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Research Article

SYNTHESIS, CHARACTERIZATION, AND ANTIMICROBIAL EVALUATION OF NEW N-PHENYLCINNAMAMIDE DERIVATIVES LINKED TO ASPIRIN AND IBUPROFEN

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ABSTRACT

Objective: The objective of this study was to synthesize phenylcinnamamide (substituted acetanilide chalcone) derivatives linked to aspirin and ibuprofen with potential antibacterial and antifungal activity.

Methods: Substituted acetanilide compounds were reacted with different arylaldehydes through Claisen-Schmidt condensation in the presence of KOH. They formed differently substituted acetanilide chalcones (1a-e) which are linked to aspirin and ibuprofen through an ester linkage to form compounds (2a-j) using ethyl chloroformate (ECF) as a catalyst.

Results: The synthesized compounds have been characterized by elemental analysis, Fourier transform infrared and ^{1}H-nuclear magnetic resonance spectroscopy. An antibacterial evaluation was achieved for Gram-positive bacteria (*Staphylococcus aureus)* and Gram-negative bacteria (*Escherichia coli*) and antifungal for *Candida albicans*.

Conclusion: Compounds (2a-j) have shown intermediate antimicrobial activity against different strains of microorganisms.

Keywords: Acetanilide, Claisen-Schmidt condensation, Chalcones, Aspirin, Ibuprofen, Antibacterial, Antifungal.

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INTRODUCTION

Antimicrobial drugs are compounds which antagonize the survival or growth of a variety of microorganisms such as bacteria, viruses, fungi, and parasite [1]. Benzalacetophenone (or benzylidene acetophenone) is the central core for a variety of important biological compounds which known as a group (chalcones or chalconoids). Chalcone is a captivating moiety which consists of two aromatic rings linked by enone bridge (or α,β-unsaturated ketone) and it belongs to flavonoid family [2]. The existence of conjugated chromophore (-CO-CH=CH-) and other auxochromes have made them colored compounds [3]. C-H·π (arene) hydrogen bonds along the c axis give the molecule a zigzag shape [4]. The synthesis and biodynamic activities of chalcones were the cornerstones of many kinds of scientific researches around the world [5]. They could be prepared synthetically or naturally (like another flavonoid family) from plants [6]. Several methods have been described for the chemical synthesis of chalcones such as Claisen-Schmidt, Knoevenagel condensations and the Meyer-Schuster rearrangement [7-9]. The conjugated ketoethylenic bridge has an important role in the behavior of chalcone moiety due to the delocalization of π electrons between two benzene rings through a bridge which gives it a flexibility in electrons movement during reactions [10], consequently it serves as starting materials for many heterocyclic compounds and therapeutic substances which are used for healing of a lot of illnesses [11]. Chalcones show diversity of pharmacological activities such as anticancer [12], cytotoxic [13], antibacterial [14], antiviral [15,16], and antifungal [17,18].

Nonsteroidal anti-inflammatory drugs (NSAIDs) are popular non-opiate compounds used worldwide for the treatment of pain, fever, and inflammation [19]. Their mechanism of action involves interfering with the cyclooxygenase (COX) pathway, which includes the conversion of arachidonic acid by the enzyme COX to prostaglandins [20]. Ibuprofen is a chiral molecule which is a derivative of phenyl propionic acid, while, aspirin is a salicylate derivative [21]. Various studies have shown potential antibacterial and antifungal activities in aspirin and ibuprofen [22,23].

Based on these observations, an attempt was considered to link aspirin or ibuprofen to differently substituted acetanilide chalcones that may afford a synergistic effect with potential antimicrobial activity. These novel conjugates would be prepared by cross-linking of these molecules through an ester bond.

METHODS

Acetanilide, benzaldehyde, p-chlorobenzaldehyde, p-nitrobenzaldehyde, vanillin, and p-hydroxybenzaldehyde were purchased from Hi-Media (India). Acetaminophen, ibuprofen, aspirin, ampicillin, and ketoconazole were donated thankfully by The State Company for Drug Industries (SDI, Samara, Iraq). Melting points were determined (uncorrected) using electrical melting point apparatus, Electrothermal 9300, USA. The infrared spectra were performed in KBr disc in the range of 400–4000 cm^{-1} by Fourier transform-infrared (FTIR) spectrophotometer/Biotech engineering management Co. Ltd (UK). ^{1}H-nuclear magnetic resonance (NMR) spectra were recorded using NMR Bruker 500 MHz - Avance III and chemical shifts were recorded in parts per million (ppm) downfield using tetramethylsilane as an internal reference. Furthermore, elemental microanalyses (CHN) were performed by EuroVector EA 3000 A, Italy, and the percentage of elements was found to be close to that of the calculated values. Physical and spectral data of the synthesized compounds are recorded in Table 1.

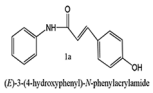
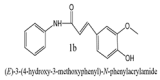
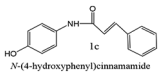
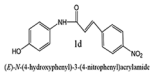
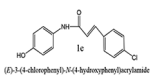
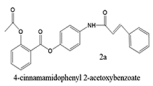
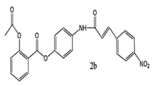
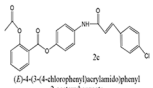
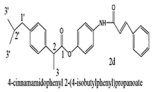
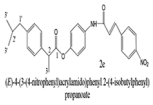
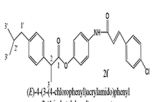
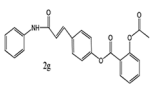
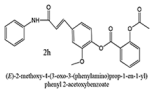
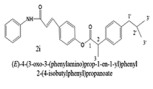
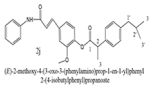
Chemical syntheses

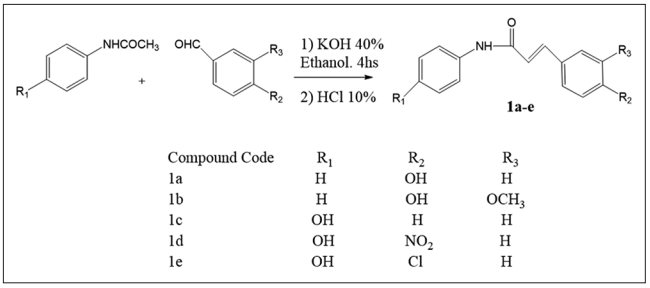
The synthesis of target compounds (1a-e and 2a-j) was achieved, as illustrated in Schemes 1 and 2.

Chemical synthesis of compounds 1a-e [24]

Equimolar quantities (0.01 mol) of substituted acetanilide compound and aryl aldehyde were dissolved in minimum volume of ethanol followed by the addition of KOH solution (40%) slowly over 10 min with stirring for 4 h and kept overnight. The reaction mixture was evaporated and acidified with cold 10% HCl and washed with cold

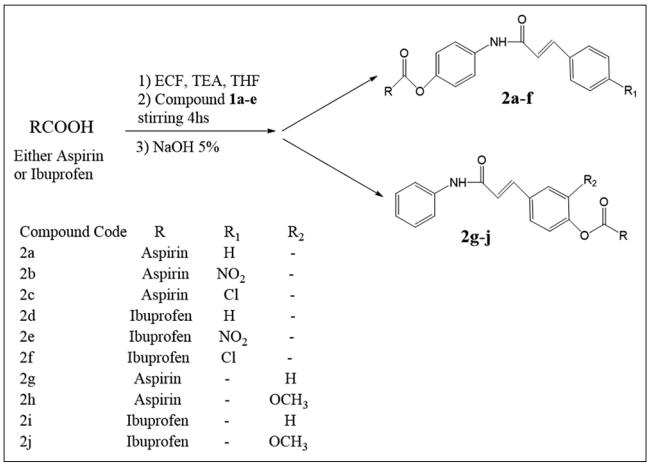
Table 1: Physical and spectral data of the titled compounds

 (*E*)-3-(4-hydroxyphenyl)-*N*-phenylacrylamide	M.F: $C_{15}H_{13}NO_2$, M.Wt: 239.27, m.p: 184–186°C, yield: 81%, elemental analysis: C-72.1%, H-5.3%, and N-5.95%. ^{1}HNMR (ppm): 9.23 (s, 1H, -NH-C=O), 6.55–7.65 (m, 9H, aromatic), 9.67 (s, 1H,-OH), 7–7.65 (d, 2H, CH=CH=C = O). IR (cm^{-1}): 3130 (OH), 1640 (C=O), 1605 (C=C) trans-alkene, 3300 (-NH)
 (*E*)-3-(4-hydroxy-3-methoxyphenyl)-*N*-phenylacrylamide	M.F: $C_{16}H_{15}NO_3$, M.wt: 369.3, m.p: 201–203°C, yield: 84%, elemental analysis: C-73.66%, H-5.45%, N-5.64%. ^{1}HNMR (ppm): 9.23, (s, 1H, -NH-C=O), 6.8–7.55 (m, 8H, aromatic), 9.5 (s, 1H,-OH), 7.05–7.36 (d, 2H, CH=CH=C = O), 3.82 (s, 3H, -OCH_3). IR (cm^{-1}): 3125 (-OH), 1635 (C=O), 1600 (C=C) trans-alkene, 3295 (NH), 1090 (C-O-C), 2950, 2870 (C-H) asymmetrical (asym.) and symmetrical (sym.) stretching vibration of -CH_3 group
 *N*-(4-hydroxyphenyl)cinnamamide	M.F: $C_{15}H_{13}NO_2$, M.wt: 239.27, m.p: 179–181°C, yield: 79%, elemental analysis: C-71.9%, H-5.34%, N-6.25%. ^{1}HNMR (ppm): 9.23(s, 1H, -NH-C=O), 6.76–7.6 (m, 9H, aromatic), 9.46 (s, 1H,-OH), 7.1–7.52 (d, 2H, CH=CH=C = O). IR (cm^{-1}): 3135 (-OH), 1635 (C=O), 1603 (C=C) trans-alkene, 3290 (NH)
 (*E*)-*N*-(4-hydroxyphenyl)-3-(4-nitrophenyl)acrylamide	M.F: $C_{15}H_{12}N_2O_4$, M.wt: 284.27, m.p: 225–227°C, yield: 72%, elemental analysis: C-60.2%, H-4.59%, N-10.38%. ^{1}HNMR (ppm): 9.23 (s, 1H, -NH-C=O), 8.37 (d, 2H, aromatic, *ortho* to NO_2), 8.07 (d, 2H, aromatic, *meta* to NO_2), 6.75 (d, 2H, aromatic, *ortho* to OH), 7.4 (d, 2H, aromatic, *meta* to OH), 9.44 (s, 1H,-OH), 7.34,7.75 (d, 1H, α and β H, respectively). IR (cm^{-1}): 3100 (-OH), 1630 (C=O), 1595 (C=C) trans-alkene, 3295 (NH), 1550 (N-O) asym. stretching, 1342 (N-O) sym. stretching
 (*E*)-3-(4-chlorophenyl)-*N*-(4-hydroxyphenyl)acrylamide	M.F: $C_{15}H_{12}ClNO_2$, M.wt: 273.72, m.p: 201–203°C, yield: 72%, elemental analysis: C-66.95%, H-4.25%, N-5.88%. ^{1}HNMR (ppm): 9.23 (s, 1H, -NH-C=O), 7.63n (d, 2H, aromatic, *ortho* to Cl), 7.7 (d, 2H, aromatic, *meta* to Cl), 6.75 (d, 2H, aromatic, *ortho* to OH), 7.38 (d, 2H, aromatic, *meta* to OH), 9.44 (s, 1H,-OH), 7.05,7.62 (d, 1H, α and β H, respectively). IR (cm^{-1}): 3095 (-OH), 1620 (C=O), 1590 (C=C) trans-alkene, 3295 (NH) (C=O), 1600 (C=C) trans-alkene, 1080 aromatic (C-Cl) stretching vibration
 4-cinnamamidophenyl 2-acetoxybenzoate	M.F: $C_{24}H_{19}NO_5$, M.wt: 401.42, m.p: 137–139°C, yield: 63%, elemental analysis: C-74.07%, H-4.54%, N-3.68%. ^{1}HNMR (ppm): 9.22 (s, 1H, -NH-C=O), 7.33–8.25 (m, 13H, aromatic), 7.05–7.52 (d, 2H, CH=CH=C = O), 2.4 (s, 3H, -CH_3). IR (cm^{-1}): 3028 (-CH of alkene), 1748 (C=O of acetic ester), 1727 (C=O of benzoic ester), 1622 (C=O of amide), 1600 (C=C) trans-alkene, 3300 (NH), 2940, 2865 (C-H) asym. and sym. stretching vibration of -CH_3 group
 (*E*)-4-(3-(4-nitrophenyl)acrylamido)phenyl 2-acetoxybenzoate	M.F: $C_{24}H_{18}N_2O_7$, M.wt: 446.42, m.p: 153–155°C, yield: 65%, elemental analysis: C-66.97%, H-4.33%, N-6.71%. ^{1}HNMR (ppm): 9.22 (s, 1H, -NH-C=O), 7.3–8.4 (m, 12H, aromatic), 7.35–7.75 (d, 2H, CH=CH=C = O), 2.38 (s, 3H, -CH_3). IR (cm^{-1}): 3025 (-CH of alkene), 1750 (C=O of acetic ester), 1728 (C=O of benzoic ester), 1620 (C=O of amide), 1590 (C=C) trans-alkene, 3300 (NH), 1548 (N-O) asym. stretching, 1340 (N-O) sym. stretching
 (*E*)-4-(3-(4-chlorophenyl)acrylamido)phenyl 2-acetoxybenzoate	M.F: $C_{24}H_{18}ClNO_5$, M.wt: 435.86, m.p: 145–147°C, yield: 67%, elemental analysis: C-63.21%, H-4.43%, N-3.39%. ^{1}HNMR (ppm): 9.21 (s, 1H, -NH-C=O), 7.26–8.21 (m, 12H, aromatic), 7.1–7.6 (d, 2H, CH=CH=C = O), 2.37 (s, 3H, -CH_3). IR (cm^{-1}): 3030 (-CH of alkene), 1751 (C=O of acetic ester), 1730 (C=O of benzoic ester), 1626 (C=O of amide), 1601 (C=C) trans-alkene, 3290 (NH), 1078 aromatic (C-Cl) stretching vibration
 4-cinnamamidophenyl 2-(4-isobutylphenyl)propanoate	M.F: $C_{28}H_{29}NO_3$, M.wt: 427.54, m.p: 105–107°C, yield: 71%, elemental analysis: C-74.92%, H-7.11%, N-3.4%. ^{1}HNMR (ppm): 9.22(s, 1H, -NH-C=O), 7.1–7.7(m, 13H, aromatic), 7.1–7.5 (d, 2H, CH=CH=C = O), 3.71 (q, 1H, -CH2), 1.6 (d, 3H, -CH_3 3), 2.45 (d, 2H, -CH_2 1'), 1.8 (m, 1H, -CH2'), 0.8 (d, 6H, -CH3'). IR (cm^{-1}): 3040 (-CH of alkene), 1758 (C=O of propanoic ester), 1622 (C=O of amide), 1604 (C=C) trans-alkene, 3295 (NH), 1380 and 1367 (d, C-H bending of isopropyl group), 2965, 2890 (C-H) asym. and sym. stretching vibration of (-CH_3) group
 (*E*)-4-(3-(4-nitrophenyl)acrylamido)phenyl 2-(4-isobutylphenyl) propanoate	M.F: $C_{28}H_{28}N_2O_5$, M.wt: 472.54, m.p: 121–123°C, yield: 73%, elemental analysis: C-74.92%, H-5.61%, N-6.2%. ^{1}HNMR (ppm): 9.22 (s, 1H, -NH-C=O), 7.12–8.39 (m, 12H, aromatic), 7.35–7.76 (d, 2H, CH=CH=C = O), 3.7 (q, 1H, -CH2), 1.58 (d, 3H, -CH_3 3), 2.43 (d, 2H, -CH_2 1'), 1.82 (m, 1H, -CH2'), 0.88 (d, 6H, -CH3'). IR (cm^{-1}): 3036 (-CH of alkene), 1758 (C=O of propanoic ester), 1625 (C=O of amide), 1602 (C=C) trans-alkene, 3290 (NH), 1382 and 1367 (d, C-H bending of isopropyl group), 2960, 2885 (C-H) asym. and sym. stretching vibration of -CH_3 group, 1550 (N-O) asym. stretching, 1340 (N-O) sym. stretching
 (*E*)-4-(3-(4-chlorophenyl)acrylamido)phenyl 2-(4-isobutylphenyl)propanoate	M.F: $C_{28}H_{28}ClNO_3$, M.wt: 461.99, m.p: 112–114°C, yield: 71%, elemental analysis: C-75.95%, H-5.81%, N-3.2%. ^{1}HNMR (ppm): 9.22 (s, 1H, -NH-C=O), 7.12–7.7 (m, 12H, aromatic), 7.05–7.62 (d, 2H, CH=CH=C = O), 3.71 (q, 1H, -CH2), 1.58 (d, 3H, -CH_3 3), 2.43 (d, 2H, -CH_2 1'), 1.82 (m, 1H, -CH2'), 0.88 (d, 6H, -CH3'). IR (cm^{-1}): 3045 (-CH of alkene), 1761 (C=O of propanoic ester), 1622 (C=O of amide), 1600 (C=C) trans-alkene, 3300 (NH), 1380 and 1365 (d, C-H bending of isopropyl group), 2950, 2875 (C-H) asym. and sym. stretching vibration of -CH_3 group, 1080 aromatic (C-Cl) stretching vibration
 (*E*)-4-(3-oxo-3-(phenylamino)prop-1-en-1-yl) phenyl 2-acetoxybenzoate	M.F: $C_{24}H_{19}NO_5$, M.wt: 401.42, m.p: 138–140°C, yield: 66%, elemental analysis: C-67.98%, H-4.93%, N-3.65%. ^{1}HNMR (ppm): 9.22 (s, 1H, -NH-C=O), 7.05–8.25 (m, 13H, aromatic), 7.05–7.62 (d, 2H, CH=CH=C = O), 2.39 (s, 3H, -CH_3). IR (cm^{-1}): 3030 (-CH of alkene), 1748 (C=O of acetic ester), 1725 (C=O of benzoic ester), 1622 (C=O of amide), 1600 (C=C) trans-alkene, 3300 (NH), 2940, 2865 (C-H) asym. and sym. stretching vibration of -CH_3 group
 (*E*)-2-methoxy-4-(3-oxo-3-(phenylamino)prop-1-en-1-yl) phenyl 2-acetoxybenzoate	M.F: $C_{25}H_{21}NO_6$, M.wt: 431.44, m.p: 149–151°C, yield: 69%, elemental analysis: C-67.02%, H-5.11%, N-3.45%. ^{1}HNMR (ppm): 9.22 (s, 1H, -NH-C=O), 7.05–8.25 (m, 13H, aromatic), 7.05–7.38 (d, 2H, CH=CH=C = O), 2.39 (s, 3H, C=OCH_3), 3.87 (s, 3H, OCH_3). IR (cm^{-1}): 3030 (-CH of alkene), 1748 (C=O of acetic ester), 1725 (C=O of benzoic ester), 1622 (C=O of amide), 1600 (C=C) trans-alkene, 3300 (NH), 1090 (C-O-C), 2957, 2868 (C-H) asym. and sym. stretching vibration of -CH_3 group
 (*E*)-4-(3-oxo-3-(phenylamino)prop-1-en-1-yl)phenyl 2-(4-isobutylphenyl)propanoate	M.F: $C_{28}H_{29}NO_3$, M.wt: 427.54, m.p: 106–108°C, yield: 79%, elemental analysis: C-77.98%, H-6.92%, N-3.39%. ^{1}HNMR (ppm): 9.22 (s, 1H, -NH-C=O), 7.07–7.56 (m, 13H, aromatic), 7.05–7.62 (d, 2H, CH=CH=C = O), 3.71 (q, 1H, -CH2), 1.58 (d, 3H, -CH_3 3), 2.43 (d, 2H, -CH_2 1'), 1.82 (m, 1H, -CH2'), 0.87 (d, 6H, -CH3'). IR (cm^{-1}): 3040 (-CH of alkene), 1762 (C=O of ester), 1620 (C=O of amide), 1598 (C=C) trans-alkene, 3300 (NH), 1384 and 1371 (d, C-H bending of isopropyl group), 2950, 2870 (C-H) asym. and sym. stretching vibration of -CH_3 group
 (*E*)-2-methoxy-4-(3-oxo-3-(phenylamino)prop-1-en-1-yl)phenyl 2-(4-isobutylphenyl)propanoate	M.F: $C_{29}H_{31}NO_4$, M.wt: 457.57, m.p: 117–119°C, yield: 81%, elemental analysis: C-77.88%, H-6.72%, N-3.21%. ^{1}HNMR (ppm): 9.22 (s, 1H, -NH-C=O), 7.07–7.56 (m, 12H, aromatic), 7.05–7.37 (d, 2H, CH=CH=C = O), 3.71 (q, 1H, -CH2), 1.58 (d, 3H, -CH_3 3), 2.43 (d, 2H, -CH_2 1'), 1.82 (m, 1H, -CH2'), 0.87 (d, 6H, -CH3'), 3.87 (s, 3H, OCH_3). IR (cm^{-1}): 3040 (-CH of alkene), 1762 (C=O of ester), 1620 (C=O of amide), 1598 (C=C) trans-alkene, 3300 (NH), 1380 and 1370 (d, C-H bending of isopropyl group), 2962, 2845 (C-H) asym. and sym. stretching vibration of -CH_3 group, 1088 (C-O-C)



Compound Code	R_1	R_2	R_3
1a	H	OH	H
1b	H	OH	OCH_3
1c	OH	H	H
1d	OH	NO_2	H
1e	OH	Cl	H

Scheme 1: Chemical synthesis of compounds 1a-e



Compound Code	R	R_1	R_2
2a	Aspirin	H	-
2b	Aspirin	NO_2	-
2c	Aspirin	Cl	-
2d	Ibuprofen	H	-
2e	Ibuprofen	NO_2	-
2f	Ibuprofen	Cl	-
2g	Aspirin	-	H
2h	Aspirin	-	OCH_3
2i	Ibuprofen	-	H
2j	Ibuprofen	-	OCH_3

Scheme 2: Chemical synthesis of compounds 2a-j

Table 2: Antimicrobial activity of compounds (2a-j) by cup plate method

Compound (200 µg/mL)	Zone of inhibition		
	S. aureus	*E. coli*	*C. albicans*
2a	18	16	10
2b	17	15	12
2c	16	19	18
2d	13	---	5
2e	15	---	6
2f	---	12	9
2g	15	18	12
2h	16	14	9
2i	---	11	5
2j	12	---	---
Ampicillin	20	21	---
Ketoconazole	---	---	20
Solvent control (DMSO)	---	---	---

---: Inactive. Results represent the average of triplicate experiments.
S. aureus: Staphylococcus aureus, E. coli: Escherichia coli, C. albicans: Candida albicans

distilled water to obtain compounds **1a-e**. These compounds were recrystallized from ethanol.

Chemical synthesis of compounds 2a-j [25,26]

The synthesis of these compounds was achieved by reacting compounds **1a-e** by mixed anhydride method with either ibuprofen or aspirin using ECFasa catalyst, as shown in Scheme 2.

NSAID (either aspirin or ibuprofen) (0.01 mol) was dissolved in 30 mL of dry tetrahydrofuran (THF) containing triethylamine (0.01 mol) and placed in a refrigerator at −5 to −10°C. A solution of ECF (0.01 mol) was added dropwise to the above mixture over a period of 10 min with continuous stirring, which maintained for further 30 min. Compound **1a-e** (0.01 mol) was dissolved in 30 mL THF previously cooled to 0°C and was added dropwise over 10 min to the above mixture with stirring for 4 h. The solvent was then evaporated, and the resultant precipitate was washed with cold NaOH solution (5%) and distilled water.

***In vitro* antimicrobial screening**

The synthesized compounds were evaluated for their antimicrobial activity using cup plate method for a zone of inhibition against *Staphylococcus aureus*, *Escherichia coli,* and *Candida albicans* [27,28]. Compounds (**2a-j**) and standard drugs (ampicillin and ketoconazole) were screened at a concentration of 200 µg/mL; additionally, dimethyl sulfoxide was used as a control. In this procedure, melted agar was poured into a sterile Petri dish and inoculated with the microorganisms. Using a sterile cork borer, wells (8 mm) were made on the surface of an agar plate and a specific volume of the screened substances is poured in them, plates were incubated at a temperature of 37°C for 48 h. The diameter of this zone (mm) was measured and shown in Table 2.

RESULTS AND DISCUSSION

Physical data, including molecular formula (M.F), molecular weights (M.wt), melting points (m.p), and spectral data along with antimicrobial activity, are shown in Tables 1 and 2, respectively. The chemical structures of the synthesized compounds were confirmed by spectrophotometric analysis (FTIR, ^{1}HNMR, and elemental analysis). The most significant characteristic IR bands that confirm the formation of compounds (**1a-e**) are the appearance of C=C stretching band around 1600 cm^{-1}, shift in C=O stretching band to a lower wave number because of the conjugation with aromatic double bond, the disappearance of symmetrical and asymmetrical stretching bands of substituted acetanilide (CH_3) group, and the appearance of other bands regarding each compound (such as OH stretching for compound 1b at 3125 cm^{-1}) as shown in Table 1. Compounds (**2a-j**) are characterized by the appearance of new ester band which is affected by the conjugation with one or both sides. The change in chemical shifts, proton counting, integration, and spin-spin splitting was distinguishable feature in^{1}HNMR, particularly the appearance of vinylic (C=C) protons at 7–7.8 (ppm) downfield (because of delocalization of π electrons which results in deshielding of these protons along with the inductive effect of the neighboring C=O group) and disappearance of OH protons due to ester formation [29].

The synthesized compounds were screened against bacterial and fungal strains. Compound 2c has the higher zone of inhibition for *E. coli* (19 mm) and *C. albicans* (18 mm) and compound 2a has the higher zone of inhibition for *S. aureus* (18 mm). The higher activity of compound 2c may be attributed to its higher lipophilicity among the aspirin linked N-phenylcinnamamide derivatives which may result in higher penetration through the microbial cell wall. Compounds (2f, 2i), (2d, 2e, 2j), and 2j show no activity on *S. aureus, E. coli,* and *C. albicans,* respectively. This could be explained by the bulkiness offered by the linking compounds **1a-e** to ibuprofen which has a great effect on the penetration and consequently the activity of compounds 2d, 2e, 2f, 2i, and 2j.

CONCLUSION

Compounds (2a-j) were successfully synthesized, confirmed (by elemental analysis, FTIR, and^{1}HNMR), and assessed for their antimicrobial activity. Regardless of the potential antimicrobial activity of the parent compounds (chalcones, aspirin, and ibuprofen), the synergism has not been achieved.

AUTHOR'S CONTRIBUTION

Ameer H. Alwashde signed the research, performed the synthesis of the compounds, and wrote the paper. Alaa M. Mahdi performed the elemental analysis, FTIR, and^{1}H-NMR spectroscopy. Haider J. Al-Karagully performed the antimicrobial evaluation.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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