

Medicinal Chemistry & Drug Discovery

Synthesis and Antimicrobial, Antiproliferative Evaluation of Novel Quinolone and Conazole Analogues via Conventional and Microwave Techniques

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1,2,4-Triazole-3-one (**3**), acquired from cinnamaldehyde was converted to the corresponding carbox(thio)amides via several steps (**6a–c**). Their reaction with sodium hydroxide gave the 1,2,4-triazole derivatives (**7a–c**). Compound **3** treatment with 2-bromo-1-(4-chlorophenyl) ethanone or 2-chloro-1-(2,4-dichlorophenyl)ethanone afforded the compounds **8a,b** and by reducing these compounds reduction products were obtained (**9a,b**). The synthesis of (**10a–e**) was carried out by the reaction compounds **9a,b** with different benzyl chlorides. Then oxadiazole derivative (**12**) was obtained by ring closure from hydrazide compound **5**. Subsequently compounds **3**, **7a–c**, and **12** were treated with various amines in the presence of formaldehyde to yield Mannich bases (**11a–e**, **14a–e**, **13a,b**).

Microwave-assisted and conventional techniques were utilized for the syntheses. The structures of newly synthesized compounds were illuminated by spectroscopic methods. Their antimicrobial (MIC method), and anticancer activities (Abay's method) were examined. Results showed that most of the compounds exhibited good antimicrobial activities. Especially compounds **14a–e** which is a mannich base showed very good antitubercular activity against *Mycobacterium smegmatis* compared with Streptomycin standard drug. Also compounds **8a** and **9b** have been found to have strong antiproliferative effects on the HeLa cervical cancer cells and also these compounds did not have a cytotoxic effects on a normal cells.

Introduction

Cancer is the result of uncontrolled growth of cells a major health concern and amongst the most important reasons for death worldwide.^[1–3] The World Health Organization's cancer agency warns that there will be 22 million new cases of cancer every year within the next two decades.^[4] Hence, cancer treatment is the primary task of today's medical research.^[5] Despite the invention of several chemotherapeutic agents, still the treatment of cancer is a major challenge, because of multi-drug resistance, toxicity, or poor bioavailability. The effectiveness of many anticancer drugs is limited by acquired resistance to drugs, side effects due to their toxicity to normal cells because of their inability to differentiate between normal and cancerous cells. In this context, there is a need to design and synthesize new, effective, and less toxic anticancer agents

throwing a challenge to medicinal chemists all over the World.^[6,7]

Infectious diseases continue to be a leading threat to human health, and the rapid development of bacterial resistance to current antibiotic chemotherapies has rendered lots of therapy weapons less effective.^[8] It is anticipated that antibiotic resistance is going to cause more than 10,000,000 deaths per year by the year 2050, posing a formidable challenge for disease treatment as pathogens become resistant to clinical drugs.^[9] The World Health Organization has launched a global action plan calling on all countries to take measures towards drug-resistant microbes, and the discovery of efficacious and safer antimicrobials with new or multiple mechanisms of action has been an urgent need to combat resistant strains.^[10,11]

Organic molecules bearing heterocyclic compounds have received significant consideration in all fields of life comprising medicinal, pharmaceutical, combinatorial, natural resources, agriculture and dyes products.^[3,12] Hybrid compounds are molecules with two or more structural fields, which have diverse dual activities and biological features. These substances generally possess the capacity to get over medicine resistance, develop pharmacokinetic structures, and abate toxicity.^[13,14]

Triazoles are an important class of aromatic five-membered heterocyclic compounds with a wide variety of biological activities. They consist of two structural isomers: 1,2,3- and 1,2,4-triazole. Compounds based on 1,2,4-triazole scaffold show diverse biological and pharmacological activities.^[15–17] The synthesized compounds having 1,2,4-triazole-3-thione skeletons have been reported to possess biological and pharmaco-

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logical activities such as anticonvulsant, urease inhibition, antioxidant, analgesic, anti-parasitic, antiulcer, anticancer, anti-HIV, anti-tuberculosis, antiamebic, anti giardial, antiepileptic, anti-inflammatory, antidepressant, and anxiolytic.^[18–25]

Quinolones are widespread pharmacophores in anti-bacterial substances. Fluoroquinolones are noted as one of the most broadly used antibacterial agents for the cure of bacterial illness. The cytotoxic activity of quinolone derivatives has become the source of new anticancer agents, which might also help to address side toxicity and resistance.^[26] Quinolones and related derivatives are useful compounds with diverse pharmaceutical applications, and some have even reached markets for the treatment of various ailments.^[27] Thus, the hybridization of quinolone with 1,2,4-triazole is inclined to present hopeful anti-bacterial agents.^[28–30]

Imidazoles and triazoles, as a group called conazoles, are currently used worldwide as fungicides for grain, vegetable, fruit, and flower production and as pharmaceuticals for the treatment of human mycoses including vaginal mycoses in pregnant women and thrush in infants.^[31]

Recently, multicomponent reactions (MCRs) have received considerable attention from synthetic organic and medicinal chemists for the construction of complex molecules having biological activity. When compared with conventional organic reactions, MCRs have some superior properties including high conversion rate, minimal reaction time, and structural complexity. Thus, MCRs are also considered green chemical processes.^[32,33] Among these, the Mannich reaction, a one-pot three-component condensation reaction, provides synthetically and biologically important β -aminoalkylated compounds, which are important intermediates for the construction of various nitrogen-containing natural products and pharmaceuticals.^[34–36]

Microwave-assisted organic synthesis of various heterocyclic moieties is an effective and environment-friendly synthetic approach and becoming an effective tool of the green chemistry method. Microwave-assisted techniques were reported to be more effective in perspective of the environment, reaction time, high yields, ease of work-up, and isolation of products. Moreover, solvents which are often expensive, toxic, difficult to remove in the case of aprotic dipolar solvents with a high boiling points, and are environmentally polluting agents, are not necessary most of microwave-assisted synthesis.^[37–40]

One of the main strategies for the discovery of new drugs is combining two or more pharmacophoric moieties in a single molecule to obtain the synergistic effect or to obtain antitumor agents that have a novel mode of action. For this purpose, in this study, various quinolone and conazole derivatives were synthesized using conventional and microwave methods, and antimicrobial and anticancer activities of these newly synthesized compounds were determined using various methods.

Results

Chemistry

The primary target of this study was to develop antimicrobial hybrid substances covering various pharmacophore structures. Reactions of last and intermediate compounds were achieved as pictorial in Scheme 1, Scheme 2, Scheme 3, and Scheme 4. The synthesis was carried out by utilizing microwave-assisted and conventional methods. The finishing of the synthesis was observed via the thin-layer chromatography (TLC) process. All product structures were based on the foundation of spectral and physicochemical data.

Antimicrobial Activity

All new products were tested for their antimicrobial properties utilizing the minimal inhibition concentration method (MIC) and the outcomes for active molecules are illustrated in Table 1. The antimicrobial activities of compounds (2–9) were tested against 4 bacteria and 3 yeasts.

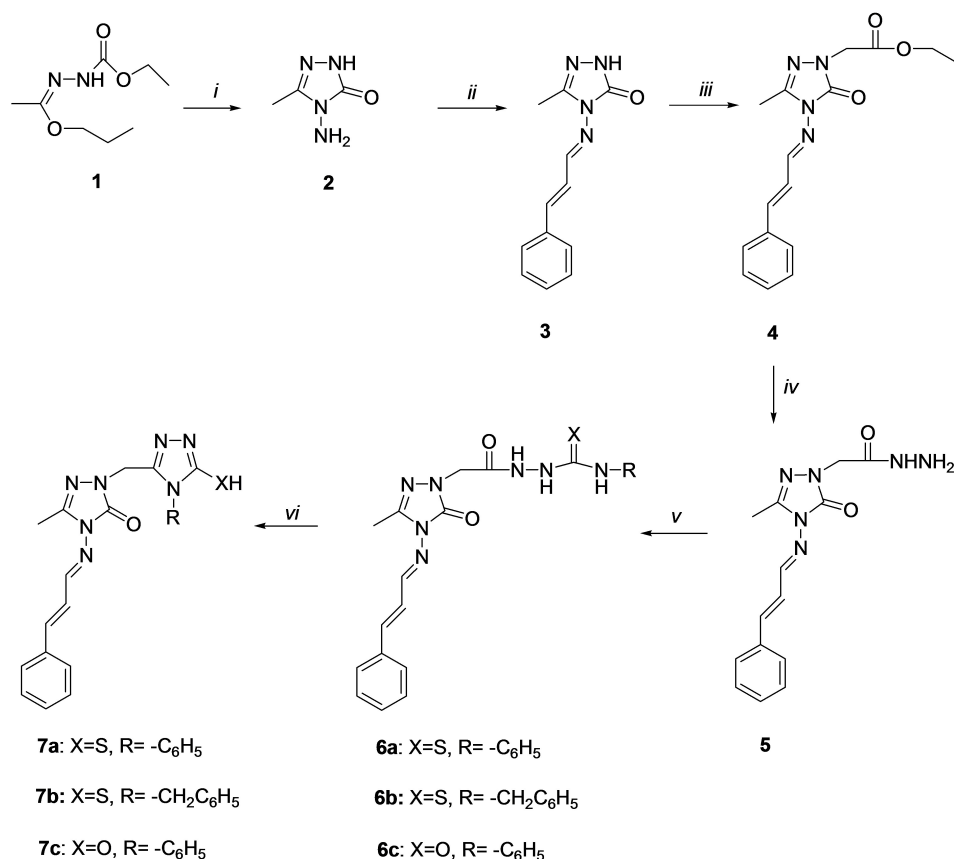
Among the synthesized compounds, compounds 3–9 displayed moderate activity in relation to testing microorganisms while showing better activities on the *M. smegmatis* and *E. coli*. That is compounds **7b** and **8b** have more effective for *M. smegmatis* than the other molecules with the MIC values of 62.5 and 1.95 $\mu\text{g}/\text{mL}$ respectively. *M. smegmatis* is one of an acid-fast, aerobic-rapidly growing bacterial species in the genus *Mycobacterium* and constitutes one of the characteristic tuberculosis agents causing death and morbidity. On the other hand, compound **9a**, an intermediate, showed excellent activity on *E. coli*, a gram-negative bacterium, at 0.24 $\mu\text{g}/\text{mL}$ MIC value. Namely, **9a** exhibited much better activity against *E. coli* than ampicillin used as a standard drug. *E. coli* which is rod-shaped, gram-negative enteric bacteria which lives in the enteric systems of humans and animals and are found in aqua and fecal substance.

Compounds **10a–e** which are conazole derivatives exhibited slight activity on the gram-positive and gram-negative bacteria and yeasts. But compound **10c** no antimicrobial effects were found towards the test microorganisms.

Mannich bases **11a–e** displayed good antibacterial activity to test microorganisms. However, these compounds presented not good antimicrobial effect against the yeast strains *C. albicans* and *S. cerevisiae*. Only compound **11e**, containing phenyl piperazine, showed a moderate activity MIC value of 156 $\mu\text{g}/\text{mL}$ on *S. cerevisiae*.

Oxadiazole compound, **12**, obtained as a result of ring closure, has low activity on all the microorganisms. But, mannich bases **13a,b** obtained from the reaction of the oxadiazole compound with the quinolone showed strong activities. Especially compound **13a** exhibited the best activity among all compounds synthesized against yeast strains with 78 $\mu\text{g}/\text{mL}$ MIC value on *S. cerevisiae*. That is **13a** has good antifungal activity.

Among the synthesized compounds, **11a–e** mannich bases demonstrated the best and excellent activity against gram-positive and gram-negative bacteria with MIC values between



Scheme 1. Reactions and conditions. *i*: hydrazine hydrate, reflux for 11 h; *ii*: cinnamaldehyde, 115–120 °C, oil bath, 2 h; *iii*: absolute ethanol, Na, ethyl bromoacetate, reflux for 8 h; *iv*: absolute ethanol, hydrazine hydrate, reflux for 15 h; *v*: phenyl isothiocyanate (for **6a**), benzyl isocyanate (for **6b**) or phenyl isocyanate (for **6c**), in dichloromethane, room temperature for 24 h; *vi*: 2 N NaOH in ethanol/water (1:1), reflux for 6 h or MW irradiation, 100 °C, 150 W for 16 min.

< 1 and 31.25 µg/mL, while showing no activity against yeast strains. At the same time, these compounds showed very good antitubercular activity against *M. smegmatis* compared with Streptomycin standard drug.

No antimicrobial effects were found against the test microorganisms in the studied concentration ranges of the **4**, **6a**, **6b**, **8a**, and **10c** compounds. Therefore, these results are not included in the table.

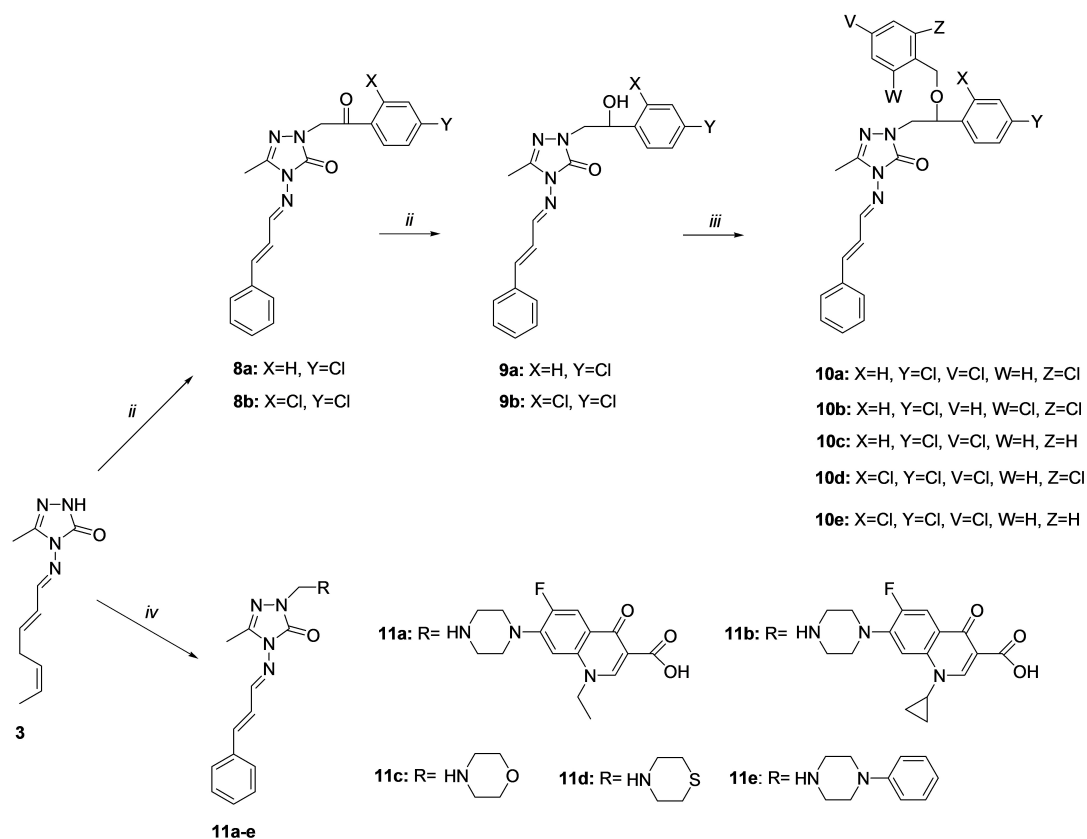
Anticancer Activity

The antiproliferative activity potentials of the molecules were examined by Abay's^[41] method against HeLa cells. Three different doses of the samples showed different antiproliferative activity against the cells (Figure 1 and Figure 2). High Cell Index (CI) values (red line) were obtained from the wells without the molecules samples. Lower CI values were obtained from the wells in which the molecules were added. Only the medium (DMEM) was added to the final three wells. These three wells were used to obtain a baseline. No impedance change was observed in these wells containing only DMEM. Therefore, the Cell Index (CI) values of these three wells did not

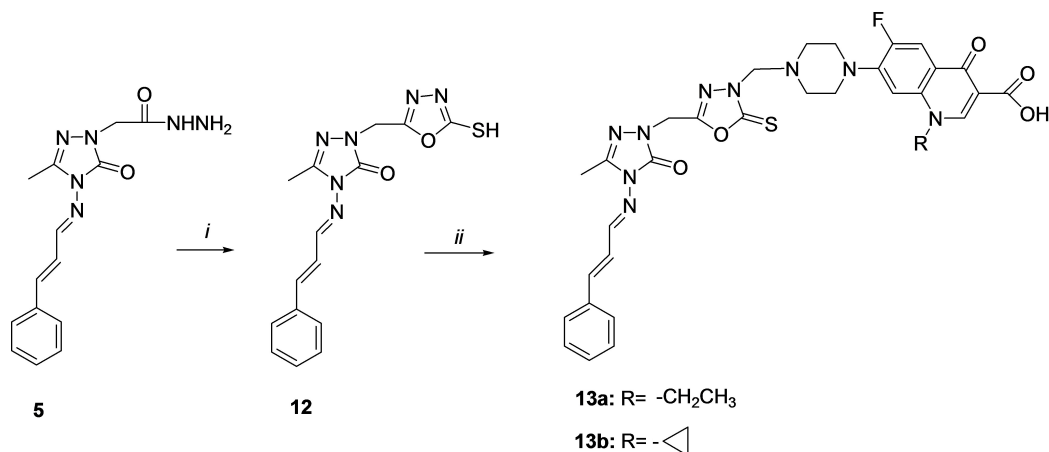
increase at all and straight continued to the end of the experiment (green line) similarly.

CI values obtained from only DMEM and cell-added wells were shown as the red line. The HeLa cells that continue to develop without encountering any obstacles have caused the CI to rise rapidly. This situation shows that the cells are attached to gold-plated microelectrodes in the well ground during the experiment and there is no proliferative negativity. The more the cells attached to the electrodes on the plate floor, the greater the impedance change. This results in an increase in CI value. On the contrary, the decrease in CI value means that the proliferation of the cells is suppressed or inhibited.

The hard CI decline seen at the 2nd hour is due to the change in the temperature of the e-Plate 96 taken from the RTCA station in the incubator (95% CO₂, 37 °C) to the sterile cabinet and the sample addition. After the addition of the molecule samples, the E-Plate 96 was inserted into the station in the CO₂ incubator again. The cells in the wells with no added samples were rapidly increased the CI values (red line). However, the proliferation of the cells in the wells the samples were added was strongly suppressed by the samples' molecules. This situation resulted in low CI values.



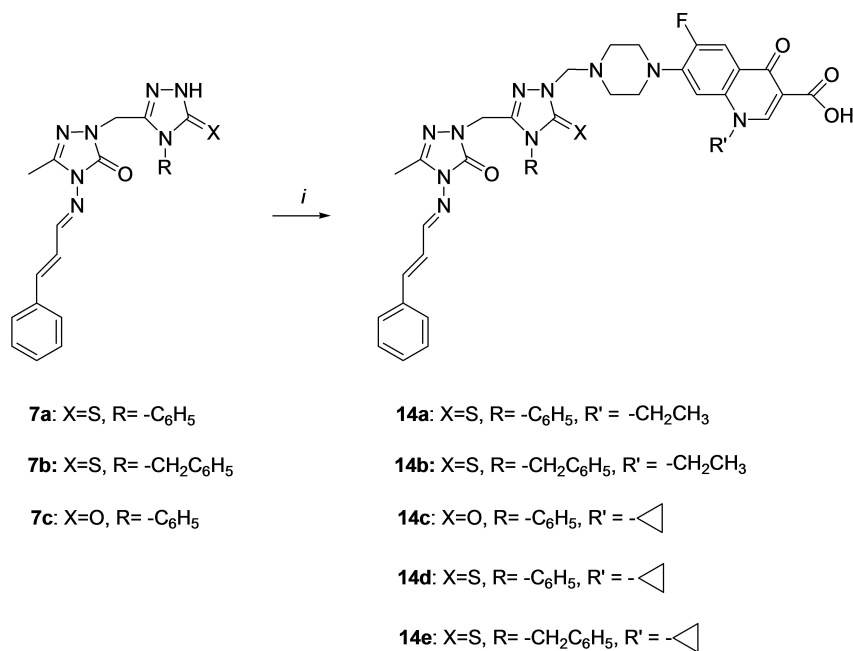
Scheme 2. Reactions and conditions. *i*: absolute ethanol, sodium ethoxide, 2-bromo-1-(4-chlorophenyl)ethanone (for **8a**) or 2-chloro-1-(2,4-dichlorophenyl)ethanone (for **8b**) reflux for 24 h or MW irradiation, 120 °C, 150 W for 6 min.; *ii*: absolute ethanol, sodium borohydride, reflux for 16 h or MW irradiation, 125 °C, 150 W for 8 min.; *iii*: tetrahydrofuran, sodiumhydride, 2,4-dichlorobenzyl chloride (for **10a**, **10d**), or 2,6-dichlorobenzyl chloride (for **10b**) or 4-chlorobenzyl chloride (for **10c**, **10e**), MW irradiation, 100 °C, 150 W for 17 min.; *iv*: HCl, formaldehyde, norfloxacin (for **11a**), ciprofloxacin (for **11b**), morpholine (for **11c**), thiomorpholine (for **11d**), 4-phenylpiperazine (for **11e**), MW irradiation, 80 °C, 100 W for 5 min.



Scheme 3. Reactions and conditions. *i*: absolute ethanol, CS₂, KOH, reflux for 24 h.; *ii*: HCl, formaldehyde, norfloxacin (for **13a**) or ciprofloxacin (for **13b**), MW irradiation, 80 °C, 100 W for 5 min.

80 minutes after the addition of the cells to the wells, the e-plate was removed from the station and taken to the sterile cabinet. The samples were added to the wells at three different concentrations (100, 50, and 10 µg mL⁻¹). Each dose of the samples were evaluated in triplicate. The antiproliferative effect

of the molecules against HeLa cells was monitored in real-time every 10 minutes and followed for 48 hours. The mean CI values from the wells were calculated automatically with the xCelligence RTCA SP software and the standard deviations are shown as vertical bars.



Scheme 4. Reactions and conditions. *i*: HCl, formaldehyde, norfloxacin (for **14a**, **14b**) or ciprofloxacin (for **14c**, **14d**, **14e**), MW irradiation, 80 °C, 100 W for 5 min.

Table 1. Antimicrobial activity of the compounds (μg/mL).

Comp. No.	Minimal Inhibition Concentration Values (μg/mL)								
	Ec	Yp	Pa	Sa	Ef	Bc	Ms	Ca	Sc
3	–	–	500	–	–	–	–	500	–
5	–	–	–	–	–	–	–	125	–
6c	–	–	–	–	250	–	–	–	–
7a	125	–	–	–	–	–	–	–	–
7b	–	–	–	–	–	–	62.5	–	–
7c	–	–	–	–	–	–	–	125	250
8b	62.5	–	–	125	–	125	1.95	–	–
9a	0.24	–	500	–	–	–	–	–	–
9b	250	–	–	–	–	–	–	–	–
10a	–	–	–	–	250	–	–	–	–
10b	–	–	–	–	–	–	–	625	–
10d	–	–	–	–	–	–	125	–	–
10e	–	–	–	–	–	–	–	625	–
11a	<1	1.9	3.9	–	3.9	7.8	3.9	–	–
11b	1.9	62.5	15.6	–	15.6	31.25	31.25	–	–
11c	–	62.5	–	–	–	–	62.5	312.5	312.5
11d	62.5	–	625	–	–	–	–	312.5	312.5
11e	15.6	–	>1000	–	–	–	–	312.5	156
12	–	–	500	–	–	500	–	250	–
13a	<1	7.8	–	156	19	39	3.9	312.5	78
13b	31.25	<1	–	9.7	9.7	9.7	<1	312.5	312.5
14a	<1	<1	<1	–	<1	1.9	<1	–	–
14b	<1	<1	<1	–	<1	<1	<1	–	–
14c	<1	<1	<1	–	<1	1.9	<1	–	–
14d	<1	<1	1.9	–	–	1.9	1.9	–	–
14e	<1	<1	3.9	–	<1	1.9	<1	–	–
Amp.	10	18	>128	35	10	15	–	–	–
Strep.	–	–	–	–	–	–	4	–	–
Flu.	–	–	–	–	–	–	–	<8	<8

Ec: *E. coli* ATCC 35218, Yp: *Y. pseudotuberculosis* ATCC 911, Pa: *P. aeruginosa* ATCC 10145, Sa: *S. aureus* ATCC 25923, Ef: *E. faecalis* ATCC 29212, Bc: *B. cereus* 709 Roma, Ms: *M. smegmatis* ATCC607, Ca: *C. albicans* ATCC 60193, *S. cerevisiae* RSKK 251, Amp.: Ampicillin, Strep.: Streptomycin, Flu.: Fluconazole, (–): no activity of test concentrations

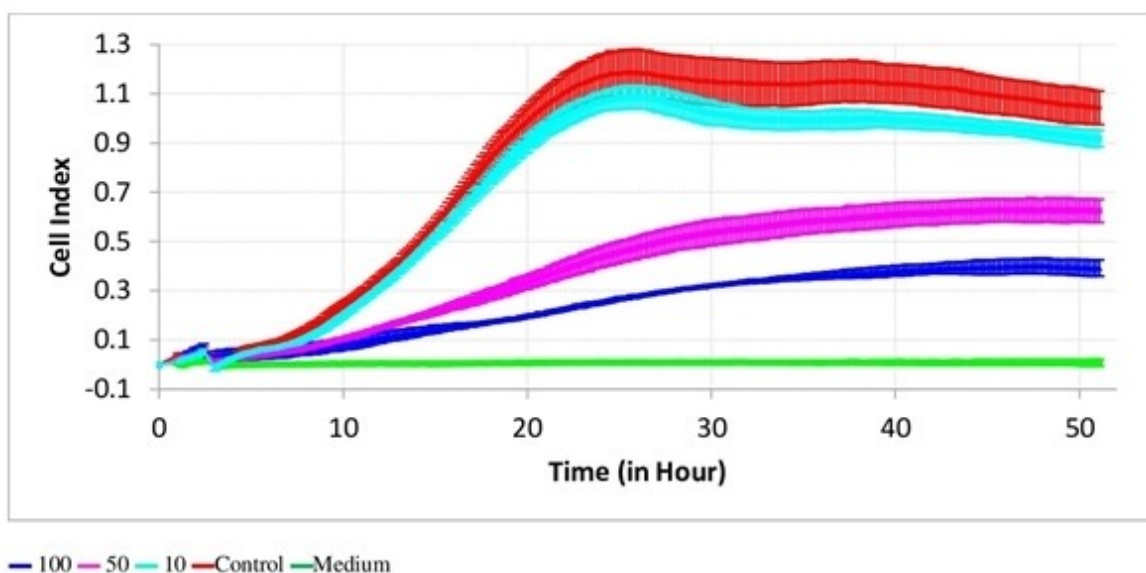


Figure 1. Time-CI (Cell Index) plot showing the antiproliferative activity test results of compound **8a** against HeLa cell line (the concentration unit is $\mu\text{g/mL}$).

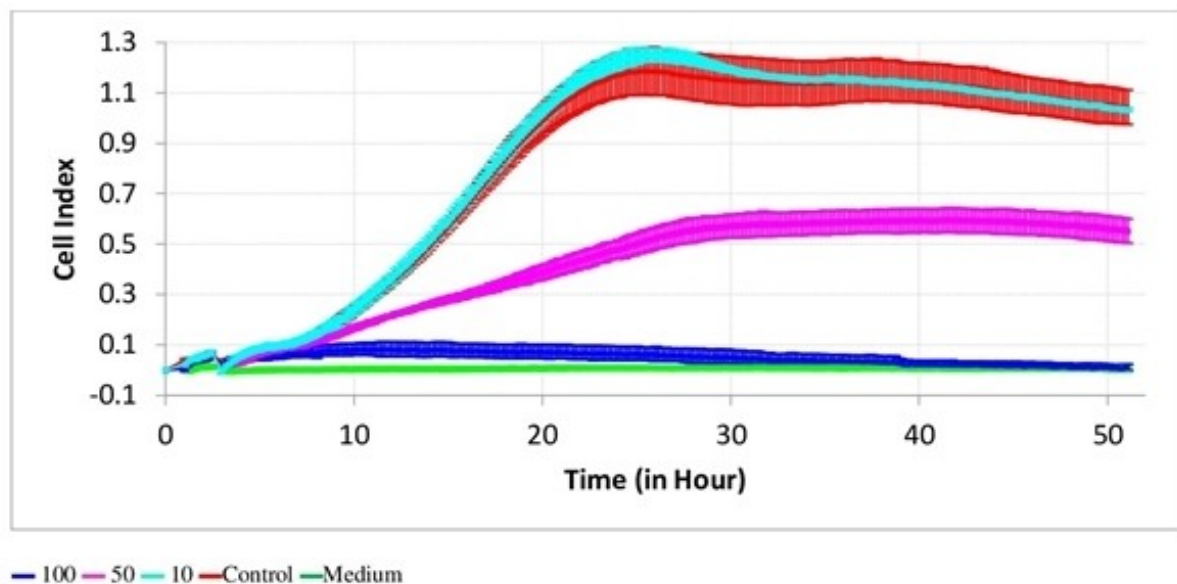


Figure 2. Time-CI (Cell Index) plot showing the antiproliferative activity test results of compound **9b** against HeLa cell line (the concentration unit is $\mu\text{g/mL}$).

Dose effect investigations are performed by considering terms such as a dose-dependent effect, dose-dependent reverse effect, hormesis, and inverse hormesis.^[42–44] Antiproliferative effects of these molecules against HeLa cells are shown in Figure 1 and Figure 2.

CI values obtained from wells with no cells increased rapidly (red line). Different doses of DMSO were added to the wells with HeLa cells and no DMSO-induced antiproliferative activity was observed (Figure 3). The effect of all doses of 5FU used as a positive control was strong, and CI values were very close to each other. None of the lower doses of the molecules

didn't show an antiproliferative effect ($10 \mu\text{g mL}^{-1}$, turquoise line). All of the low doses of the molecules produced the same CI as the control group. Only the low dose of compound **8a** partially dissociated from the control group towards the end of the experiment (after 35 hours). However, this situation cannot be considered as a net antiproliferative effect. On the 5FU graph (Figure 4) used as a positive control, it is seen that the low dose (turquoise line) has a clearly different CI value from the red-colored CI values (negative control).

Middle doses of **8a** and **9b**, molecules ($50 \mu\text{g mL}^{-1}$, pink line) showed strong antiproliferative activity. They maintained

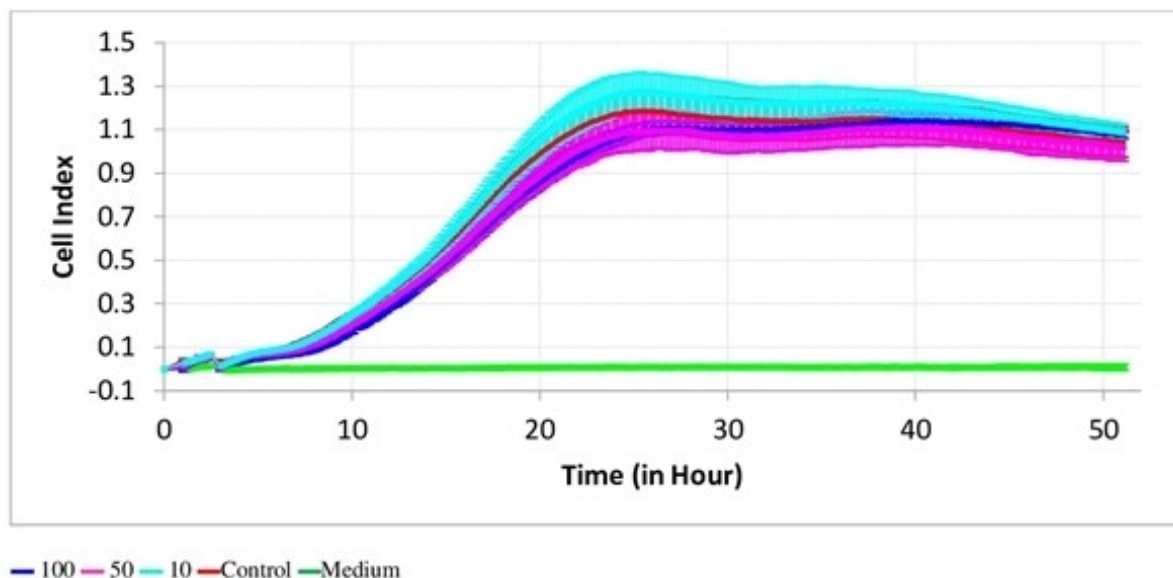


Figure 3. Adding different doses of DMSO to HeLa cell wells (the concentration unit is $\mu\text{g/mL}$).

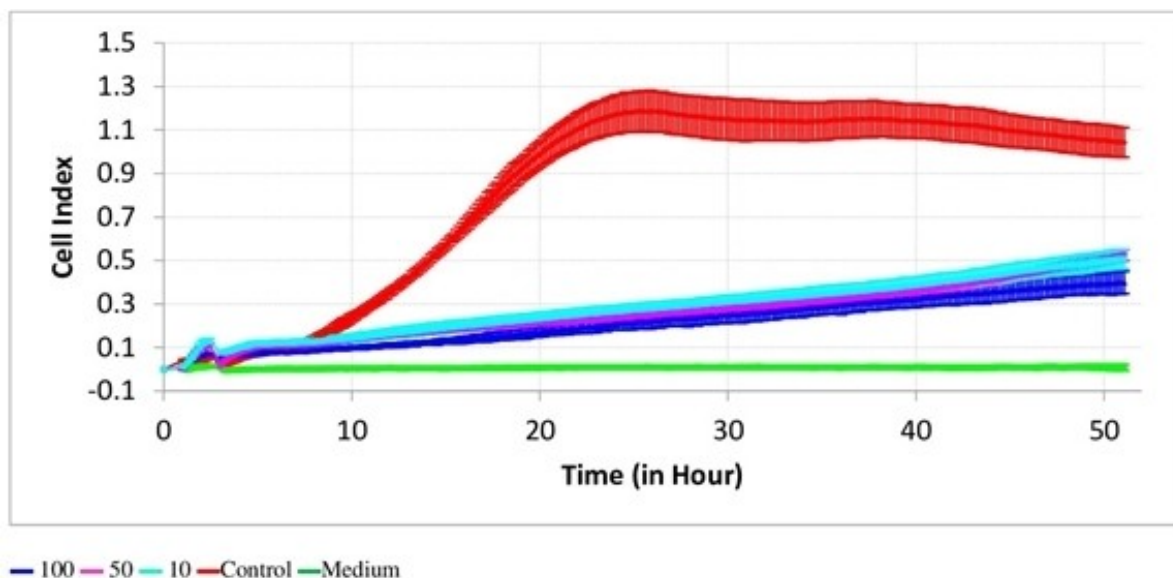


Figure 4. Effect of all 5FU doses used as positive control (the concentration unit is $\mu\text{g/mL}$).

their antiproliferative effects throughout the experiment. High doses of molecules have also been found to have high antiproliferative activities. High doses of the **9b** molecule ($100 \mu\text{g mL}^{-1}$, dark blue line) showed very strong antiproliferative activity. High doses of the **8a** molecule also showed a strong antiproliferative effect ($100 \mu\text{g mL}^{-1}$, dark blue line) on HeLa cells. The effects of high doses of the **9b** molecules were so potent that the resulting CI values were the same as the 0 CI values (green line) obtained from wells with no added cells. This strong effect continued throughout the experiment.

The dose-effect differences of these molecules were most clearly seen in **8a** and **9b**. These effects of molecules with

strong antiproliferative effects are due to their structural forms. The antiproliferative activity potentials of the molecules that didn't show any effect or have a weak effect against HeLa cells should be examined against other cancer cell lines and their effects should be investigated.

Discussion

Schiff base (**3**) was obtained from the reaction of 3-alkyl-4-amino-4,5-dihydro-1H-1,2,4-triazole-5-one (**2**) compound with cinnamaldehyde, which was obtained from the reaction of ester ethoxycarbonylhydrazone (**1**) and hydrazine hydrate.^[45]

The object was to combine the 1,2,4-triazole nucleus with the cinnamaldehyde since it is known that more efficacious antimicrobial substances can be discovered by adding two biologically effective components together into a single molecular structure.^[46,47] Thereafter product (3) was transformed to the corresponding hydrazide derivative (5) by the creation of ester (4). With the introduction of hydrazide function in the molecule, two signals appeared at 4.23 and 0.88 ppm as D₂O exchangeable singlets at the ¹H NMR data of the molecule (5). With the introduction of the hydrazide group in the compound, two signals emerged at 5.25 and 9.17 ppm as D₂O exchangeable singlets at the ¹H NMR data of molecule.

Molecules (6a–c) were performed by the treatment of molecule (5) with phenyl- (for 6a), or benzyl isothiocyanate (for 6b), or phenyl isocyanate (for 6c) in dichloromethanolic solution in good yields, and molecule constructions were confirmed via FT-IR, ¹H NMR, ¹³C NMR, mass data.

The intramolecular cyclization of products (6a–c) at basic media afforded in the transformation of carbox(thio)amide function alter to 5-oxo(mercapto)-1,2,4-triazole derivatives and so molecules 7a–c were synthesized. These compounds were characterized by the presence of a signal at 13.70 and 14.02 ppm in the ¹H NMR data as a D₂O exchangeable singlet confirming the existence of a –SH function (7a,b) and 10.77 ppm–NH function (for 7c). The stretching band derived from these groups appeared at 2929 and 2932 cm^{−1}, and C=O (for 7c) was observed at 1626 cm^{−1} at the FT-IR data of these molecules (Scheme 1).

Alkylation of products 3, via 2-bromo-1-(4-chlorophenyl)-ethanone or 2-chloro-1-(2,4-dichlorophenyl)-ethanone in ethanol performed compound 8a,b. These reactions, which took place in 1440 minutes in the conventional method, took place in 6 minutes in the microwave irradiated method. Studies related to microwave synthesis which supports organic synthesis in a shorter time and higher efficiency are available in the literature.^[48–50] NH proton attached to the triazole group disappeared for compound 3 at the ¹H NMR spectra. New aromatic peaks were resonated in the region 7.27–7.67 ppm. In ¹³C NMR data of molecules, the carbon atom (C=O) was observed between 192.56 and 194.43 ppm for the newly added carbonyl group.

Compounds 9a,b was obtained with the reduction of the carbonyl structure of products 8a,b with sodium borohydride utilizing both classical heating and MW irradiation. When we compare the traditional and microwave method MW irradiation reduced the reaction time from 960 min. to 8 min. and increased the yields. Looking at compound numbers 9a,b, the carbonyl group peak has evanesced at the ¹³C NMR data and OH peak added between 5.41 and 6.44 ppm in the ¹H NMR. The spreading band obtained in this group (OH) appeared between 3374 and 3251 cm^{−1}, in the FT-IR data of molecules.

Reactions of molecules 10a–e were afforded reaction of molecule 9a,b and benzyl chlorides, such as 2,4-dichloro-, 2,6-dichloro- and 4-chlorobenzyl chlorides in an ambience with of NaH via MW synthesis method at 80 °C and 100 W for 5 min. In both FT-IR and ¹H NMR data of the molecules, the peaks due to

the –OH group have disappeared. Other peaks approving molecule structures were displayed at the concerned chemical ranges in the ¹H NMR and ¹³C NMR spectra. Moreover, [M + 1] ion signals were appeared at the concerned m/z ranges auxiliary the offered structures of molecules 10a–e (Scheme 2).

Oxadiazole compound (12) was obtained as a result of ring closure reaction of hydrazide compound (5) with CS₂ in basic media. The NH and NH₂ peaks resulting from the hydrazide compound disappeared in both the FT-IR and ¹H NMR data of the oxadiazole derivative compound. Instead of those peaks, SH peaks were added at 14.66 ppm in ¹H NMR and 2749 cm^{−1} in the FT-IR. In addition, synthesized molecules confirmed ¹³C NMR and Mass spectral data and elemental analysis results consistent with the assigned structures (Scheme 3).

Mannich reaction is a three-component condensation reaction involving active hydrogen-containing compound, formaldehyde and a secondary amine. The amino alkylation of aromatic substrates by the Mannich reaction is of considerable importance for the synthesis and modification of biologically active compounds.^[51] Mannich bases found numerous practical applications in the field of medicinal chemistry, it could be responsible for enhancing physicochemical properties.^[52] Mannich bases linked 1,2,4-triazole derivatives as containing a significant biological activity that has been reported in the literature.^[53,54] Furthermore, several Mannich bases of triazole derivatives including piperazine, thiomorpholine, or morpholine moiety were synthesized as antimicrobial agents in our laboratory.^[55,56] Fluoroquinolones are known as the most broadly utilized synthetic antimicrobial substances; privileged with wide spectrum antibacterial property, relatively low occurrence of toxic and adverse effects along with a perfect safety profile.^[45]

Considering these facts in this research, the aminoalkylation of structures 3, 7a–c, and 12 with different amines, such as norfloxacin (for 11a, 13a, 14a, 14b), ciprofloxacin (for 11b, 13b, 14c, 14d, 14e), morpholine (for 11c), thiomorpholine (11d), and 4-phenylpiperazine (for 11e) in an ambience with formaldehyde was performed using the MW-assisted Mannich synthesis reactions (Scheme 2, Scheme 3 and Scheme 4). No signal symbolizing the presence of the NH band exists on the ¹H NMR and FT-IR spectra of products (11a–e, 13a,b, 14a–e), and in the ¹H NMR and ¹³C NMR spectra of molecules extra signals originated from amine moieties were observed at the concerned chemical ranges. These molecules displayed mass spectral datum records reasonable with their constructions.

The use of microwave (MW) irradiation method consequences in very influential and clean results with notable developments compared to classical processes. The process via MW irradiation ensured the more helpful road with developed synthesis yields and shorter synthesis times.^[57] Green Chemistry would like the high yield of synthetic processes, the use of less toxic solvents, and the decrease in phases of synthetic schemes.^[58]

Conclusions

This study states the synthesis of novel compounds having various bioactive units via microwave irradiation and conventional techniques. The microwave method provided a more efficient way for the synthesis of desired compounds. Also, the antibacterial and antiproliferative activity of the synthesized molecules were determined. Among the synthesized compounds, the best antimicrobial activities were found to show compounds **14a–e** which are Mannich bases. Especially these compounds showed very good antitubercular activity against *M. smegmatis* compared with Streptomycin standard drug. And also they exhibited better activity against *E. coli* than ampicillin used as a standard drug. Middle and high doses of compounds **8a** and **9b** were found to have strong anticancer activity on the HeLa cervical cancer cells.

Supporting Information Summary

You will find the synthetic route, yields, melting points and spectral data, and FT-IR, ¹H NMR, ¹³C NMR and mass spectra in the Supporting Information file of newly synthesized compounds. And also you will see the antimicrobial and anticancer activity determination methods.

Acknowledgement

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Conflict of Interest

The authors declare no conflict of interest.

Keywords: anticancer · antimicrobial activity · mannich base · 1,2,4-triazole · quinolone

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