Click synthesis of new 7-chloroquinoline derivatives by using ultrasound irradiation and evaluation of their biological activity

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**ABSTRACT**

This study describes the click synthesis of new 7-chloroquinoline derivatives by using ultrasound irradiation and evaluation of their activity as antimicrobial, antimalarial and the anticancer. All the compounds show moderate antimalarial activity with IC\textsubscript{50} < 100 \mu M, six of them showed high antimalarial activity (2, 3, 4, 6, 8 and 9) with IC\textsubscript{50} < 50 \mu M. The most active 7-chloroquinoline derivative is a compound (9). Also, the newly synthesized compounds were screened for their antitumor activity towards three lines of cancer cells, MCF-7 (human breast cancer), HCT-116 (colon carcinoma) and Hela (Cervical carcinoma) cell lines. Compounds (3) and (9) exerted the highest activity on all cell lines and showed special selectivity toward MCF-7 cells and the antibacterial screening data showed moderate to good inhibition zone (12.5 ± 0.63 – 23.8 ± 1.5) towards all the tested compounds. Elucidation of the structures of these new pure compounds was based on, IR, \textsuperscript{1}H NMR, \textsuperscript{13}C NMR, MS and their elemental analysis.

1. Introduction

Quinolines and their derivatives are present in numerous natural products and have highly antimalaria, antiasthmatic, antiinflammatory, antibacterial and antihyper-sensitive activities (1). Few methods have been reported for the preparation of quinolines derivatives such as the Skraup, Doebner von Miller and Combes procedures (2, 3). Malaria is a contagious disease, caused by protozoa parasites from the genus Plasmodium that is transmitted by mosquitoes of the genus Anopheles. Plasmodium falciparum is responsible for the most lethal form of malaria (4). Chloroquine was the most effective antimalarial clinically used drug but parasite resistance led to its substitution by artemisinin and its semi-synthetic derivatives (artemether, artesunate) (5, 6). So, new drugs to treat malaria are critically required. Synthesis of molecular hybrids containing different moieties which are representatives of known or putative antimalarial compounds is presently being extensively explored. Recently, the synthesis of 1,2,3-triazoles by a process known as Cu-mediated click chemistry (7) has been explored to combine different molecules affording new analogs of chloroquine (8), chalcones (9), naphthoquinones (10) several other hybrid antimalarial molecules have been synthesized (11–13).

In this sense, ultrasonic irradiation has picked up ubiquity in the previous decades as a useful tool in most of the industrial and academic applications. The utilization of sanction as the energy source of organic synthesis (sonochemistry) is very much recorded (14). This energy source has been proven to be able to accelerate reactions and selectivities through the development of new receptive intermediates and compounds not usually observed under ordinary thermal conditions (14). Furthermore, ultrasound irradiation can be considered as earth amiable procedures, being less vitality concentrated and creating decreased amounts of side items (15).
In this study, the sonochemical technique was used to synthesize new derivatives of 7-chloroquinoline and evaluation as antimicrobial, antimalarial and the anticancer activity of the new compounds.

2. Results and discussion

2.1. Chemistry

The application of ultrasound in the synthesis of compounds (2) and (3) is fulfilling some of the goals of “green and sustainable chemistry” as it has some advantages comparing with the traditional thermal methods in terms of reaction times, yields and purity of the products (16, 17). The reaction of 4,7-dichloroquinoline and o-phenylenediamine in the presence of ethanol under reflux in an ultrasonic bath, for 30 min at 90°C yielded N-(7-chloroquinolin-4-yl)-benzene-1,2-diamine (2) (cf. Scheme 1).

The synthesized quinoline derivative (2) was then reacted with carbonyl compounds such as acetyl naphthalene and 3,4-dimethoxy acetophenone in ethanol under reflux in an ultrasonic bath, for 30 min at 90°C forming Schiff’s bases (E)-N1-(7-chloroquinolin-4-yl)-N2-(1-(naphthalene-8-yl)ethylidene)-benzene-1,2-diamine (5) and 7(E)-N1-(7-chloroquinolin-4-yl)-N2-(1-(3,4-dimethoxyphenyl)-ethylidene)-benzene-1,2-diamine (6), respectively (cf. Scheme 2).

2-(7-chloroquinolin-4-yl)hydrazinecarbothioamide (3) was prepared by nucleophilic substitution reaction involving 4,7-dichloroquinoline and thiosemicarbazide. The click reactions were achieved in ethanol under reflux in an ultrasonic bath, for 30 min at 90°C (cf. Scheme 1). Compound (3) which upon cyclization with ethylacetocetate in an ultrasonic bath, for 40 min at 90°C gave 3-[(7-chloroquinolin-4-yl)amino]-6-methyl-2-thioxo-2,5-dihydro pyrimidin-4(3H)-one (9) in excellent yield, then the reaction of compound (3) with carbonyl compounds (acetyl naphthalene and 3,4-dimethoxy acetophenone) in ethanol under reflux in an

![Scheme 1.](image1)

![Scheme 2.](image2)
ultrasonic bath, for 30 min at 90°C yielded the Shiff's bases (E)-1-(7-chloroquinolin-4-yl)-4-(1-(naphthalen-1-yl)ethylidene)thiosemicarbazide (7) and 2-(7-chloroquinolin-4-yl)-N-[(1Z)-1-(3,4-dimethoxyphenyl)ethylidene]hydrazine carbothioamide (8), respectively (cf. Scheme 3). Finally, the nucleophilic substitution of 4,7-dichloroquinoline with 3-Amino-1,2,4-triazole in ethanol under reflux in an ultrasonic bath, for 30 min at 90°C gave 7-chloro-N-(1H-1,2,4-triazol-3-yl)-quinolin-4-amine (4). The yields for the several click reactions reported here were in the range of 78–89%, synthetic route of the compounds is outlined in Schemes 1, 2 and 3. The structure of the compounds (2)–(9) was confirmed by FT-IR, $^1$H NMR, $^{13}$C NMR, elemental analysis and mass spectral data.

The first step of the proposed strategy was the synthesis of the key derivatives (2)–(4) which carried out via nucleophilic substitution on the suitably position of 4,7-dihloroquinoline. It should be noted that the chloroquinoline ring can be considered as the prototype electron poor aromatic system. The electronegative nitrogen substituted on the ring has it’s aromaticity disrupted through a strong permanent dipole by the inductive polarization that causes fractional positive charge on the C2 and C4 atoms of the chloroquinoline ring. Therefore, 4,7-dihloroquinoline ring can be pictured as experiencing mesomeric electron withdrawal by the nitrogen atom, and more importantly, experiences additional inductive withdrawal from the chlorine atom at the C4 (18–21). This means that the chloroquinoline preferably undergoes nucleophilic aromatic substitution via an addition of a nucleophile at C4, followed by the elimination of chlorine atom (SNAE). The present research, in combination with prior studies clearly demonstrates that regioselectivity is often achievable, this regioselectivity is also in agreement with that predicted using the $^1$H NMR guidelines reported earlier by this group (22). Thus, the chemical shift values for the 7 and 4 positions of quinoline are 7.26 and 8.00, respectively, thereby indicating that C4 should be the more reactive site for SNAE reactions. It is also in agreement with the regioselectivity predicted by the bond dissociation energy calculations reported by Houk and co-workers for the corresponding chloroquinolines (96.2 kcal/Mol for C4 and 97.5 kcal/Mol for C7) (23–25).

2.2. Biological activity

2.2.1. Antimalarial activity

The eight 7-chloroquinoline derivatives were assessed for their in vitro antimalarial action against *P. falciparum*. Table 1 shows the values of IC$_{50}$ for the vitro antimalarial assay. All newly synthesized compounds showed moderate antimalarial with IC$_{50}$ < 100 μM, six of them showed high antimalarial activity with IC$_{50}$ < 50 μM in the range of 11.92–79.71 μM. The compounds (2), (3), (4), (6), (8)

| Compound | 2   | 3   | 4   | 5   | 6   | 7   | 8   | 9   | CQ* |
|----------|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Yield    | 78% | 80% | 81% | 88% | 83% | 85% | 89% | 87% |     |
| IC$_{50}$ (μM) | 35.29 | 25.37 | 42.61 | 77.60 | 49.68 | 79.85 | 38.71 | 11.92 | 0.18 |

*Standard dose (0.01 μM)*
and (9) showed high activities due to the amination of 4,7-dichloroquinoline with o-phenylenediamine, thiosemicarbazide and 3-Amino-1,2,4-triazole via SNAE, then treated with different carbonyl compounds which increase their activities through the substituents on the amino group. The most active 7-chloroquinoline derivative was the compound (9) with an IC$_{50}$ of 11.92 μM that is because this compound contains thioxopyrimidinone ring, suggesting that its presence could contribute to the activity (26). Interestingly, the other active compound is the compound (2) with an IC$_{50}$ of 35.29 μM, compound (3) with an IC$_{50}$ of 25.37 μM, compound (4) with an IC$_{50}$ of 42.61 μM, compound (6) with an IC$_{50}$ of 49.68 μM and compound (8) with an IC$_{50}$ of 38.71 μM. The significant activity was observed for compounds (6) and (8) which having two -OCH$_3$ group on quinoline moiety, the presence of this group could elevate the activity (27, 28) where this functional group can do an electron transfer to the protein of the plasmodium parasite that led to the destruction and death of the parasite (28). However, compounds (5) and (7) showed less antimalarial activity with an IC$_{50}$ >50 μM, the absence of active substituent on the amino group might resulted in less biological activities.

### 2.2.2. Antitumor activity

Compounds (2)–(9) were screened for their antitumor activity on three tumor cell lines, MCF-7 (human breast cancer) cell lines, HCT-116 (colon carcinoma) cell lines, Hela (Cervical carcinoma) cell lines and as a control cell, the human normal liver cell lines HL-7702 were employed to discern an unspecific of new synthesized compounds. All compounds have been made visible antitumor activity. In general, there is less difference between the antitumor activities of all compounds. Thus, compounds (3), (7) and (9) exerted the highest activities on all cell lines and showed special selectivity toward MCF-7 cells with IC$_{50}$ 14.68, 14.53 and 5.74 μM, respectively (cf. Table 2 and Figures 1–3). The presence of sulfur and nitrogen atoms in the heterocyclic rings in the compounds (3) and (9) prompts altogether greater selectivity in the direction of MCF-7 cell lines.

### Table 2. The 50% inhibitory concentration (IC$_{50}$) of 7-chloroquinoline derivatives (2)–(9) against HELA, HCT-116 and MCF-7 cell lines.

| Compounds | Hela IC$_{50}$ (µM) | MCF-7 IC$_{50}$ (µM) | HCT-116 IC$_{50}$ (µM) | Unspecific IC$_{50}$ (µM) |
|-----------|---------------------|----------------------|------------------------|---------------------------|
| 2         | 100.05 ± 1.02       | 61.71 ± 1.02         | 55.71 ± 1.01           | 123.05 ± 1.02             |
| 3         | 50.03 ± 0.92        | 14.68 ± 1.02         | 23.49 ± 1.02           | 279.94 ± 1.02             |
| 4         | 372.45 ± 0.23       | 218.76 ± 1.01        | 364.36 ± 1.04          | 328.56 ± 1.04             |
| 5         | 113.94 ± 1.04       | 36.34 ± 1.04         | 54.29 ± 1.01           | 61.97 ± 1.01              |
| 6         | 64.76 ± 1.03        | 20.91 ± 1.01         | 27.26 ± 1.04           | 298.64 ± 0.84             |
| 7         | 74.35 ± 1.01        | 15.53 ± 0.84         | 72.84 ± 1.01           | 280.86 ± 1.04             |
| 8         | 51.67 ± 1.04        | 27.58 ± 1.03         | 51.68 ± 1.01           | 258.23 ± 1.02             |
| 9         | 21.41 ± 0.95        | 7.54 ± 1.04          | 21.41 ± 1.05           | 346.14 ± 1.04             |
The elucidation for this could be either in the ability of these atoms to communicate (bind) with cellular macromolecules (proteins and/or DNA) and to stimulate a similar reaction in tumor cells (e.g. DNA-damage response), or the most mindful usefulness for this activity is the thiosemicarbazide moiety with the quinoline ring. 7-Chloroquinoline derivatives (3), (6) and (9) have a more pronounced antitumor effect on HCT-116 (colon carcinoma) cells with IC_{50} 23.39, 27.26 and 21.41 µM, respectively. All compounds showed mild activity toward Hela cell lines except (3), (8) and (9) which has IC_{50} 50.03, 51.67 and 21.41 µM, respectively. On the other hand, the compound (4) presented less antitumor activity against all cell lines. Regarding the on the human normal liver cell line HL-7702, in general, all newly synthesized compounds are not toxic to normal human cells, however, the low activity was detected for the compound (9) IC_{50} 346.14 µM. The compound (5) was the most toxic compound showing IC_{50} 61.97 µM.

### 2.2.3. Antibacterial activity

The study examined the antibacterial information of all newly synthesized compounds (2)–(9) which showed a very good to moderately good activities towards different strains of microorganisms (12.5 ± 0.63–23.8 ± 1.5) (Table 3). The compounds (3), (4), (7) and (9) showed relatively perfect activity with all the bacterial strains. The best activity is attributed to the presence of pharmacologically active groups at position 4 of quinoline, –NH– and triazole ring attached to quinoline ring. Introduction of thiosemicarbazide group such as NH–CS–NH2 to the ring quinoline at position 4 promoted activity while the introduction of o-phenylene diamine derivatives group at quinoline caused a reduction in activity versus most of the bacterial strains. Compounds (7) and (9) demonstrated greater activity against the gram-negative bacterial species Staphylococcus aureus, however, compounds (4) and (8) exhibit a good action versus the gram-negative bacterial species Bacillus subtilis. Fulfillment of gram-negative antibacterial, compounds (4) and (9) demonstrated amazing activity against Salmonella typhimurium, while compounds (7) and (8) showed very good activities against Escherichia coli. DMSO was used as a control solvent and Ampicillin and Ciprofloxacin, as reference drugs.

The compounds showed relatively very good activities against all the fungal strains. These compounds include biologically active groups, –NH– and triazole ring attached to quinoline ring. The compounds (3), (4), (7) and (9) exhibited higher activity against all fungal strains. DMSO was used as a control solvent and Ampotericin B, as a reference drug. It is worth noting that the presence of hetero rings at the fourth position of the quinoline system significantly increases the biological effect against fungal strains.

### 3. Materials and methods

#### 3.1. Chemical syntheses - general

Melting points were measured with a Gallen Kamp melting point apparatus. Silica-gel-coated aluminum plates used to test the purity of the compounds. Infra-red spectra (λ-cm⁻¹) were recorded on Bruker Vector (Germany) and on Mattson FT-IR 1000 (Taibah University, Saudi Arabia), using KBr disks. ¹H NMR spectra were recorded on Gemini 300 MHz, C¹³ NMR spectrometer, in DMSO-d₆ using dimethyl sulfoxide as a solvent and tetramethylsilane (TMS) as an internal standard (Chemical shift in δ, ppm); ¹³C NMR spectra were recorded on Gemini 50 MHz NMR spectrometer. Mass spectra were measured on GCQ Finnigan MAT and Elemental analyses were performed at the micro-analytical Center, Cairo University, Giza, Egypt. Biological activity was determined in a laboratory by the Regional Center for Mycology and Biotechnology (RCMB), Al-Azhar University, Cairo, Egypt. All the chemicals were purchased from Sigma–Aldrich.

#### 3.1.1. General procedure for synthesis 1-(7-chloroquinolin-4-yl) derivatives (2)–(4)

(0.01 Mol) 4,7-dichloroquinoline (1) was mixed with (0.01 Mol) of the appropriate amine, o-phenylenediamine, thiosemicabazide and 3-amino-1,2,4-triazole in ethanol (15 ml) and refluxed in an ultrasonic bath for 30 min at ambient temperature. TLC monitoring was used to ensure the completion of the reaction. Then we added CH₂Cl₂ (150 ml) as an organic solvent, then washed the mixture with NaOH (1N, 150 ml) to give an organic layer and aqueous layer. The resulting crude poured into ice water to produce compounds (2)–(4) and the solid formed was collected by filtration and dried.

#### 3.1.2. General procedure for synthesis Schiff bases (5)–(8), (0.01 Mol) of a compound (2) or (3) (0.01 Mol) of carbonyl compounds as acetyl naphthalene, 3,4-dimethoxy acetophenone, in 20 ml absolute ethyl alcohol were refluxed in an ultrasonic bath, for 30 min at 90°C, until TLC analysis showed the complete consumption of 1-(7-chloroquinolin-4-yl) derivatives by using a proper eluent. By concentrating the filtered it gave compounds (5)–(8) which purified by preparative column chromatography to give the desired product in good to excellent yields.
3.1.3. General procedure for synthesis 3-(7-chloroquinolin-4-ylamino)-tetrhydro-6-methyl-2-thioxopyrimidin-4(1H)-one (9)

(0.01 Mol) of a compound (3) and (0.01 Mol) of ethyl acetoacetate was refluxed in an ultrasonic bath, for 40 min at 90°C, to give brown crystals which recrystallized from ethyl alcohol to give the product (9).

N1-(7-chloroquinolin-4-yl)benzene-1,2-diamine (2): Show the following data; a brown precipitate which was washed with ether and dried. Yield: 88%; mp 237–239°C, Rf 0.38 (3:1 EtOAc–hexane); IR (KBr) cm⁻¹: 3184 (NH), 3020 (Ar–C–H), 2941 (CH₃ str.), 1626 (C–N); ¹H NMR(300 MHz, DMSO-d₆) δ 8.85 (d, J = 5.45 Hz, 1H, N=CH, quinoline), 8.16(d, J = 8.34 Hz, 1H, Ar- H), 7.89(d, J = 8.46 Hz, 1H, Ar-H), 7.88(d, J = 8.43 Hz, 1H, Ar- H), 7.81(d, J = 8.41 Hz, 1H, Ar-H), 7.79(s, 1H, Ar- H), 7.77(dd, J = 7.42 Hz, J = 8.42 Hz, 1H, Ar- H), 7.75(dd, J = 8.42 Hz, J = 7.22 Hz 1H, Ar-H), 7.70 (s, 1H, ArC- NH), 7.35–7.45 (m, 7H,Ar-H), 6.47 (d, J = 5.39 Hz, 1H, Ar- H), 2.66 (s, 3H, CH₃); ¹³C NMR (50 MHz, CDCl₃) δ 160.27, 155.17, 150.43, 145.32, 142.34, 140.26, 137.54, 135.24, 133.78, 132.11, 130.63, 130.56, 130.45, 128.15, 126.87, 126.48, 126.25, 125.73, 125.30, 124.70, 124.10, 123.67, 123.11, 117.40, 113.52, 94.45. Mass spectra (M⁺) at m/z 421. Anal. Calcd for C₂₂H₂₃N₃Cl: C, 76.86; H, 4.78; N, 9.96. Found: C, 76.91; H, 4.52; N, 9.88%.

(E)-N₁-(7-chloroquinolin-4-yl)N₂-(1-(3,4-dimethoxy-phenyl)-ethyldiene)-benzene-1,2-diamine (6): Show the following data; a yellowish red precipitate which purified by column chromatography by using ethyl acetate and hexane (3:1) to give yellow crystals. Yield: 83%; mp 249–251°C, Rf 0.48(3:1 EtOAc– CHCl₃); IR (KBr) (cm⁻¹) :3162 (NH), 3041 (Ar-C–H), 2952 (CH₃ str.), 1615 (C=O); ¹H NMR(300 MHz, DMSO-d₆) δ 8.89 (d, J = 5.37 Hz, 1H, N=CH, quinoline), 8.32 (s, 1H, ArC- NH), 8.29(d, J = 5.42 Hz, 1H, Ar-H), 8.17(d, J = 8.48 Hz, 1H, Ar-H), 7.91(d, J = 8.43 Hz, 1H, Ar- H), 7.88 (s, 1H, Ar- H), 7.79 (d, J = 8.41 Hz, 1H, Ar- H), 7.77(d, J = 8.38 Hz, 1H, Ar-H), 7.61 (dd, J = 7.22 Hz, J = 8.32 Hz, 1H, Ar-H), 7.51(dd, J = 7.02 Hz, J = 8.34 Hz, 1H, Ar-H), 7.41 (1H, Ar-H), 7.36 (d, J = 8.29 Hz, 1H, Ar-H), 7.33 (d, J = 8.33 Hz, 1H, Ar-H), 3.81–3.84 (s, 6H, 2OCH₃), 2.50 (s, 3H, CH₃); ¹³C NMR (50 MHz, CDCl₃) δ 169.41, 154.82, 154.31, 153.12, 151.76, 151.54, 150.17, 149.49, 149.09, 144.28, 143.54, 139.91, 133.42, 31.11, 127.53, 124.2, 123.90, 123.05, 122.17, 119.83, 117.56, 116.98, 116.03, 111.08, 96.15, 58.16, 55.66, 30.60. Mass spectra (M⁺) at m/z 431. Anal. Calcd for C₂₂H₂₃N₃Cl: C, 69.66; H, 5.09; N, 9.69%.

(E)-N₁-(7-chloroquinolin-4-yl)-N₂-(1-(naphthalen-8-yl)ethyldiene)-benzene-1,2-diamine (7): Show the following data; a brown oil which purified by column chromatography by using ethyl acetate and hexane (3:1) to give yellow crystals. Yield: 85%; mp 210–212°C, Rf 0.42(3:1 EtOAc– CHCl₃); IR (KBr) (cm⁻¹) :3172 (NH), 3025 (Ar–C–H), 2943 (CH₃ str.), 1623(C= N), 1580 (NH bend), 1224 (C=S); ¹H NMR (300 MHz, DMSO-d₆) δ 2.71 (s, 3H, CH₃), δ8.87 (d, J = 5.25 Hz, 1H, N=CH, quinoline), 8.57 (d, J = 8.17 Hz, 1H,
Ar-H), 8.43 (s, 1H, Ar-H), 8.31(d, J = 8.43 Hz, 1H, Ar-H), 8.16 (s, 1H, NH), 8.00 (s, 1H, NHCS), 7.29–7.51 (m, 7H, Ar-H), 6.64(d, J = 5.29 Hz, 1H, Ar-H); 13C NMR (50 MHz, CDCl3) δ 187.57, 162.64, 151.34, 149.02, 145.84, 136.91, 135.89, 134.15, 124.93, 127.73, 126.59, 126.32, 125.06, 122.76, 122.21, 121.06, 114.26, 109.44, 98.36, 26.71. Mass spectra (M±) at m/z 404. Anal. Calcd for C23H20N2ClO2S: C, 57.90; H, 4.46; N, 13.50; Found: C, 57.73; H, 4.32; N, 13.62%.

(E)-1-(7-chloroquinolin-4-yl)-4-((3,4-dimethoxyphenyl)ethyldiene)thiosemicarbazide (8): Show the following data; a brown precipitate which was purified by column chromatography by using ethyl acetate and CHCl3 (3:1) to give a brown crystal. Yield: 89%; mp 251°C Rf 0.48(1:2 EtOAc-petroleum ether); IR (KBr) cm⁻¹ : 3165 (NH), 1674 (C=O), 1618 (C=O), 1543, 1532, 1495, 1487, 1477, 1373, 12805, 1275, 121.26, 119.50, 116.74, 115.60, 114.09, 109.91, 108.54, 103.38, 102.57, 80.72, 25.80. Mass spectra (M±) at m/z 318. Anal. Calcd for C20H19N4ClO2S: C, 57.75; H, 4.17; N, 13.88%.

Figure 4. Evaluation of antitumor activities of 7-chloroquinoline derivatives (2)-(9) against HELa cell line.
3.2.2. Determination of antitumor activity against MCF-7, HCT-116 and Hela cell lines

The antitumor activities of all new synthesized 7-chloroquinoline derivatives were tested for three cancer cell lines MCF-7 cells (human breast cancer), HCT-116 (colon carcinoma) and Hela (Cervical carcinoma). As control cell, the human normal liver cell line HL-7702 was employed to discern an unspecific cytotoxicity of newly synthesized 7-chloroquinoline derivatives. All cell lines were gotten from the VACSERA Tissue Culture Unit. The effect of new compounds on the cell was calculated and the microplate reader (SunRise, TECAN, Inc., U.S.A.) was utilized to gauge the optical density and to determine the number of viable cells and the percentage of viability which calculated as [1-(ODt/ODc)] × 100% where ODt is the mean Optical Density of wells dealed with the tested sample and ODc is the mean Optical Density of untreated Cells (34, 35).

3.2.3. Determination of antimicrobial activity

The antimicrobial activity was measured for the newly synthesized compounds (2)–(9). Each microbial strain of culture collection was given by the RCMB, Al-Azhar University, Cairo, Egypt. The antimicrobial profile was tested against two Gram-positive bacteria species (B. subtilis, S. aureus), two Gram-negative bacterial species (E. coli, S. typhimurium), two fungi (Aspergillus fumigatus and Candida albicans) utilizing an adjusted well dissemination strategy (36–38).

4. Conclusions

The present study describes the synthesis and antimalarials, antimicrobial, and the anticancer activity of a novel series of 7-chloroquinoline derivatives via click chemistry by using ultrasound irradiation energy source. All the compounds exhibit potent antimalarial activity in vitro. Further, the synthesized compounds (2)–(9) were screened for antibacterial activity against two Gram-positive bacteria species (B. subtilis, S. aureus), two Gram-negative bacterial species (E. coli, S. typhimurium), two fungi (A. fumigatus and C. albicans) two pathogenic strains (E. coli and B. subtilis). The results appear clearly that the most of the new compounds have shown very good biological activities.

Disclosure statement

No potential conflict of interest was reported by the authors.

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Asmaa Aboelnaga was born in Cairo, Egypt. She received a Ph.D. degree from the Ain Shams University, Egypt; she...
worked as a faculty member in the chemistry department in Ain Shams University, Egypt, and Taibah University, KSA. Her research group has been working for the last 10 years and continues to work on various aspects of cycloaddition reaction with the main objective of developing this reaction into a useful and powerful synthetic tool in organic chemistry. Green chemistry is another important area of her research interest.

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