Synthesis of new 4,7Chloroquinoline Derivaties by using Ultrasound irradiation evaluation of their Biological activity

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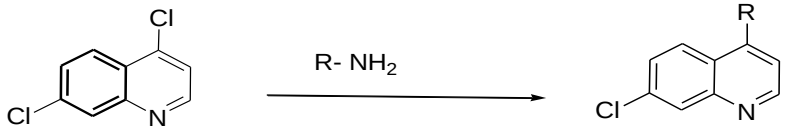
Abstract: This study describes the click synthesis of new 4, 7-chloroquinoline derivatives by using ultrasound irradiation and evaluation of their compounds show activity antimicrobial, anti malarial and the anticancer. All high compounds chow moderate anti malarial activity with 100 MM, sis of them showed anti malarial activity chloroquinoline derivative screened for their antitumor cancer) 2. 3. 4. 68 and 95 with IC50 M The compound 19 Also the newly synthesized compounds we were activity towards three lines of cancer cells. MCF-7 (human breast HCT-116 (colon cartinomal (9) exerted the highest activity and Hela (Cervical carcinoma) cell lines. Compound (3) and on all cell lines and showed special selectivity toward MCF-7 cells and the antibacterial screening data showed moderate ta 11.3) towards the entire tested good inhibition zone (12.5-0.63-238 compounds. Elucidation of the structures of these new pure compounds was based on, IR, 'H NMR, C NAMR, MS and their elemental analysis.

Keywords: Ultrasonic radiation Antibacterial activity, Antifungal activity.

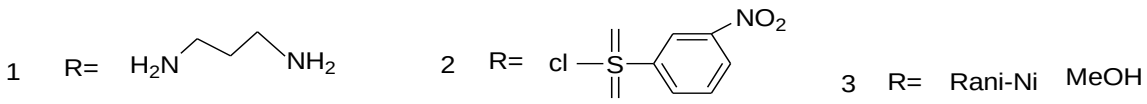
INTRODUCTION

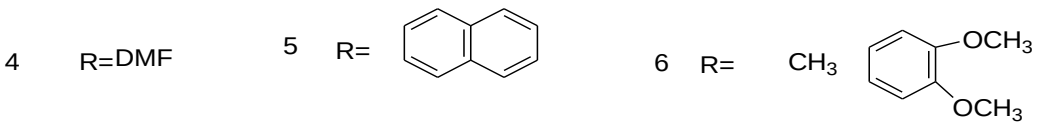
Quinolines and their derivatives are present in numerous natural products and have highly anti malaria, anti hypersionmantic, anti-inflammatory, antibacterial and ant hypersensitive activities [1]. Few methods have been reported for the preparation of quinolines derivatives such as the Skraup, Doebner 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 anti malarial clinically used drug but parasite resistance led to its substitution by artemisinin and its semi-synthetic (artemether, artesunate) [5], [6]. Therefore, there is an urgent need for new medications to treat malaria. There is extensive documentation of the synthesis of molecular hybrids with various moieties that represent known or suspected (sonochemistry) [7]. Through the creation of novel receptive intermediates and compounds that are not typically seen under typical thermal conditions, this energy source has been shown to be able to speed up reactions and selectivities [8]. In addition, ultrasonic irradiation can be regarded as an earth-friendly process because it concentrates less vitality and produces fewer side effects [9].

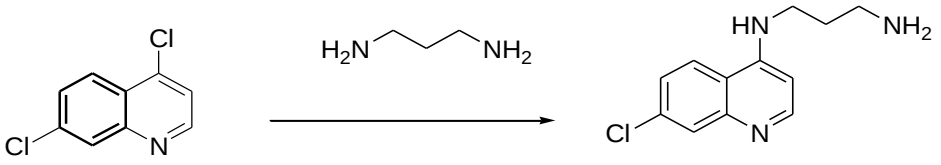
This indicates that dimethoxyphenyl) ethylidene) hydrazine is eliminated after the chloroquinoline preferentially undergoes nucleophilic aromatic substitution by adding a nucliophile at C_4. The synthesis of the important derivatives (2)–(4) was the initial stage of the suggested approach [10]. This was done by nucleophilic substitution on the appropriately positioned 4-7-dihloroquinoline. It should be mentioned that the prototypical electron-poor aromatic system is the chloro-quinoline ring. The inductive polarization that results in fractional positive charge on the C_2 and C_4 atoms of the chloroquinoline ring disrupts the aromaticity of the electronegative nitrogen replaced on the ring by creating a strong permanent dipole [11]. This means that when a nucliophile is added at C_4, the chloroquinoline preferentially undergoes nucleophilic aromatic substitution, which results in the elimination of dimethoxyphenyl) ethylidene) hydrazine [12]. The first step in the proposed method was the synthesis of the significant derivatives (2)–(4). Nucleophilic substitution on the correctly positioned 4-7-dihloroquinoline was used to accomplish this [13].



Scheme -1

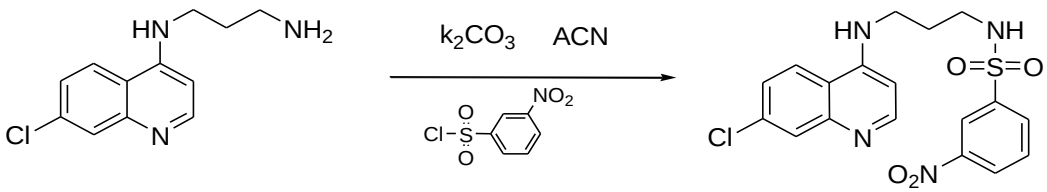






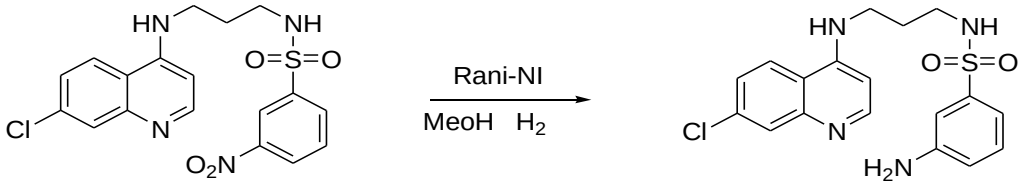
1 1-2

Scheme -2



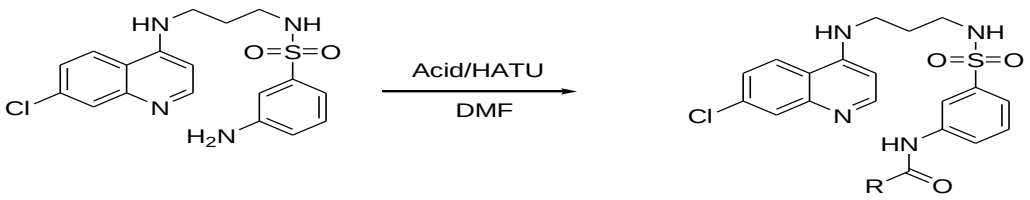
2 2-3

Scheme -3



3-4

Scheme-4



4 4-5

Scheme -5

Biological activity

Antimalarial action the antimalarial activity of the eight 4, 7-chloroquinoline derivatives against P. falciparum was evaluated in vitro. The IC values for the in vitro antimalarial test are displayed in Table 1. Six of the newly synthesized compounds shown significant antimalarial activity with IC 50 µM in the range of 11.92-79.71 µM, while all of them demonstrated moderate antimalarial activity with IC < 100 MM. Due to the presence of 4,7-dicloroquinoline with N-(3-(7-Chloroqunoline-4yl amino) propyl3-nitrobenzene sulphonamide, the compounds (2), (3), (4), and (5) exhibited high activity. These compounds were further treated with other carbonyl compounds, which boost their activities by substituting the amine group. With an ICs of 11.92 M, the most active 4, 7-chloroquinoline derivative was the one that had no rings, indicating that its prevalence might have contributed to the activity [14]. It's interesting to note that compound (2), with an ICs of 35.29 µM, is the other active chemical. compound (4) with a path b KnD of 42.61 µM, compound (6) with a K*C_{50} of 49.65 µM, compound (5) with a K_{50} of 38.71 M, and compound with a Wedt of 25.37 µM Compounds (4) and (5), which include two -OCH groups on the quinoline moiety, showed the most activity; the presence of these groups may increase the activity [15], where the plasmodium parasite 1781 was destroyed and killed as a result of this functional group's ability to transmit electrons to its protein. However, with a K_{30} > 50mu*M, compounds (4) and (5) had decreased anti-malarial efficacy. Less biological activity may have resulted from the amino group's lack of an active substituent [16].

Table1. The yield of click reaction affording 4, 7 chloro quinoline derivatives 2-4 in vitro antimalarial activity (IC_{50}µM) again Plasmodium falciparum.

Compound	2	3	4	5
Yield	68%	72%	75%	80%
IC_{50}9 (µM)	25.25	22.37	35.27	72.14

Antitumor activity

In order to identify an unspecific of newly synthesized compounds, compounds (2)–(9) were tested for their antitumor activity on three tumor cell lines: MCF-7 (human breast cancer), HCT-116 (colon carcinoma), and Hela (cervical carcinoma). The human normal liver cell lines HL-7702 were used as a control cell. Every chemical has demonstrated anticancer action. Overall,[17] there is less variation in each compound's antitumor properties. With I*C{50} 14.68, 14.53, and 7.54 µ.M., compounds (3), (7), and (9) demonstrated the highest activity on all cell lines and demonstrated unique selectivity for MCF-7 cells. Accordingly (see Figures 1-3 and Table 2). The compounds (3) and (5) exhibit a significantly higher degree of selectivity towards MCF-7 cell lines due to the presence of nitrogen and sulfur atoms in their heterocyclic rings. The explanation for this could be found in the atoms' capacity to communicate with cellular macromolecules (such as DNA) and to trigger a similar response in tumor cells' leg DNA damage response. The thiasemicarbsazide moiety with the quinoline ring is the most useful component for this activity. On HCT-116 (colon carci normal cells), 7-chloroquinoline derivatives and have a stronger anticancer activity with 23.59, 27.26, and 21.41 M, respectively. With the exception of (3), all drugs exhibited modest action toward Hela cell lines. W VB 50.03, 51.07, and 21.41 M are found in (4) and (5) respectively. However, the anticancer activity of compound (4) against all cell lines was lower. In reference to the human normal liver cell line HL-7702, the newly synthesized compounds are generally not hazardous to normal human cells; however, compound (9) K apr 346.14 µM was found to have modest activity. With an IC of 61.97 µ.M., chemical (5) was the most hazardous.

Table2. The 50% inhibitory concentration IC_{50}) 4,7 chloroquinoline derivative 2-4 against HTC-116 and MCF-7 Cell lines.

Compound	Hela	MCF-7	HTC-116	Human normal liver HL-770
2	95.02 ± 0.02	58.29 ± 0.01	45.04 ± 0.02	98.05 ± 0.02
3	45.03 ± 0.02	10.04 ± 0.02	19.04 ± 0.02	210.05 ± 0.0
4	310.34 ± 0.02	200.26 ± 0.01	310.32 ± 0.02	287.23 ± 0.02

5	93.54 ± 0.02	21.24 ± 0.04	32.19 ± 0.02	42.92 ± 0.02

MATERIALS AND METHODS

General chemical syntheses A Gallen Camp melting point instrument was used to measure melting points. Aluminum plates covered with silica gel are used to assess the compounds' purity. Bruker Vector (Germany) and Mattson FT-IR 1000 (Taibah University, Saudi Arabia) were used to record infrared spectra (lambda*e * m^-1) using KBr disks. "Using tetramethylsilane (TMS) as an internal standard (Chemical shift in &, ppm) and dimethylsulfoxide as a solvent, H NMR spectra were acquired in DMSO-d on a Gemini 300 MHz, c ^ 11 NMR spectrometer; C [18]. The Gemini 50 MHz NMR spectrometer was used to record the NMR spectra. Biocal activity was evaluated in a laboratory by the Regional Center for Mycology and Biotechnology (RCMB), Al-Azhar University, Cairo, Egypt, and mass spectra were measured on GCQ+ Finnegan MAT [19]. Elemental studies were carried out at the 5/10 analytical Center, Cairo University, Giza, Egypt. The supplier of all the chemicals was Sigma-Aldrich [20].

CONCLUSION

The synthesis and antimalarial, antibacterial, and anticancer properties of a novel family of 4,7-chloroquinoline derivatives using click chemistry and an ultrasound irradiation energy source are described in this paper. In vitro, all of the compounds show strong antimalarial activity. Additionally, two Gram-positive bacterial species (B. subrills, S. aureus), two Gram-negative bacterial species (E. coli, S. typhimurium), two fungi (A. fumigatus and Calbicans), and two pathogenic strains (E. coli and B. subtilis) were tested for antibacterial activity using the synthesized compounds (2)–(4). The findings make it abundantly evident that the majority of the novel compounds have demonstrated excellent biological activity.

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