$^+$ mode: $m/z = 302.1662$ $[M]^+$, 303.1664 $[M + H]^+$.

*(**2e**) N-(2-Nitrophenyl)cinnamamide.* 70.34% yield. ^{1}H NMR ($CDCl_3$, 300 MHz, 298 K) δ (ppm), 10.61 (br, 1H, -NH), 8.92 (1H, d, $J = 7.8$ Hz, Ar-H), 8.22 (1H, d, $J = 8.4$ Hz, Ar-H), 7.75 (d, 1H, $J = 15.6$ Hz, CH=CH), 7.64–7.70 (t, 1H, Ar-H), 7.56–7.59 (dd, 2H, Ar-H), 7.39–7.41 (m, 3H, Ar-H), 7.17–7.20 (t, 1H, Ar-H), 6.58 (d, 1H, $J = 15.6$ Hz, CH=CH). ^{13}C NMR (d6-DMSO, 300 MHz,): 164.9 (**C**=O), 144.2 (NO_2-Ar$_{\text{-}\mathbf{C}}$), 136.9 (Ar-**C**H=CH), 136.4, 135.8, 134.8, 130.9, 129.5, 128.7, 126.3, 123.6, 122.8 (Ar), 121.6 (CH=**C**H-C=O). JEOL JMS 600, EI$^+$ mode: $m/z = 268.2617$ $[M]^+$.

*(**2f**) N-(3-Nitrophenyl)cinnamamide.* 72.95% yield, ^{1}H NMR (d6-DMSO, 300 MHz, 298 K) δ (ppm), 10.68 (br, 1H, -NH), 8.77 (1H, s, Ar-H), 8.02 (d, 1H, $J = 7.8$ Hz, Ar-H), 7.89 (d,

Table 1: Antimicrobial activity of compounds **2a–2g** and **3a-3b**.

Microbial strain	pMIC								
	2a	**2b**	**2c**	**2d**	**2e**	**2f**	**2g**	**3a**	**3b**
E. coli K99	2.45	3.68	2.81	2.58	2.83	3.13	*	*	*
E. coli 306	2.45	3.38	2.81	2.88	2.83	2.83	*	2.41	*
E. coli K88	2.45	3.68	3.11	2.58	3.13	2.83	*	*	*
E. coli LT37	3.95	3.68	4.41	2.58	4.03	4.43	4.03	3.61	3.85
E. coli 872	2.75	3.68	2.81	2.58	3.13	2.83	*	*	3.54
E. coli ROW 7/12	2.75	3.68	3.11	2.58	2.83	3.13	2.83	*	*
E. coli 3:37C	2.75	3.68	2.81	2.58	2.83	2.53	2.53	*	2.34
E. coli CD/99/1	2.75	3.38	3.11	2.58	2.83	3.13	2.53	*	2.34
Salmonella TyphiTy2	3.95	3.68	2.51	*	*	*	2.53	*	2.64
Shigella dysenteriae 1	*	2.78	2.51	*	2.53	2.53	2.83	*	2.94
Shigella dysenteriae 8	*	3.68	2.51	*	2.83	2.53	3.13	*	2.94
Shigella sonnei 1	*	2.78	*	*	2.53	*	3.83	2.71	2.64
Shigella boydii D13629	*	3.08	2.51	*	2.53	*	2.53	*	3.85
Shigella flexneri Type 6	*	3.08	2.51	*	2.53	2.53	3.13	2.71	2.94
Vibrio cholerae 1313	2.45	3.68	3.11	*	2.53	2.53	2.53	*	*
Vibrio cholerae 293	2.45	3.38	3.11	2.58	2.53	2.83	2.53	2.41	2.34
Vibrio cholerae 1315	3.05	3.38	3.11	2.58	3.13	2.83	3.13	*	*
Vibrio cholerae 85	3.95	3.38	3.11	2.58	4.03	2.53	2.83	3.31	2.94
Staphylococcus aureus ML267	*	2.78	2.51	*	*	4.03	3.43	*	2.94
Bacillus pumilus 82	2.75	3.38	*	*	*	2.53	*	3.01	3.24
Bacillus subtilis ATCC 6633	3.95	3.68	3.71	*	*	2.53	*	*	*

[*] No antimicrobial activity was observed in the concentration range of 5–800 μg/mL.

1H, J = 7.8 Hz, Ar-H), 7.44–7.72 (m, 7H, Ar-H, CH=CH), 6.82 (d, 1H, J = 15.6 Hz, CH=CH). ^{13}C NMR (d6-DMSO, 300 MHz,): 164.6 (**C**=O), 148.5 (NO_2-Ar$_{\text{-C}}$), 141.6 (Ar-**C**H=CH), 140.9, 135.0, 130.4, 129.4, 128.3, 125.6, 122.1, 113.9 (Ar), 118.1 (CH=**C**H-C=O). JEOL JMS 600, EI$^+$ mode: m/z = 268.2615 [M]$^+$.

*(**2g**) N-(4-Nitrophenyl)cinnamamide*. 68.23% yield, ^{1}H NMR (d6-DMSO, 300 MHz, 298 K) δ (ppm): 10.90 (s, 1H, -NH), 8.22 (d, 2H, J = 8.7 Hz, Ar-H), 7.93 (d, 2H, J = 7.8 Hz, Ar-H), 7.69–7.43 (m, 6H, Ar-H, CH=CH), 6.85 (d, 1H, J = 15.0 Hz, CH=CH). ^{13}C NMR (d6-DMSO, 300 MHz,): 164.9 (**C**=O), 146.1 (NO_2-Ar$_{\text{-C}}$), 142.8, 142.4 (Ar), 142.2 (Ar-**C**H=CH), 135.0, 129.5, 128.5, 125.7, 121.9 (Ar-C), 119.6 (CH=**C**H-C=O). JEOL JMS 600, EI$^+$ mode: m/z = 268.2615 [M]$^+$, 269.2657 [M + H]$^+$.

*(**3a**) N,N-Dimethylcinnamamide*. 73.34% yield, ^{1}H NMR ($CDCl_3$, 300 MHz, 298 K) δ (ppm): 7.66–7.71 (d, 1H, J = 15.6 Hz, CH=CH), 7.53 (d, 2H, J = 7.8 Hz, Ar-H), 7.35 (m, 3H, Ar-H), 6.68 (d, 1H, J = 15.0 Hz, CH=CH), 3.12 (s, 6H, -CH_3). ^{13}C NMR (300 MHz, $CDCl_3$): 167.0 (**C**=O), 142.9 (Ar-**C**H=CH), 135.5, 129.8, 129.0, 128.0 (Ar), 117.3 (CH=**C**H-C=O), 37.0 (**C**H_3). JEOL JMS 600, EI$^+$ mode: m/z = 175.0993 [M]$^+$, 176.1403 [M + H]$^+$.

*(**3b**) N,N-Diethylcinnamamide*. 76.85% yield, ^{1}H NMR ($CDCl_3$, 300 MHz, 298 K) δ (ppm): 7.73 (d, 1H, J = 15.9 Hz, CH=CH), 7.55 (m, 2H, J = 7.8 Hz, Ar-H), 7.39 (m, 3H, Ar-H), 6.85 (d, 1H, J = 15.0 Hz, CH=CH), 3.40–3.50 (m, 4H, CH_2), 1.25 (m, 6H, CH_3). ^{13}C NMR (300 MHz, $CDCl_3$): 165.7 (**C**=O), 142.3 (Ar-**C**H=CH), 135.5, 129.4, 128.7, 127.7 (Ar), 117.7 (CH=**C**H-C=O), 42.3 (**C**H_2-CH_3), 13.2 (-**C**H_3). JEOL JMS 600, EI$^+$ mode: m/z = 203.2913 [M]$^+$, 204.2732 [M + H]$^+$.

2.2. Antimicrobial Activity. The antimicrobial activity of the synthesized compounds was tested *in vitro* against twenty-one microorganisms. Stock solutions (1 mg/mL) of synthesized compounds **2a**–**2g** and **3a**-**3b** were prepared by dissolving each compound in dimethyl sulfoxide. Calculated volumes of stock solutions were dispensed in series of McCartney bottles previously containing calculated volumes of sterile cooled molten nutrient agar media (40–45°C) to prepare the volume of 30 mL each with dilutions of 5, 10, 25, 50, 100, 200, 400, and 800 μg/mL. These sterile nutrient agar media solutions were poured into Petri plates and allowed to solidify. These plates were kept in the refrigerator at 4°C for 24 h to allow the uniform diffusion of the compounds throughout the nutrient agar medium. Before spot inoculation, plates were kept at 37°C for 2 h. One loop full (loop diameter: 3 mm) of an overnight grown peptone water culture of each microorganism was inoculated, and the location of the inoculation was marked by the checkerboard technique. The spot inoculated plates were incubated at 37°C for 24 h and the minimum inhibitory concentration (MIC, mM) values were obtained. The calculated pMIC ($-\log_{10}$MIC) values are presented in Table 1. Experiments were done in triplicate, and the results were presented as mean values of the three measurements.

2.3. Antioxidant Activity. The antioxidant activity of the synthesized compounds (**2a**–**2g**, **3a**-**3b**) was evaluated using the DPPH free radical scavenging assay [18]. The 200 μL of test sample solution (1 mg/mL) was added to 4 mL of 100 μM methanolic DPPH. The solution was allowed to incubate for 20 minutes at 25°C, and the absorbance was measured at 517 nm. Ascorbic acid (1 mg/mL) was used as reference standard. A blank was prepared without adding the standard or test compound. The lower absorbance of the reaction mixture indicates higher free radical scavenging activity. The capability to scavenge the DPPH radical was calculated using the following equation:

$$\% \text{ inhibition} = \frac{A_{\text{control}} - A_{\text{sample}}}{A_{\text{control}}} \times 100, \qquad (1)$$

where A_{control} is the absorbance of the DPPH alone and A_{sample} is the absorbance of DPPH in the presence of compounds **2a**–**2g**, **3a**-**3b**. All determinations were performed in triplicate ($n = 3$). The results are presented in Figure 1.

3. Results and Discussions

3.1. The Synthesis. The amide derivatives of cinnamic acid **2a**–**2g** and **3a**-**3b** were synthesized to study the effect of amide nitrogen substituents on the antimicrobial activity. As shown in Scheme 1, the reaction of cinnamoyl chloride with corresponding aromatic or aliphatic amines gave compounds **2a**–**2g** and **3a**-**3b**. All compounds were obtained in good yield, purified by recrystallization, and characterized by ^{1}H NMR, ^{13}C NMR, and mass spectrometry.

3.2. Antimicrobial Activity. The pMIC (− log(MIC)) values of compounds **2a**–**2g**, **3a**-**3b** are presented in Table 1. Except compound **2d**, all compounds showed a good antibacterial activity against Gram-negative compared to Gram-positive bacterial strains. Compound **2b** showed strong antimicrobial activity against all microorganisms with the pMIC values ranging from 2.78 to 3.68. However, compound **2d** demonstrated little (pMIC = 2.58) or no antibacterial activity in the tested concentration domain. Similarly, compound **3a** also showed very poor or no antimicrobial activity against the tested microorganisms. Therefore, compounds **2d** and **3a** were considered as poor antimicrobial compounds. Compounds **2c**, **2e**–**2g** showed the highest antimicrobial activity against *E. coli LT37* with the pMIC of 4.03–4.43. Moreover, compounds **2e** and **2f** demonstrated strong activity against *Vibrio cholerae 85* and *Staphylococcus aureus ML267*, respectively.

Compound **2a** demonstrated strongest activity against *E. coli LT37*, *Salmonella* Typhi Ty2, *Vibrio cholerae 85*, and *Bacillus subtilis ATCC 6633* with the pMIC value of 3.95. Compound **2b** showed strong activity against all microorganisms except for *Shigella dysenteriae 1*, *Shigella sonnei 1*, and *Staphylococcus aureus ML267* with the lowest pMIC value of 2.78. Compound **2c** did not show any antibacterial activity against *Shigella sonnei 1* and *Bacillus pumilus 82*. Compound **3b** showed the strongest activity against *E. coli LT37* and *Shigella boydii D13629* with the pMIC of 3.85.

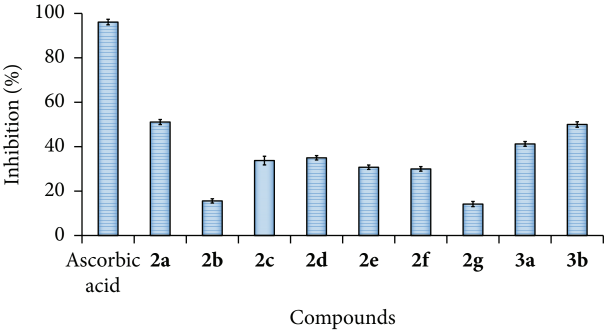


Figure 1: DPPH radical scavenging activity of compounds **2a**–**2g** and **3a**-**3b**.

From the results of the microbiological studies, it is evident that substituents on the amide nitrogen of cinnamamide derivatives **2a**–**2g** and **3a**-**3b** play a critical role in their antimicrobial activities. Derivatives **2a**–**2g** and **3a**-**3b** were obtained from primary amines (aniline derivatives) and secondary amines, respectively. It is important to notice that compound **2b**, which contains *o*-hydroxyphenyl substituent on the amide nitrogen, showed a significant increase in the antimicrobial activity as compared to compound **2a**, which contains only phenyl group. Compound **2c** containing *p*-chlorophenyl substituent on the amide nitrogen showed strong activity as compared to compound **2d**, which contains *p*-bromophenyl substitution on the amide nitrogen. Among the compounds containing the nitrophenyl substituents on the amide nitrogen, compound **2e** showed strong activity as compared to compounds **2f** and **2g**. The *m*-nitrophenyl substituent in compound **2e** endows it with a strong antibacterial activity as compared to the *o*-nitrophenyl and *p*-nitrophenyl substituents in compounds **2f** and **2g**, respectively. It is also important to notice that the aromatic substituents on the amide nitrogen allow overall strong activity as compared to the aliphatic substituents. The presence of bulky ethyl groups on the amide nitrogen of compound **3b** allows it to demonstrate strong activity as compared to compound **3b** containing methyl groups.

3.3. Antioxidant Activity. DPPH radical scavenging is considered as a good *in vitro* model and is widely used to assess antioxidant efficacy [19, 20]. The DPPH free radical scavenging assay was employed to evaluate the antioxidant activity of the synthesized compounds. The DPPH radical scavenging activity of compounds **2a**–**2g**, **3a**-**3b** (50 μg/mL) was compared with that of ascorbic acid at the same concentration. As presented in Figure 1, the results of antioxidant screenings were expressed as % of inhibition of the DPPH radical.

As depicted in Figure 1, most compounds showed moderate-to-good antioxidant activity. Compounds **2a**, **3a**, and **3b** showed strong activity as indicated by the % inhibition of the DPPH radical, 51% (±1.14), 41% (±1.01), and 50% (±1.23), respectively. Compounds **2b** and **2g** showed very low activity with the % inhibition of 16% (±1.12) and 14% (±1.09), respectively. Compounds **2c**, **2d**, **2e**, and **2f** showed moderate activity with the % inhibition of 34% (±1.96), 35% (±0.98), 31% (±0.97), and 30% (±1.02), respectively. The results clearly indicate the electron donating groups on the amide nitrogen (**3a**-**3b**) play an important role in scavenging the free radicals. Moreover, compound **2a**, which contains phenyl group on amide nitrogen, demonstrates almost similar radical scavenging activity to that of compounds **3a**, **3b**, which contain dimethyl and diethyl substituents on amide nitrogen, respectively.

However, the electron withdrawing substituents such as *p*-chloro, *p*-bromo, and *o*-nitro, *m*-nitro, and *p*-nitro on phenyl ring in compounds **2c**, **2d**, and **2e**–**2g**, respectively, significantly decrease radical scavenging activity. The results obtained in this study are in line with other findings [21].

4. Conclusion

Most of the amide derivatives of cinnamic acid mentioned in this showed moderate-to-high antibacterial and antioxidant activities. The investigation of antimicrobial potentials of the compounds demonstrated a strong activity against 21 bacterial strains comprising Gram-positive and Gram-negative bacteria. Compounds **2a**, **2b**, and **3b** showed strong antimicrobial activity against all microorganisms with the pMIC value ranging from 2.45 to 3.68. Compounds **2a**, **3a**, and **3b** demonstrated strong antioxidant activity. These findings encourage the synthesis of new amide derivatives of cinnamic acid. These findings indicate that the amide derivatives of the cinnamic acid afford strong antibacterial and antioxidant activities.

Conflict of Interests

All authors declare that there is no conflict of interests.

Acknowledgment

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References

[1] T. Hintz, K. K. Matthews, and R. Di, “The use of plant antimicrobial compounds for food preservation,” *BioMed Research International*, vol. 2015, Article ID 246264, 12 pages, 2015.

[2] A. Lucera, C. Costa, A. Conte, and M. A. Del Nobile, “Food applications of natural antimicrobial compounds,” *Frontiers in Microbiology*, vol. 3, article 287, 2012.

[3] K. W. Lee and G. Y. H. Lip, “The role of omega-3 fatty acids in the secondary prevention of cardiovascular disease,” *QJM*, vol. 96, no. 7, pp. 465–480, 2003.

[4] H.-S. Wu, W. Raza, J.-Q. Fan, Y.-G. Sun, W. Bao, and Q.-R. Shen, “Cinnamic acid inhibits growth but stimulates production of pathogenesis factors by *in vitro* cultures of *Fusarium oxysporum* f.sp. *niveum*,” *Journal of Agricultural and Food Chemistry*, vol. 56, no. 4, pp. 1316–1321, 2008.

[5] K. Bagchi and S. Puri, “Free radicals and antioxidants in health and disease,” *EMHJ—Eastern Mediterranean Health Journal*, vol. 4, no. 2, pp. 350–360, 1998.

[6] Y.-W. Kim and T. V. Byzova, “Oxidative stress in angiogenesis and vascular disease,” *Blood*, vol. 123, no. 5, pp. 625–631, 2014.

[7] I. S. Young and J. V. Woodside, “Antioxidants in health and disease,” *Journal of Clinical Pathology*, vol. 54, no. 3, pp. 176–186, 2001.

[8] D. K. Pal and S. B. Nimse, “Screening of the antioxidant activity of *Hydrilla verticillata* plant,” *Asian Journal of Chemistry*, vol. 18, no. 4, pp. 3004–3008, 2006.

[9] H.-J. Suh, M.-S. Chung, Y.-H. Cho et al., “Estimated daily intakes of butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT) and tert-butyl hydroquinone (TBHQ) antioxidants in Korea,” *Food Additives and Contaminants*, vol. 22, no. 12, pp. 1176–1188, 2005.

[10] S. Lafay and A. Gil-Izquierdo, “Bioavailability of phenolic acids,” *Phytochemistry Reviews*, vol. 7, no. 2, pp. 301–311, 2008.

[11] M. N. Clifford, “Chlorogenic acids and other cinnamates—nature, occurrence, dietary burden, absorption and metabolism,” *Journal of the Science of Food and Agriculture*, vol. 80, no. 7, pp. 1033–1043, 2000.

[12] P. De, M. Baltas, and F. Bedos-Belval, “Cinnamic acid derivatives as anticancer agents-a review,” *Current Medicinal Chemistry*, vol. 18, no. 11, pp. 1672–1703, 2011.

[13] P. Sharma, “Cinnamic acid derivatives: a new chapter of various pharmacological activities,” *Journal of Chemical and Pharmaceutical Research*, vol. 3, no. 2, pp. 403–423, 2011.

[14] M. Sova, “Antioxidant and antimicrobial activities of cinnamic acid derivatives,” *Mini-Reviews in Medicinal Chemistry*, vol. 12, no. 8, pp. 749–767, 2012.

[15] S. Vishnoi, V. Agrawal, and V. K. Kasana, “Synthesis and structure–activity relationships of substituted cinnamic acids and amide analogues: a new class of herbicides,” *Journal of Agricultural and Food Chemistry*, vol. 57, no. 8, pp. 3261–3265, 2009.

[16] C. Sánchez-Moreno, “Review: methods used to evaluate the free radical scavenging activity in foods and biological systems,” *Food Science and Technology International*, vol. 8, no. 3, pp. 121–137, 2002.

[17] T.-C. Wang, Y.-L. Chen, K.-H. Lee, and C.-C. Tzeng, “Lewis acid catalyzed reaction of cinnamanilides: competition of intramolecular and intermolecular Friedel-Crafts reaction,” *Synthesis*, no. 1, pp. 87–90, 1997.

[18] C. Sánchez-Moreno, J. A. Larrauri, and F. Saura-Calixto, “A procedure to measure the antiradical efficiency of polyphenols,” *Journal of the Science of Food and Agriculture*, vol. 76, no. 2, pp. 270–276, 1998.

[19] M. Oktay, I. Gülçin, and Ö. I. Küfrevioğlu, “Determination of in vitro antioxidant activity of fennel (*Foeniculum vulgare*) seed extracts,” *LWT—Food Science and Technology*, vol. 36, no. 2, pp. 263–271, 2003.

[20] S. B. Nimse and D. Pal, “Free radicals, natural antioxidants, and their reaction mechanisms,” *RSC Advances*, vol. 5, no. 35, pp. 27986–28006, 2015.

[21] H. M. Ali, A. Abo-Shady, H. A. S. Eldeen et al., “Structural features, kinetics and SAR study of radical scavenging and antioxidant activities of phenolic and anilinic compounds,” *Chemistry Central Journal*, vol. 7, no. 1, article 53, 9 pages, 2013.


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