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SYNTHESIS AND BIOLOGICAL EVALUATION OF NOVEL QUINOLINE / CHALCONE HYBRID AS POTENTIAL ANTIBACTERIAL AGENTS

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ABSTRACT: A series of new quinoline/chalcone hybrids 3a-e and 4a-e were designed and synthesized. The structures of all new target molecules 3a-e and 4a-e have been confirmed by various spectral techniques and elemental analyses. The newly synthesized compounds were screened for their antibacterial activity using agar disc diffusion method. Results showed that most of the newly synthesized compounds showed good antibacterial activity comparable with that of the standard drug Gatifloxacin against all tested strains (*B. cereus*, *E. coli*, and *S. marcescens*) except for *P. aeroginosa* where it does not respond to most of the newly synthesized compounds, and that compounds 3c, 4c, 4d, and 4e showed good antibacterial activity (53-78% that of Gatifloxacin) towards some bacterial strains (*Bacillus cereus*, *Escherichia coli*, and *Serratia marcescens*) when compared to standard drug Gatifloxacin. Amongst all the tested compounds, 4e exhibited excellent activity against *S. marcescens* (88% that of Gatifloxacin).

INTRODUCTION: Quinolines are a wide class of natural and synthetic compounds that show anti-inflammatory [1], antimalarial [2], anticancer [3], anti-hypertensive [4], antibiotic [5], tyrokinase PDGF-RTK inhibiting agents [6], and anti-HIV [7, 8]. Moreover, chalcones (1,3-diaryl-2-propen-1-ones) constitute an important class of natural products belonging to the flavonoid family, which displayed interesting biological activities including antimicrobial [9, 10], antimalarial [11], antifungal [12], anti-Alzheimer's disease [13], antiplatelet aggregation [14], anti-oxidant [15], anti-inflammatory [16, 17], and anticancer [18] activities.

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Due to their abundance in plants and ease of synthesis, this class of compounds has provoked great interest for possible therapeutic uses. Furthermore, in the design of new drugs, the development of hybrid molecules through the combination of different biologically active entities may lead to compounds with interesting biological profiles. Moreover, a single molecule containing more than one pharmacophore, each with the different mode of action could be beneficial for the treatment of bacterial infections. Therefore, guided and inspired by the aforementioned information, the current work aims at designing of novel quinoline/ chalcone hybrids **Fig. 1** gathering two bioactive entities in one compact structure for increasing the potential antibacterial effect.

EXPERIMENTAL:

Chemistry: Melting points were determined on an electrothermal melting point apparatus [Stuart Scientific, model SMP3, England, UK], and were

uncorrected. A pre-coated silica gel plate (kieselgel 0.25 mm, 60G F254, Merck, Germany) was used for TLC monitoring of reactions. The developing solvent system *n*-hexane/ethyl acetate (3:2 v/v) was used, and the spots were detected at 254 nm wavelength using an ultraviolet lamp (Spectroline, model CM-10, USA). IR spectra were carried out as KBr disc on Shimadzu Infrared Spectro-photometer 200-91527 at the Faculty of Science, Sohag University. ^{1}H NMR spectra were carried out on 400 MHz Brucker spectrometer, using TMS as an internal reference. Chemical shift (δ) values are given in parts per million (ppm) relative to CDCl3 (7.29) or DMSO-d6 (2.5) and coupling constants (J) in Hertz. Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; dd, the doublet of doublet; m, multiplet. Elemental microanalyses for carbon, hydrogen, and nitrogen were performed on Perkin-Elmer, 240 C Elemental Analyzer at the Regional Center for Mycology and Biotechnology, Al-Azhar University, Cairo, Egypt. Reagents used for synthesis were purchased from Sigma-Aldrich (Gillingham - Dorest, UK) and Merck (Schuchardt, Germany). All solvents were obtained from commercial suppliers and used without further purification. The starting materials 2-chloro-quinoline-3-carbaldehyde derivatives (1a-e) [19] and (4- Acetyl- phenoxy) acetic acid (2) [20] were synthesized according to reported procedures.

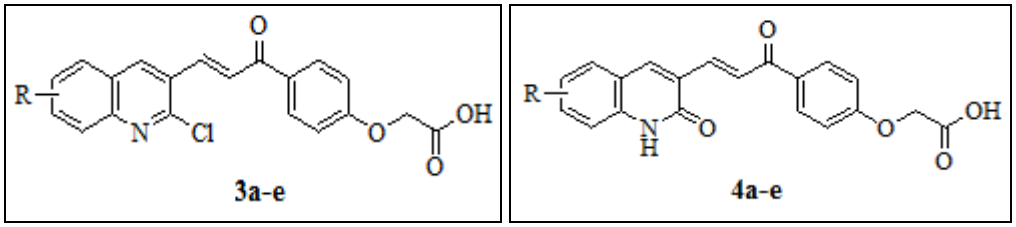


FIG. 1: GENERAL STRUCTURE OF THE TARGET COMPOUNDS 3a-e AND 4a-e

General Method for the Synthesis of {4- [3- Arylacryloyl] phenoxy- acetic acid 3a-e: To a vigorously stirred suspension of (4-acetylphenoxy) acetic acid (2) (1.94 g, 10 mmol) and the appropriate 2 -chloroquinoline -3 -carbaldehyde derivatives (1a-e) (10 mmol) in ethanol (20 ml) at room temperature, 10% aqueous sodium hydroxide (6 ml) was added dropwise and the stirring is continued for an additional 15 min. After acidification of the reaction mixture with dilute hydrochloric acid, the precipitated crystals were filtered off and washed with water and cold methanol. The crystals are allowed to dry and recrystallized from the appropriate solvent.

{4- [3- (2 -Chloro -quinolin-3 -yl)- acryloyl]-phenoxy-acetic acid 3a: Yield 82%; M.P. 167-8 °C; IR (KBr) (υ, cm^{-1}) 2911-3066 (OH), 1712 (CO-OH), 1656 (CO-C=C), 831 (*p*-C=C); ^{1}H NMR (400 MHz, DMSOd$_6$) δ (ppm):^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 13.10 (s, 1H, OH), 9.22 (s, 1H, Ar-H), 8.21 (d, 2H, *J* = 8 Hz, Ar-H), 7.91 (d, 2H, *J* = 8 Hz, Ar-H), 7.89 (d, 1H, *J* = 16 Hz, CH=CH-C=O), 7.75 (d, 1H, *J* = 16 Hz, CH=CH-C=O) 7.67 (t, 1H, *J* = 8 Hz, Ar-H), 7.58 (t, 1H, *J* = 8 Hz, Ar-H), 7.11 (d, 2H, *J* = 8 Hz, Ar-H), 4.85 (s, 2H, CH$_2$); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 187.34 (C=O), 170.11 (C=O), 162.51 (C-O), 150.10, 147.64, 137.95, 132.38, 129.30, 126.93, 115.16, 65.18; Anal. calcd. for $C_{20}H_{14}ClNO_4$: C, 65.31; H, 3.84; N, 3.81. Found: C, 65.25; H, 3.88; N, 3.78%.

{4- [3- (2 -Chloro -6-methyl- quinolin-3 -yl)-acryloyl] -phenoxy} -acetic acid 3b: Yield 79%; M.P. 158-9 °C; IR (KBr) (υ, cm^{-1}) 2979-3052 (OH), 1715 (CO–OH), 1660 (CO–C=C), 823; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 13.10 (s, 1H, OH), 9.09 (s, 1H, Ar-H), 8.20 (d, 2H, *J* = 8 Hz, Ar-H), 7.99 (d, 2H, *J* = 8 Hz, Ar-H), 7.88 (d, 1H, *J*= 16 Hz, CH=CH-C=O), 7.80 (d, 1H, *J* = 16 Hz, CH=CH-C=O) 7.71 (t, 1H, *J* = 8 Hz, Ar-H), 7.69 (t, 1H, *J* = 8 Hz, Ar-H), 7.13 (d, 1H, *J* = 8 Hz, Ar-H), 4.85 (s, 2H, CH$_2$), 2.53 (s, 3H, CH$_3$); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 187.34 (C=O), 170.11 (C=O), 162.49 (C-O), 149.21, 146.28, 138.08, 134.52, 127.94, 126.76, 115.16, 65.18, 21.16; Anal. calcd. for $C_{21}H_{16}ClNO_4$: C, 66.06; H, 4.22; N, 3.67. Found: C, 66.01; H, 4.18; N, 3.62%.

{4- [3- (2 –Chloro -6-methoxy -quinolin-3 -yl)-acryloyl]-phenoxy}-acetic acid 3c: Yield 73%; M.P. 179-180 °C; IR (KBr) (υ, cm^{-1}) 2910-3079 (OH), 1718 (CO–OH), 1657(CO–C=C), 826; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 13.07 (s, 1H,

OH), 9.05 (s, 1H, Ar-H), 8.19 (d, 2H, *J* = 8 Hz, Ar-H), 7.98 (d, 2H, *J* = 8 Hz, Ar-H), 7.86 (d, 1H, *J* = 16 Hz, CH=CH-C=O), 7.82 (d, 1H, *J* = 16 Hz, CH=CH-C=O) 7.46 (t, 1H, *J* = 8 Hz, Ar-H), 7.36 (t, 1H, *J* = 8 Hz, Ar-H), 7.12 (d, 1H, *J* = 8 Hz, Ar-H), 4.85 (s, 2H, CH_2), 3.92 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ (ppm): 187.25 (C=O), 170.08 (C=O), 162.48 (C-O), 158.48, 147.44, 146.28, 138.08, 134.52, 127.94, 126.76, 115.16, 106.56, 65.18, 56.07; Anal. calcd. for $C_{21}H_{16}ClN O_5$: C, 63.40; H, 4.05; N, 3.52. Found: C, 63.35; H, 4.02; N, 3.48%.

{4- [3- (2 –Chloro -7-methyl -quinolin-3 -yl)-acryloyl]-phenoxy}-acetic acid 3d: Yield 82%; M.P. 147-8 °C; IR (KBr) (υ, cm^{-1}) 2906-2977 (OH), 1721 (CO–OH), 1647 (CO–C=C), 834; ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ (ppm): 13.10 (s, 1H, OH), 9.14 (s, 1H, Ar-H), 8.20 (d, 2H, *J* = 8 Hz, Ar-H), 7.98 (d, 2H, *J* = 8 Hz, Ar-H), 7.94 (d, 1H, *J* = 16 Hz, CH=CH-C=O), 7.75 (d, 1H, *J* = 16 Hz, CH=CH-C=O) 7.56 (t, 1H, *J* = 8 Hz, Ar-H), 7.54 (t, 1H, *J* = 8 Hz, Ar-H), 7.13 (d, 1H, *J* = 8 Hz, Ar-H), 4.85 (s, 2H, CH_2), 2.54 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ (ppm): 187.32 (C=O), 170.11 (C=O), 162.47 (C-O), 149.21, 146.28, 138.08, 134.52, 127.94, 126.76, 115.14, 65.18, 22.01; Anal. calcd. for $C_{21}H_{16}ClNO_4$: C, 66.06; H, 4.22; N, 3.67. Found: C, 66.02; H, 4.17; N, 3.64%.

{4- [3- (2 -Chloro -7-methoxy -quinolin-3 -yl)-acryloyl]-phenoxy}-acetic acid 3e: Yield 79%; M.P. 168-9 °C; IR (KBr) (υ, cm^{-1}) 2909-2969 (OH), 1716 (CO–OH), 1648 (CO–C=C), 831; ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ (ppm): 9.00 (s, 1H, Ar-H), 8.16 (d, 2H, *J* = 8 Hz, Ar-H), 7.97 (d, 2H, *J* = 8 Hz, Ar-H), 7.91 (d, 1H, *J* = 16 Hz, CH=CH-C=O), 7.89 (d, 1H, *J* = 16 Hz, CH=CH-C=O) 7.28 (t, 1H, *J* = 8 Hz, Ar-H), 7.36 (t, 1H, *J* = 8 Hz, Ar-H), 7.12 (d, 1H, *J* = 8 Hz, Ar-H), 4.82 (s, 2H, CH_2), 3.92 (s, 3H, OCH_3); ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ (ppm): 187.18 (C=O), 170.11 (C=O), 162.48 (C-O), 158.48, 147.44, 146.28, 138.08, 134.52, 127.94, 126.76, 115.16,106.56, 65.18, 56.11; Anal. calcd. For $C_{21}H_{16}ClNO_5$: C, 63.40; H, 4.05; N, 3.52. Found: C, 63.37; H, 4.01; N, 3.49%.

General Method for the Synthesis of Compounds 4a-e: To a solution of the chalcone derivatives 3a-e (0.01mol) in aqueous acetic acid (30 ml), the reaction mixture was heated under reflux for 6 h. After cooling, the separated solid was filtered and recrystallized from ethanol to give 2-Oxo-1, 2-dihydroquinoline derivatives 4a-e.

{4- [3- (2 -Oxo-1, 2-dihydro -quinolin-3 -yl)-acryloyl]-phenoxy}-acetic acid 4a: Yield 69%; M.P. 172-4 °C; IR (KBr) (υ, cm^{-1}) 2957-3150 (OH), 1713 (CO–OH), 1664 (CO–C=C), 829; ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ (ppm): 13.05 (s, 1H, OH), 12.03 (s, 1H, NH), 8.59 (s, 1H, Ar-H), 8.30 (d, 2H, *J* = 8 Hz, Ar-H), 8.06 (d, 2H, *J* = 8 Hz, Ar-H), 7.82 (d, 1H, *J* = 16 Hz, CH=CH-C=O), 7.74 (d, 1H, *J* = 16 Hz, CH=CH-C=O) 7.59 (t, 1H, *J* = 8 Hz, Ar-H), 7.38 (t, 1H, *J* = 8 Hz, Ar-H), 7.12 (d, 2H, *J* = 8 Hz, Ar-H), 4.85 (s, 2H, CH_2); ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ (ppm): 188.28 (C=O), 170.13 (C=O), 162.17 (C=O), 161.42 (C-O), 150.10, 147.64, 137.95, 132.38, 129.30, 126.93, 115.16, 65.15; Anal. calcd. for $C_{20}H_{15}$ NO_5: C, 68.76; H, 4.33; N, 4.01. Found: C, 68.81; H, 4.40; N, 4.04%.

{4-[3-(6-methyl-2 -Oxo-1, 2-dihydro-quinolin-3-yl)-acryloyl]-phenoxy}-aceticacid 4b: Yield 68%; m.p. 160-2°C; IR (KBr) (υ, cm^{-1}) 2977-3138 (OH), 1687 (CO–OH), 1658(CO–C=C), 828; ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ (ppm): 12.94 (s, 1H, OH), 11.95 (s, 1H, NH), 8.49 (s, 1H, Ar-H), 8.30 (d, 2H, *J* = 8 Hz, Ar-H), 8.05 (d, 2H, *J* = 8 Hz, Ar-H), 7.76 (d, 1H, *J* = 16 Hz, CH=CH-C=O), 7.41 (d, 1H, *J* = 16 Hz, CH=CH-C=O) 7.28 (t, 1H, *J* = 8 Hz, Ar-H), 7.26 (t, 1H, *J* = 8 Hz, Ar-H), 7.12 (d, 1H, *J* = 8 Hz, Ar-H), 4.83 (s, 2H, CH_2), 2.51 (s, 3H, CH_3);^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ (ppm): 188.32 (C=O), 170.13 (C=O), 162.15 (C=O), 161.31 (C-O), 150.10, 147.64, 137.95, 132.38, 129.30, 126.49, 115.13, 65.14, 20.83; Anal. calcd. for $C_{21}H_{17}NO_5$: C, 69.41; H, 4.72; N, 3.85. Found: C, 69.38; H, 4.67; N, 3.81%.

{4-[3-(6-methoxy-2-Oxo-1, 2-dihydro-quinolin-3-yl)-acryloyl]-phenoxy}-acetic acid 4c: Yield 74%; M.P. 182-3°C; IR (KBr) (υ, cm^{-1}) 2974-3149 (OH), 1707 (CO–OH), 1658 (CO–C=C), 828; ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ (ppm): 12.93 (s, 1H, OH), 11.94 (s, 1H, NH), 8.50 (s, 1H, Ar-H), 8.34 (d, 2H, *J* = 8 Hz, Ar-H), 8.08 (d, 2H, *J* = 8 Hz, Ar-H), 7.80 (d, 1H, *J* = 16 Hz, CH=CH-C=O), 7.32 (d, 1H, *J* = 16 Hz, CH=CH-C=O) 7.24 (t, 1H, *J* = 8 Hz, Ar-H), 7.22 (t, 1H, *J* = 8 Hz, Ar-H), 7.12 (d, 1H, *J* = 8 Hz, Ar-H), 4.85 (s, 2H, CH_2), 3.82 (s, 3H, OCH_3); ^{13}C

NMR (100 MHz, DMSO-d_6) δ (ppm): 188.32 (C=O), 170.15 (C=O), 162.35 (C=O), 161.70 (C-O), 150.10, 147.64, 137.95, 132.38, 129.30, 126.49, 115.13, 98.21, 65.17, 56.01; Anal. calcd. for $C_{21}H_{17}NO_6$: C, 66.49; H, 4.52; N, 3.69. Found: C, 66.42; H, 4.48; N, 3.66%.

{4-[3-(7 -methyl-2-Oxo-1, 2-dihydro-quinolin-3-yl)-acryloyl] -phenoxy}-acetic acid 4d: Yield 72%; M.P. 150-2 °C; IR (KBr) (υ, cm^{-1}) 2980-3080 (OH), 1734 (CO–OH), 1659 (CO–C=C), 842; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 13.06 (s, 1H, OH), 11.94 (s, 1H, NH), 8.51 (s, 1H, Ar-H), 8.30 (d, 2H, *J* = 8 Hz, Ar-H), 8.07 (d, 2H, *J* = 8 Hz, Ar-H), 7.80 (d, 1H, *J* = 16 Hz, CH=CH-C=O), 7.61 (d, 1H, *J* = 16 Hz, CH=CH-C=O) 7.15 (t, 1H, *J* = 8 Hz, Ar-H), 7.11 (t, 1H, *J* = 8 Hz, Ar-H), 7.09 (d, 1H, *J* = 8 Hz, Ar-H), 4.83 (s, 2H, CH_2), 2.51 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 188.11 (C=O), 170.13 (C=O), 162.11 (C=O), 161.01 (C-O), 150.10, 147.64, 137.95, 132.38, 129.30, 126.49, 115.13, 65.14, 20.73; Anal. calcd. for $C_{21}H_{17}NO_5$: C, 69.41; H, 4.72; N, 3.85. Found: C, 69.40; H, 4.77; N, 3.82%.

{4-[3-(7-methoxy-2-Oxo-1, 2-dihydro-quinolin-3-yl)-acryloyl]-phenoxy}-acetic acid 4e: Yield 71%; M.P. 170-2 °C; IR (KBr) (υ, cm^{-1}) 2971-3054 (OH), 1730 (CO–OH), 1697 (CO–C=C), 829; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 12.89 (s, 1H, OH), 11.89 (s, 1H, NH), 8.49 (s, 1H, Ar-H), 8.27 (d, 2H, *J* = 8 Hz, Ar-H), 8.06 (d, 2H, *J* = 8 Hz, Ar-H), 7.78 (d, 1H, *J* = 16 Hz, CH=CH-C=O), 7.66 (d, 1H, *J* = 16 Hz, CH=CH-C=O) 7.11 (t, 1H, *J* = 8 Hz, Ar-H), 6.89 (t, 1H, *J* = 8 Hz, Ar-H), 6.86 (d, 1H, *J* = 8 Hz, Ar-H), 4.82 (s, 2H, CH_2), 3.85 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 188.22 (C=O), 170.13 (C=O), 162.85 (C=O), 161.71 (C-O), 150.10, 147.64, 137.95, 132.38, 129.30, 126.49, 115.13, 98.21, 65.17, 56.11; Anal. calcd. for $C_{21}H_{17}NO_6$: C, 66.49; H, 4.52; N, 3.69. Found: C, 66.44; H, 4.49; N, 3.67%.

Antibacterial Activity:

Organisms and Culture Conditions: The used bacterial cultures were obtained from Assiut University Mycological Center (AUMC), Assiut University, Assiut. The antibacterial activity of compounds 3a-e and 4a-e was determined according to the agar disc diffusion method [21]. Six bacterial species were used to test the antibacterial activity of the target compounds: *Bacillus cereus* (AUMC B70), *Staphylococcus aureus* (AUMC B71) and *Micrococcus luteus* (AUMC B68) as representatives of gram-positive strains, while the gram-negative strains were represented by *Escherichia coli* (AUMC B69), *Pseudomonas aeruginosa* (AUMC B72) and *Serratia marcescens* (AUMC B67).

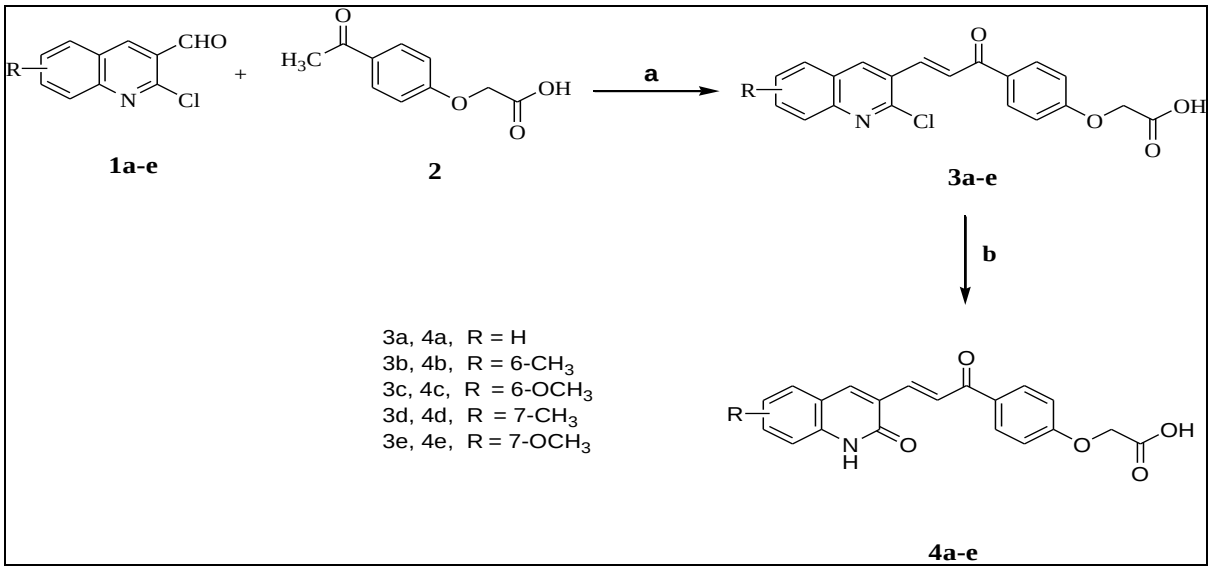
MATERIALS AND METHODS: Cell suspension of bacterial strains was prepared from 48 h old cultures grown on nutrient agar (NA) in sterilized water [21]. One ml suspension was added to Petri dishes of 9 cm in diameter, and then 15 ml of NA was poured into the plates. Plates were shaken gently to homogenize the inocula. Sterile 5-mm filter paper disc (Whatman) was saturated with 10 µl solutions of the test compounds or Gatifloxacin as a reference drug (53 µmol-mL^{-1} in DMSO). Also, other disks were impregnated with the solvent (DMSO) and served as a negative control. The discs were then dried for 1 h and placed in the center of each plate. The seeded plates were incubated at 35 ± 2 °C for 24-48 h. The radii of inhibition zones (in mm) were measured in triplicate, and the results are given in **Table 1**.

RESULTS AND DISCUSSION:

Chemistry: The starting materials (1a-e) and (2) were prepared according to a reported procedure and their structures were confirmed by comparison of its physical and spectral data with the reported ones [19, 20]. The synthesis of aryloxyacetic acid derivatives containing 2-chloroquinoline chalcone 3a-e was accomplished using the reported simple and fast method [22]. This method involves a one-pot base catalyzed Claisen- Schmidt condensation of compound 2 with 2-chloroquinoline-3-carbaldehyde derivatives1a-using aqueous NaOH as a base in the presence of ethanol as a solvent **Scheme 1**.

Reagent and Reaction Conditions: (a) Ethanol, 10% NaOH, 15 min then HCl. (b) aq. acetic acid; reflux. IR, NMR spectroscopy and elemental analyses, confirmed structures of chalcones 3a-e. IR spectra of compounds 3a-e showed the presence of absorption bands at 315-2906 cm^{-1} corresponding to OH group, strong absorption bands at 1734-1687 cm^{-1} attributed to CO-OH group and strong absorption band at 1697-1640 cm^{-1} assigned for CO-C=C group.

The ^{1}H NMR spectra of compounds 3a-e showed characteristic singlet at δ 13.10-12.89 ppm assigned for COOH group. The singlet at δ 4.85-4.82 ppm assigned for the two protons of the CH_2. All other signals appear at their expected values. The ^{13}C NMR spectra of compounds 3a and 3b revealed a peak at δ 187.34 ppm corresponds to CO-C=C group and a peak at δ 170.11 ppm assigned for COOH group. The peak at δ 65.18 ppm is characteristic for the carbon of CH_2 group. Also, compound 3c showed a characteristic peak at 56.07 ppm corresponding to the carbon of the OCH_3 group. All other carbons appear at their expected values.



SCHEME 1: SYNTHESIS OF TARGET COMPOUNDS 3a-e AND 4a-e

The target compounds 4a-e were prepared by treating 3a-e with aqueous acetic acid as a solvent under reflux to afford the desired 2-Oxo-1,2-dihydroquinoline derivatives 4a-e **Scheme 1**. IR, NMR spectroscopy and elemental analyses, confirmed structures of chalcones 4a-e. The ^{1}H NMR spectra of compounds 4a-e showed characteristic singlet at δ 13.10-12.89 ppm assigned for COOH group and a singlet at δ 12.03-11.89 ppm assigned for the NH group. All other signals appear at their expected values. The ^{13}C NMR spectra of compounds 4a-revealed a peak at δ 187.34 ppm corresponds to CO-C=C group, a peak at δ 170.11 ppm assigned for COOH group and a peak at 162.83-162.15 for N-C=O group. All other signals appear at their expected values.

Antibacterial Activity: The newly synthesized compounds were screened for their antibacterial activity against six bacterial species: *Bacillus cereus*, *Staphylococcus aureus*, and *Micrococcus luteus* as representatives of Gram-positive strains, and *Escherichia coli*, *Pseudomonas aeruginosa* and *Serratia marcescensas* representatives of gram-negative strains [22]. Results of the antibacterial activity **Table 1** indicated that *S. aureus* and *M. luteus* were completely resistant to the tested compounds, while *B. cereus*, *E. coli*, and *S. marcescens* were the most sensitive organisms to the tested compounds. Also, the test compounds were inactive against *P. aeruginosa* except for compounds 4c and 4e which are moderately active.

On the other hand, the majority of the tested compounds appeared to be moderately active against *B. cereus*. Nevertheless some of them, 4a, 4c and 4e showed good activity, and, compounds 3c, 4c, and 4e exhibited moderate to good activity against *E. coli* correlated to the standard drug Gatifloxacin. Moreover, some of the test compounds showed good activity against *S. marcescens*, and compound 4e exhibited excellent activity.

SAR:

- Generally, it was observed that compounds containing 2-Oxo-1,2-dihydroquinoline nucleus 4a-e seem to be more effective than their precursor's 2-chloroquinoline derivatives 3a-e.
- The most active compounds seem to be compounds containing 7-OCH_3 as an R substituent.

- It was also noticed that the introduction of a CH_3 group in compounds 3b, 3d, 4b, and 4d resulted in a decrease of their antibacterial activity.

TABLE 1: PERCENTAGE INHIBITION ZONES OF COMPOUNDS 3a-e, 4a-e, AND GATIFLOXACIN

Compound no.	% Inhibition zone			
	Gram-positive		Gram-negative	
	B. cereus	*E. coli*	*P. aeroginosa*	*S. marcescens*
3a	44.2	47.8	-	44.7
3b	42.2	38.7	-	39.5
3c	52.9	60.0	-	46.5
3d	48.2	47.1	-	42.4
3e	51.2	50.6	-	46.8
4a	58.2	50.7	-	68.6
4b	51.2	50.9	-	63.7
4c	72.2	68.3	52.9	74.7
4d	53.7	52.1	-	61.6
4e	78.7	74.1	60.1	88.2
Gatifloxacin	100	100	100	100

- No inhibition

CONCLUSION: A number of 2-Oxo-1,2-dihydro-quinoline derivatives 4a-e and their precursor's 2-chloroquinoline derivatives 3a-e were prepared and tested for their antimicrobial activity. The anti-bacterial data indicated that most of the test compounds showed good activity against *B. cereus*, *E. coli* and *S. marcescens* and some of them showed antibacterial activity against and *P. aeroginosa*. On the other hand, they showed no activity against *S. aureus* and *M. luteus*. Generally, compounds containing 2-Oxo-dihydroquinoline4a-enucleus seems to be more effective as antibacterial than their precursor's 2-chloroquinoline derivatives 3a-e. It was also noticed that the methoxy-substituted derivatives were the most active ones.

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