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Antibacterial Activity of 3-Amino (Substituted)-2-phenyl quinazolin-4-ones

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Abstact: Different quinazoline derivatives have been reported for their antibacterial, antifungal, anti-HIV, anthelmintic, CNS depressant and antitubercular activities. In this work, we evaluated antimicrobial potential of 3-amino (substituted) -2-phenyl quinazolin-4-ones. The antibacterial efficacy was performed against the bacterial strains $S1^+$,$S2^+$, $S8^+$,$E6^-$,$V6^-$ and $SG7^-$ using agar serial dilution method. Ciprofloxacin was used as reference antibacterial compound.

Key words: Anti-Bacterial, Quinazolinone agar serial dilution, bacterial strain

Introduction

Quinazoline compounds are widely used in agrochemicals as plant virucides, antifungal agents and herbicides. According to recent data, quinazoline nucleus has attracted the attention of medicinal chemists due to its well-known anticancer activity, and many substituted quinazoline derivatives have recently earned great interest in chemotherapy as antitumor drugs [1]. Different quinazoline derivatives have been reported for their antibacterial, antifungal, anti-HIV, anthelmintic, CNS depressant and antitubercular activities. Antitumor activities are also reported for 2,3-dihydro-2-aryl-4-quinazolinones.[2] Quinazolinones and their derivatives constitute an important class of heterocyclic compounds. They occupy an important position in medicinal and pesticide chemistry, presenting a wide range of bioactivities. In light of the growing number of applications in recent years there has been an enormous increase in the interest among biologists and chemists in their synthesis and bioactivity of quinazoline derivatives.when a ketone group is present in 4th position of the Quinazoline then it is known as quinazolones [3].

Quinazolinone is a versatile lead molecule for designing potential bioactive agents**.** A deceptive simple quinazolone shows cardiotonic activity. One such derivative was synthesised from tonnage chemical vanilline [4]. Quinazolinone derivatives has structural similarity with thiazide diuretic. It is not surprising that quinazolones have a diuretic effect similar to that of thiazides and the side effect are also same. Quinazolinone diuretic have a long duration of action [5].

Quinazolines have been frequently used in medicine because of their wide spectrum of biological activities [6]. Different quinazoline derivatives have been reported for their antibacterial, antifungal, anti-HIV [7,8], anthelmintic [9], CNS depressant [10] and antitubercular [11], anticancer activities. Antitumor activities are also reported for 2,3-dihydro-2-aryl-4-quinazolinones [12,13]. Some reports have suggested that 2-styrylquinazolin-4-ones (SQZ) [14,15] could be effective inhibitors of tubulin polymerization. Keeping in view, the medicinal importance of 3-amino-2-phenyl quinazolin-4-one the authors have attempted the anti-bacterial efficacy of titled compounds in present work.

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Materials and methods

Preparation of nutrient agar media

Sodium chloride (2.5 g), peptone (5.0 g), beef extract (5.0 g), agar (10.0 g) were dissolved in required amount of distilled water by keeping the media in the steam bath, the agar was melted out and the indicator was added and the volume was made up with distilled water, pH was adjusted at 7.2-7.4. Then the flask was plugged and wrapped in paper then autoclaved at 15 PSI pressure at 121°C for 15 minutes.

Preparation of luria broth media

Sodium chloride (2.5 g), peptone (5.0 g), yeast extract (2.5 g) were dissolved in required amount of distilled water by keeping the media in the steam bath, and the volume was made with distilled water, PH was adjusted at 7.2-7.4. Then the flask was plugged and wrapped in paper and then autoclaved at 15 PSI pressure at 121°C for 15 minutes.

Determination of minimum inhibitory concentration (MIC)

The MIC was determined by the standard agar dilution method**.** The titled compounds were synthesized by reported methods (Table 1). The synthesized product was dissolved in DMF, as they are not freely soluble in water and then diluted by sterile distilled water to make up the volume. The drug solution was then added to the molten nutrient agar in different test tubes to give final concentration of 100, 200, 300, 400, 500, 600, 700, 800, 900 and 1000 µg/ml. The molten nutrient agar media containing various concentration of the synthesized compound were poured and solidified into sterile 100 mm Petri dishes to give sterile nutrient agar plate with varying dilution of synthesized drug. Then these plates were kept in a refrigerator (4°C) for 24 hrs for uniform diffusion of the synthesized drug into the nutrient agar media. The plates were then dried at 37°C for 2 hours before spot inoculation.

Petri plates were sterilized by dry heat sterilizer (160°C for 1 hr). For the preparation of inoculums, firstly the luria broth media was transferred into 6 test tubes (5 ml each). In three test tubes gram positive (*S. aureus* NCTC 6571, *S. aureus* NCTC 8530, *S. aureus* ML275) and in another three test tubes gram negative bacterial strains (*E. coli* HD10, *V. cholerae* 71, *S. dysentriae*) were inoculated individually. Then these test tubes were incubated over night at 37°C. Solid agar media was transferred into the test tubes (9 ml each). One loop full (diameter: 3 mm) of the overnight grown luria broth culture of each test organism was placed in petridish marked by checker board technique.

The final number of c.f.u. inoculated on to the agar plates was 10^{10} for all strains. The spot inoculated plates were incubated at 37°C for 24 hrs. and the MIC values were obtained. The lowest concentration of the plates which did not show any visible growth after incubation was considered as MIC. The agar plates containing only sterile distilled water were served as control. [26, 27].

Result and discussion

All the synthesized compounds were screened for antibacterial activity and results are tabulated in Table 2. Minimum inhibitory concentration (MIC) of the synthesized compounds was determined against *Staphylococcus aureus* NCTC 6571, *Staphylococcus aureus* NCTC 8530, *Staphylococcus aureus* ML275, *Escherichia coli* HD10 and *Vibrio cholerae* 71, *Shigella dysentriae*. It has been found that all the compounds have anti-bacterial activity when compared with control. The result of the experiment indicates that all the synthesized compounds exhibit almost same level of activity. Compound, SQ5 showed promising antibacterial effect, being equipotent to ciprofloxacin, followed by compound SQ1 particular against the bacterial strains *Escherichia coli*, *Vibrio cholerae*, and *Shigella dysenteriae*, responsible for diarrhea.

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Table 1. Molecular formula and structures of titled compounds

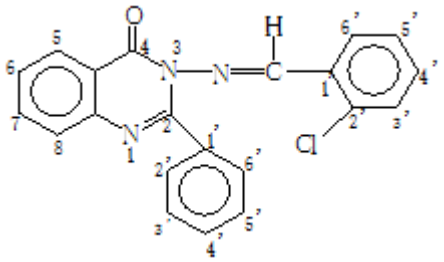
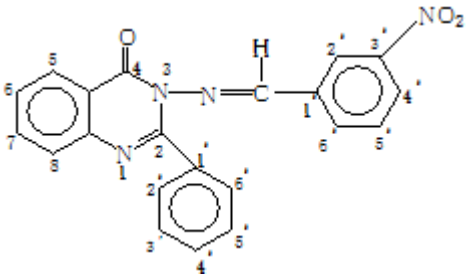
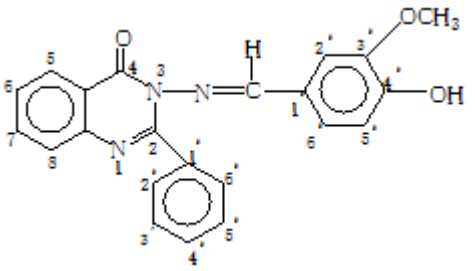
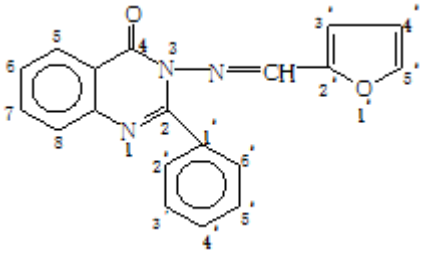
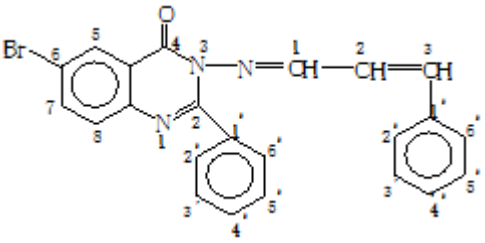
Compound code	Molecular Formula	IUPAC name	Structure
SQ1	$C_{21}H_{14}N_3OCl$	3-[2-chloro benzalamino]-2-phenyl quinazolin-4-one	
SQ2	$C_{21}H_{14}N_4O_3$	3[3 nitro benzalamino]-2-phenyl quinazolin-4-one	
SQ3	$C_{22}H_{17}N_3O_3$	3-[3-methoxy 4-hydroxy benzalamino]-2-phenyl quinazolin-4-one	
SQ4	$C_{19}H_{13}N_3O_2$	3-[furfural amino]-2-phenyl quinazolin-4-one	
SQ5	$C_{23}H_{16}N_3O_{Br}$	3-[phenyl propen1-yl-amino]-2-phenyl-6-bromo-quinazolin-4-one	

Table 2. MIC (in μg) of titled compounds

Compounds (μg/ml)	Strains S1$^+$	S2$^+$	S8$^+$	E6$^-$	V6$^-$	SG$^-$	CP
SQ1	60	80	50	60	40	80	50
SQ2	50	80	70	80	80	60	50
SQ3	80	100	80	80	100	100	50
SQ4	70	100	60	40	80	80	50
SQ5	60	60	60	50	50	60	50

S1, S2$^+$, S8$^+$, E6$^-$, V6$^-$, SG7$^-$ and CP indicates *Staphylococcus aureus* NCTC 6571, *Staphylococcus aureus* NCTC 8530, *Staphylococcus aureus* ML275, *Escherichia coli* HD10, *Vibrio cholerae* 71, *Shigella dysenteriae* and *ciprofloxacin* respectively.

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