Biological Screening of Some Newly Synthesized N-phenyl-4-aryl-Polyhydroquinolines

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Abstract- *In this paper we are discussing about the biological activity of newly synthesized substituted quinoline compounds was evaluated by agar well diffusion method. Quinolines are having most potent biological activity like, here N-phenyl-4-aryl-polyhydroquinolines. All the twelve synthesized target compounds (**4a-4l**) were assayed for their in vitro antimicrobial activity against S. aureus and B. subtilis representing Gram-positive bacteria, E. coli and P. fluorescens representing Gram-negative bacteria, and S. cerevisiae and C. albicans representing fungal yeasts by agar well diffusion method using ciprofloxacin against bacteria and fluconazole against fungi as the reference drugs. The results were recorded for each tested compound as the average diameter of inhibition zones of microbial growth surrounding the well in mm.The minimum inhibitory concentration (MIC) shown in Table 4.1 &4.2.*

Keywords- anti-bacterial activity, antifungal activity, dihydropyridines, polyhydroquinoline

I. INTRODUCTION

Quinoline and some of its derivatives are the most widespread N-heterocyclic compounds associated into the structures of most pharmaceutical and antimicrobial drugs [1]. Recently, much interest has been dedicated to the synthesis of polyhydroquinoline compounds because of their diverse therapeutic and pharmacological properties. Various quinoline derivatives characterize moderate toxicity and central nervous system stimulants [2,3]. naturally occurring quinolone derivatives as 2-methyl-1,2,3,4-tetra-hydroquinoline exist in human brain. Dynemycin is acting as antitumor and antibiotic effectives[4]. antifungal [5], and antiviral [6,7] activities. Much interest has been dedicated to the synthesis of polyhydroquinoline compounds due to their diverse therapeutic and pharmacological properties, such as antitumor, ant atherosclerotic, vasodilator, geroprotective, bronchodilator and hepatoprotective activity [8].

In vitro antimicrobial activity of all synthesized compounds 8aet was determined by broth micro dilution method according to National Committee for Clinical Laboratory Standards(NCCLS) [9]. Quinolines are an important class of nitrogen containing heterocycles due to its presence in numerous biologically active compounds. They have proved to be promising pharmaceutical candidates because of their broad spectrum of biological activities such as antioxidant[10-12],antimalarial[13,14],anticancer[15,16] and anti microbial[17-18].

II. MATERIALS AND METHOD

The *in vitro* antimicrobial activity of the compounds (**4a-4l**) was evaluated by agar well diffusion method. Overnight broth culture of the respective bacterial as well as fungal strains was adjusted to approximately 10^8 colony forming units (CFU/mL) with sterile distilled water and 100 µL of diluted inoculum was spreaded over the petriplates containing 25 mL of Nutrient Agar media (in case of bacteria) or Sabouraud Dextrose Agar (SDA, pH 5.6) media (in case of fungi). Five equidistance wells (8 mm in diameter) were made in each of the plates using a sterile cork borer. The test compounds were dissolved in dimethylsulfoxide (DMSO) and then antimicrobial effect of the target compounds was tested. The wells were filled with 100 µL of the test compound having concentration 4.0 mg/mL. The plates were incubated at 37 °C for 48 h (in case of bacteria) or at 30 °C for 72 h (in case of fungi). The antibacterial activity was evaluated by measuring the zone of growth inhibition of bacteria surrounding the wells after 24 h and 48 h. Similarly, antifungal activity was evaluated after 48 h and 72 h. Ciprofloxacin (4.0 mg/mL) served as antibacterial control and fluconazole (4.0 mg/mL) served as antifungal control while DMSO was taken as negative control in both the cases.
The minimum inhibitory concentration (MIC) of each compound giving an inhibitory zone at the concentration of 4.0 mg/ mL in both the cases (bacteria as well as fungi) was also tested with the agar well diffusion method.[19] Different concentrations (4000 to 0.004 µg/mL) of a single compound were applied to number of wells in the agar plates. The determinations were performed in triplicates and the results were averaged.

Table 4.1. *In vitro* antimicrobial activity of compounds (4a-4l) through agar well diffusion method.

Compound[a]	Diameter of growth of inhibition zone (mm)[b]					
	S. aureus	*B. subtilis*	*E. coli*	*P. fluorescens*	*S. cerevisiae*	*C. albicans*
4a	18±0.10	14±0.14	24±0.18	16±0.22	–	16±0.15
4b	24±0.13	12±0.20	12±0.17	24±0.24	10±0.24	10±0.24
4c	16±0.22	12±0.24	12±0.13	16±0.13	10±0.20	12±0.12
4d	16±0.28	12±0.14	12±0.15	14±0.15	–	12±0.10
4e	18±0.24	26±0.23	12±0.20	12±0.21	10±0.18	–
4f	14±0.12	12±0.20	12±0.12	18±0.12	-	12±0.12
4g	14±0.22	16±0.22	22±0.16	18±0.20	-	12±0.14
4h	16±0.14	12±0.15	12±0.17	18±0.19	-	18±0.25
4i	14±0.20	10±0.12	14±0.14	14±0.20	-	–
4j	14±0.15	12±0.14	12±0.13	14±0.20	14±0.24	18±0.24
4k	12±0.19	14±0.10	12±0.12	16±0.15	16±0.16	14±0.15
4l	18±0.22	12±0.18	12±0.37	14±0.23	-	10±0.22
Ciprofloxacin	26±0.25	26±0.02	25±0.44	23±0.42	Nt	Nt
Fluconazole	Nt	Nt	Nt	Nt	24±0.50	16±0.45

[a]Concentration 4.0 mg/mL.
[b]Values, including diameter of the well (8 mm), are means of three replicates.
–Noactivity
Nt: Not tested

Table 4.2. Minimum inhibitory concentration (MIC) (in µg/ml) of compounds (**4a**-**4l**)

Compound	*S. aueus*	*B.subtilis*	*E. coli*	*P. fluorescens*	*S. cervisiae*	*C. albicans*
4a	4.0	40	0.04	4.0	-	4.0
4b	0.04	40	40	0.04	400	400
4c	4.0	40	40	4.0	400	40
4d	4.0	40	40	40	-	40
4e	4.0	0.04	40	40	400	-
4f	40	40	40	4.0	-	40
4g	40	4.0	0.04	4.0	-	40
4h	4.0	40	40	4.0	-	4.0
4i	40	400	40	40	-	-
4j	40	40	40	40	40	4.0
4k	40	40	40	4.0	4.0	40
4l	4.0	40	40	40	-	400
Ciprofloxacin	0.4	0.4	0.4	4.0	Nt	Nt
Fluconazole	Nt	Nt	Nt	Nt	0.4	40

Nt: Not tested

III. CONCLUSIONS

The objective of the present work was to synthesize *N*-phenyl-4-arylpolyhydroquinolines containing 1,4-dihydropyridine scaffold and their evaluation as antimicrobial agents On the basis of zone of inhibition against the test bacterium, compound **4b** was found to be the most effective against *S. aureus* and P. *fluorescens* showing zone of inhibition of 24±0.13 mm and 24±0.24 mm respectively, **4a** and **4g** against *E. coli* showing zone of inhibition of 24±0.18 mm and 22±0.16 respectively, and **4e** against *B. subtilis* with 26±0.24 mm zone of inhibition when compared with standard drug ciprofloxacin which showed the zone of inhibition of 26±0.25 mm and 26±0.02 mm against *S. aureus* and *B. subtilis* respectively, 25±0.44 mm against *E. coli* and 23±0.42 mm against *P. fluorescens*. MICs of **4a**, **4b**, **4e** and **4g** were found to be ten times less (0.04 µg/ml) as compared to ciprofloxacin (0.4 µg/ml) corresponding to the same bacteria.

In case of fungal yeasts, compounds **4a**, **4h** and **4j** were found to be the most active against *C. albicans* showing zone of inhibition 16±0.15 mm, 18±0.25 mm and 18±0.26 mm respectively whereas **4k** showing maximum zone of inhibition of 16±0.18 mm against *S. cerevisiae* when compared with standard drug fluconazole showing zone of inhibition of 16±0.45 mm and 24±0.50 mm against *C. albicans* and *S. cerevisiae* respectively. MICs of **4a**, **4h** and **4j** were found to be ten times less (4.0 µg/ml) as compared to fluconazole (40 µg/ml) corresponding to the same yeasts.

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