Original Research Article

Synthesis and antimicrobial activities of some new 6-iodoquinazoline-based Schiff bases

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ABSTRACT

A library of thirteen new quinazoline-based Schiff bases was synthesized by simple, straightforward documented chemical procedures. Their skeletal structure was confirmed by IR, NMR, MS, and elemental analyses. The final compounds were also screened for their activities against eight selected microbial strains (two gram-positive and two gram-negative bacteria in addition to four fungal strains). Nine out of the thirteen tested compounds showed remarkable antimicrobial activities. However, six compounds, namely **7**, **10**, **13**, **15**, **16** and **18,** showed antibacterial and antifungal activities, while compounds **9**, **14** and **17** were devoid of antifungal and showed only antibacterial activities. The best activity was obtained by compounds **10** and **15,** which were against *Bacillus subtilis*. The best MIC (1.90 µg/ml) and (3.9 µg/ml) were obtained by compound **10** against *Bacillus subtilis* and *Staphylococcus aureus*, respectively. *Aspergillus fumigatus* and *Syncephalastrum racemosum* were the most sensitive filamentous fungi, where compound **10** inhibited their growth at MIC (15.63 and 62.50 µg/ml), respectively.

Keywords: Quinazoline; Schiff's Bases; Antibacterial; Antifungal.

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Received: 07 Nov 2023; accepted: 05 March 2024
Available online: 25 March 2024
http://doi.org/10.24191/IJPNaCS.v7i1.02

1.0 Introduction

Hospital infection is a major health problem that concerns the medical community around the world, as it makes the management of such diseases more precarious. It was estimated that for every 100 patients in acute care hospitals, seven patients in high-income countries and fifteen in low and middle-income countries may catch at least one health care-associated infection while receiving health care for another condition. On average, one out of ten affected patients will die from such infection.

Therefore, there is a critical need for new effective entities (1, 2). Infections initiated by antibiotic resistant strains continue to challenge the global medical community, as indicated by the higher rate of prescription and abuse of antibiotics compared to other medications (3-5). It became well known that treatment failures can occur not only through traditional microbial antibiotic resistance mechanisms but also through recent less defined ones, mainly those developed by microbes in response to their quorum sensing systems and biofilm machinery (6, 7). More recent work in this respect has focused on the evaluation of the clinical influence of antibiotic resistance on the ideal antibiotic choices for treatment, in addition to alternative strategies to combat such serious problems (8-10).

Over the last few decades, significant developments have been made in many areas of the design and development of new molecules to meet the pressing need for new medication (11-14). However, these efforts were hampered by a number of problems which still remain and the therapeutic potential has been compromised by the developed toxicity and low safety profile (15-17).

Quinazoline-containing compounds form an important class of synthetic products and represent an attractive scaffold for the design of small molecules of diverse biological effects. They have attracted interest over the past years, notably as tyrosine kinase as well as carbonic anhydrase inhibitors as potential chemotherapeutic agents (18-20). On the other hand, the antimicrobial activity of nitro-containing molecules is one of the widest effects observed, not only in human or veterinary medicines, but also in developing new agents with such aims (21-23). The same could be found for quinazoline derivatives, which display a wide diversity of enzyme inhibitory activity, and so many researchers expected them to be useful for patients with acquired immune deficiency syndrome (AIDS), cancer chemotherapy, and organ transplantation. Recently, it was discovered that quinazoline-sulfonamide scaffold furnishes a new class of B-cell lymphoma 2(Bcl-2) family inhibitors with low nano-molar activity. Some of these derivatives exhibited sub-micromolar in human small-cell lung carcinoma. It was the first successful quinazoline sulfonamide core as an effective antitumor agent (24-28).

In addition, Schiff bases have a sound pharmacological impact in different areas of medical applications. We decided to synthesize certain new quinazoline molecules equipped with this functionality by simple condensation of 3-amino-2-methyl-3H-quinaolin-4-one with some selected aromatic aldehydes for evaluation as potential antimicrobial and antifungal agents in addition to studying their preliminary safety through liver and kidney function tests (29-31).

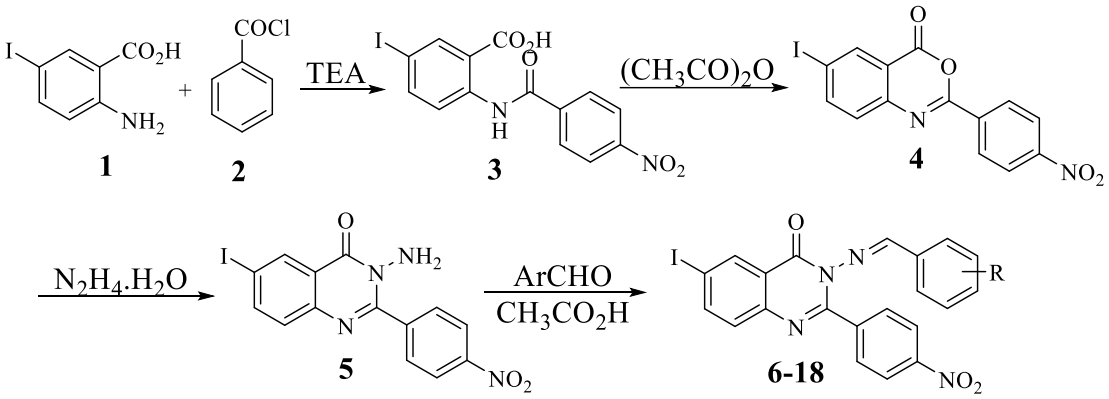
2.0 Materials and Methods

2.1 Chemistry

2.1.1.1 Synthesis of N-(4-nitrobenzoyl)- 5-iodoanthranilic acid 3 (32-35).

4-Nitrobenzoyl chloride 2 (1.85 g, 0.05 mol) was added dropwise to a stirred solution

2.1.1 Scheme 1



6: R= H. **7:** R= 4-CH_3. **8:** R= 4-$N(2CH_3)_2$. **9:** R= 2,4-(2Cl).
10: R= 2-OH. **11:** R= 4-OH. **12:** R=2,4(2OH). **13:** R= 2-OCH_3.
14: R= 4-OCH_3. **15:** R= 4-OH, 3-OCH_3. **16:** R=2,4,5(3OCH_3).
17: R=2,4,6(3OCH_3). **18:** R=3,4,5(3OCH_3).

of 5-iodoanthranilic 1 (6.85 g, 0.05 mol) and triethylamine (2 ml) in dichloromethane (70 ml) and the reaction mixture was stirred at room temperature for 2 hours. The separated solid was filtered, washed several times with water, dried, and crystallized from ethanol.

2.1.1.2 2-(4-Nitrophenyl)-4H-6-iodo-3,1-benzoxazin-4-one 4 (32-35).

A mixture of *N*-(4-nitrobenzoyl)- 5-iodoanthranilic acid 3 (8.58 g, 0.03 mol) and acetic anhydride (7.5 g, 0.07 mol) was heated under reflux for 3 hours. The solvent was removed under reduced pressure. The residue was triturated with water. The separated solid was collected by filtration, washed with water, dried and crystallized from ethanol.

Yield percentages, melting points, molecular formulae and micro-analytical data are shown.

2.1.1.3 2-(4-Nitrophenyl)-3-amino-3,4-dihydro-6-iodoquinazolin-4-one 5 (32-35).

This compound was prepared by the following three methods:

Method A

A mixture of 2-(4-nitrophenyl)-6-iodo-4*H*-3,1-benzoxazin-4-one 1 (0.804 g, 0.003 mol) and 98 % hydrazine hydrate (0.6 g, 0.018 mol), in ethanol (10 ml) was heated under reflux for 10 hours. The reaction mixture was cooled, and the separated solid was filtered and dried. The solid obtained was separated on a column using chloroform as an eluent to afford compound 5 in 15 % yields.

Method B

2-(4-nitrophenyl)-6-iodo-4*H*-3,1-benzoxazin-4-one 1 (0.804 g, 0.003 mol) and 98 % hydrazine hydrate (0.6 g, 0.018 mol), in *n*-butanol (10 ml) was heated under reflux for 10 hours. The reaction mixture was cooled, and the separated solid was filtered and dried. The solid obtained was separated on a column using chloroform as an eluent to afford compound 5 in 30 % yields.

Method C

2-(4-nitrophenyl)-6-iodo-4*H*-3,1-benzoxazin-4-one 1 (0.804 g, 0.003 mol) and

98 % hydrazine hydrate (0.6 g, 0.018 mol) were heated under reflux for 3 hours. On cooling, the separated solid was filtered, washed with water and crystallized from ethanol to afford 5 in 50 % yield.

M.P.: 240-2 °C. Yield: 71.0 %. IR, KBr, υ cm^{-1}: 3350, 3300 (NH_2), 1680 (C=O). ^{1}H NMR ($CDCl_3$, δ ppm): 5.7-5.8 (bs, 2H, NH_2, D_2O exchanged), and 7.4-8.5 (m, 7H, Ar-*H*). ^{13}C NMR: 120.6, 121.5, 123.9, 124.2, 127.9, 128.6, 132.8, 134.1, 149.0, 153.8, 160.2 (Ar-C), 164.1 (CO). MS *m/z* (Rel. Int.) 309 (M^+, 86.0). Anal. ($C_{14}H_{10}IN_4O_3$, 282.25) C, H, N. The product obtained by these methods has the same physical constants.

2.1.1.4 2-(4-Nitrophenyl)-3-(arylideneamino)-3,4-dihydro-6-iodoquinazolin-4-ones 6-18 (32-35).

General procedure:

A mixture of 2-(4-nitrophenyl)-3-amino-3,4-dihydro-6-iodoquinazolin-4-one 5 (0.408 g, 0.001 mol) and the appropriate aldehyde (0.001 mol) in acetic acid (5 ml) was heated under reflux for 2 hours. On cooling, the separated solid was filtered, washed with water and crystallized from acetic acid.

a. 2-(4-Nitrophenyl)-3-(benzylideneamino)-3,4-dihydro-6-iodoquinazolin-4-one 6:

Yield, 87%; m.p. 195-197 ˚C; IR υ 1669 (C=O) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 7.60-8.51 (m, 12H, Ar), 9.11 (s, 1H, N=CH). ^{13}C NMR: 92.0, 121.62. 121.7, 123.9, 124.2, 127.9, 128.6, 128.8, 130.3, 132.8, 134.1, 138.4, 139.9, 142.6, 149.0, 149.2, 163.2, 164.7 (CO). MS *m/z* (Rel. Int.) 496 (M^+, 66.0). Anal. ($C_{21}H_{13}IN_4O_3$, 370.36) C, H, N.

b. 2-(4-Nitrophenyl)-3-(4-methylbenzylideneamino)-3,4-dihydro-6-iodoquinazolin-4-one 7:

Yield, 87%; m.p. 133-135 ˚C. IR υ 1660 (C=O) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 2.34 (s, 3H, CH_3), 7.6-8.28 (m, 11H, Ar), 8.44 (s, 1H, N=CH). ^{13}C NMR: 21.3, 92.8, 120.9, 121.4, 122.1, 127.8, 128.2, 128.7, 129.4, 131.6, 132.5, 134.1, 140.1, 141.7, 149.1, 152.0, 160.2, 164.4, 165.2 (CO). MS *m/z* (Rel. Int.) 510 (M^+, 38.0). Anal. ($C_{22}H_{15}IN_4O_3$) C, H, N.

c. 3-((4-(Dimethylamino) benzylidene)amino)-6-iodo-2-(4-nitrophenyl)quinazolin-4(3H)-one 8:

Yield, 52%; m.p. 200-202 ˚C. IR υ 1667 (C=O) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 2.91 (s, 6H, $2CH_3$), 6.66-7.87 (m, 11H, Ar), 8.32 (s, 1H, N=CH). ^{13}C NMR: 18.5, 91.7, 112.7, 112.9, 119.3, 120.2, 121.7, 122.5, 128.6, 132.3, 140.2, 150.5, 151.6, 152.2, 164.3, 164.67 (CO). MS *m/z* (Rel. Int.) 539 (M^+, 47.0). Anal. ($C_{23}H_{18}IN_5O_3$) C, H, N.

d. 3-((2,4-Dichlorobenzylidene)amino)-6-iodo-2-(4-nitrophenyl)quinazolin-4(3H)-one 9:

Yield, 82%; m.p. 225-227 ˚C. IR υ 1662 (C=O) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 7.19-8.08 (m, 10H, Ar), 8.89 (s, 1H, N=CH). ^{13}C NMR: 91.9, 120.8, 121.5, 122.2, 128.1, 128.2, 128.5, 128.8, 129.9, 130.9, 132.8, 134.5, 135.4, 140.8, 143.7, 152.6, 164.5, 165.31 (CO). MS *m/z* (Rel. Int.) 565 (M^{+2} + 4, 8.0), 563 (M^{+1} + 21, 68.0), 561 (M^+, 71.0). Anal. ($C_{21}H_{11}ICl_2N_4O_3$) C, H, N.

e. 3-((2-Hydroxybenzylidene)amino)-6-iodo-2-(4-nitrophenyl)quinazolin-4(3H)-one 10:

Yield, 80%; m.p. 178-180 ˚C; IR υ 3385 (OH), 1666 (C=O) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 5.28 (S, 1H, OH), 7.51-8.33 (m, 11H, Ar), 9.1 (s, 1H, N=CH). ^{13}C NMR: 95.1, 119.6, 120.9, 123.5, 124.0, 127.1, 128.6, 128.8, 130.5, 132.4, 134.0, 138.2, 139.7, 142.0, 146.2, 148.2, 163.2, 163.9 (CO). MS *m/z* (Rel. Int.) 512 (M^+, 80.0). Anal. ($C_{21}H_{13}IN_4O_4$) C, H, N.

f. 3-((4-Hydroxybenzylidene)amino)-6-iodo-2-(4-nitrophenyl)quinazolin-4(3H)-one 10 11:

Yield, 79%; m.p. 214-216 ˚C. IR υ 3394 (OH), 1668 (C=O) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 5.91 (s, 1H, OH), 7.62-7.35 (m, 11H, Ar). 8.72 (s, 1H, N=CH). ^{13}C NMR: 92.0, 116.9, 119.7, 120.0, 120.3, 120.5, 122.8, 124.5, 128.4, 128.7, 129.5, 132.5, 140.4, 149.4, 152.6, 159.6, 164.3, 164.2 (CO). MS *m/z* (Rel. Int.) 386 (M^+, 91.0). Anal. ($C_{21}H_{13}IN_4O_4$) C, H, N.

g. 3-((2,4-Dihydroxybenzylidene)amino)-6-iodo-2-(4-nitrophenyl)quinazolin-4(3H)-one 10 12:

Yield, 87%; m.p. 274-276 ˚C. IR υ 3382 (2OH). 1668 (C=O) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 5.51 (s, 2H, 2OH), 6.68-7.81 (m, 10H, Ar), 8.87 (s, 1H, N=CH). ^{13}C NMR: 55.9, 91.4, 116.6, 119.4, 120.26, 120.5, 121.6, 122.17, 127.0, 127.3, 128.56, 128.78, 132.60, 135.39, 140.11, 143.7, 145.0, 148.8, 152.6, 164.4, 165.1 (CO). MS *m/z* (Rel. Int.) 527 (M^+, 53.0). Anal. ($C_{21}H_{13}IN_4O_5$) C, H, N.

h. 3-((4-Hydroxy-3-methoxybenzylidene)amino)-6-iodo-2-(4-nitrophenyl)quinazolin-4(3H)-one 13:

Yield, 85%; m.p. 185-187 ˚C; IR υ 3402 (OH), 1671 (C=O) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 3.83 (s, 3H, OCH_3), 5.70 (S, 1H, OH), 7.91-8.53 (m, 10H, Ar), 8.80 (s, 1H, N=CH). ^{13}C NMR: 55.6, 92.9, 118.4, 119.1, 119.7, 120.3, 120.6, 120.7, 121.9, 122.7, 125.6, 128.5, 128.7, 131.9, 132.5, 140.2, 144.8, 152.4, 157.8, 164.4, 165.9 (CO). MS *m/z* (Rel. Int.) 542 (M^+, 91.0). Anal. ($C_{22}H_{15}IN_4O_5$) C, H, N.

i. 3-((2-Methoxybenzylidene)amino)-6-iodo-2-(4-nitrophenyl)quinazolin-4(3H)-one 14:

Yield, 87%; m.p. 145-147 ˚C. IR υ 1681 (C=O) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 3.81 (s, 3H, OCH_3), 5.91-8.62 (m, 11H, Ar), 9.10 (s, 1H, N=CH). ^{13}C NMR: 55.64, 92.3, 108.9, 112.9, 115.4, 119.5, 120.4, 120.5, 120.7, 122.4, 122.5, 125.1, 128.6, 128.7, 128.7, 132.4, 140.6, 148.3, 149.2, 149.7, 152.6, 164.4, 164.9 (CO). MS *m/z* (Rel. Int.) 526 (M^+, 28.0). Anal. ($C_{22}H_{15}IN_4O_4$) C, H, N.

j. 3-((4-Methoxybenzylidene)amino)-6-iodo-2-(4-nitrophenyl)quinazolin-4(3H)-one 15:

Yield, 86%; m.p. 151-153 ˚C. IR υ 1664 (C=O) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 3.60 (s, 3H, OCH_3). 6.69-7.78 (m, 11H, Ar), 8.41 (s, 1H, N=CH). ^{13}C NMR: 55.91, 94.1, 114.6, 119.3, 120.8, 122.1, 126.9, 128.5, 128.7, 128.9, 131.5, 132.5, 134.7, 142.4, 148.9, 152.6, 160.3, 162.7, 165.0 (CO). MS *m/z* (Rel. Int.) 527 (M^+, 65.0). Anal. ($C_{22}H_{15}IN_4O_4$) C, H, N.

k. 3-((2,4,5-Trimethoxybenzylidene) amino)-6-iodo-2-(4-nitrophenyl)quinazolin-4(3H)-one 16:

Yield, 80%; m.p. 227-229 ˚C. IR υ 1675 (C=O) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 3.39 (s, 9H, $3OCH_3$), 7.71-8.30 (m, 9H, Ar), 8.39 (s, 1H, N=CH). ^{13}C NMR: 55.9, 92.2, 108.1, 112.9, 119.7, 120.3, 121.3, 122.5, 125.2, 128.7, 128.9, 129.7, 132.5, 139.2, 140.6, 149.9, 152.3, 153.8, 164.6, 165.1 (CO). MS *m/z* (Rel. Int.) 543 (M^+, 83.0). Anal. ($C_{21}H_{13}IN_4O_6$) C, H, N.

l. 3-((2,4,6-Trimethoxybenzylidene)amino)-6-iodo-2-(4-nitrophenyl)quinazolin-4(3H)-one 17:

Yield, 87%; m.p. 215-217 ˚C. IR υ 1672 (C=O) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 3.95 (s, 9H, 3 OCH_3), 7.55-7.9 (m, 9H, Ar), 8.32 (s, 1H, N=CH). ^{13}C NMR: 92.05 119.36, 120.3, 122.7, 128.4, 128.5, 132.4, 134.5, 135.2, 136.0, 140.2, 143.6, 144.9, 152.2, 152.6, 153.6, 164.4, 164.7 (CO). MS *m/z* (Rel. Int.) 543 (M^+, 65.0). Anal. ($C_{21}H_{13}IN_4O_6$) C, H, N.

m. 3-((3,4,5-Trimethoxybenzylidene)amino)-6-iodo-2-(4-nitrophenyl)quinazolin-4(3H)-one 18:

Yield, 85%; m.p. 217-219 ˚C. IR υ 1663 (C=O) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 3.92 (s,

9H, 3OCH_3), 7.56-7.80 (m, 3H, Ar), 8.30 (s, 1H, N=CH). ^{13}C NMR: 94.6, 119.6, 120.1, 122.5, 128.1, 128.6, 131.8, 133.9, 136.1, 137.3, 141.5, 144.2, 145.4, 153.1, 154.7, 155.1, 162.8, 163.5 (CO). MS *m/z* (Rel. Int.) 544 (M^+, 73.0). Anal. ($C_{21}H_{13}IN_4O_6$) C, H, N.

2.2 Antimicrobial screening

Antimicrobial screening and determination of the minimum inhibitory concentration (MIC) of compounds was carried out using the disc diffusion method (15). Filter paper discs (5 mm in diameter) were separately soaked in the solution of the compounds and at different concentrations (for determination of MIC) and transferred to the surface of the growth medium seeded with the test organism. After the incubation, the diameter of the inhibition zone around the discs was measured in millimetres (32-34).

Representatives of Gram-negative bacteria; *Escherichia coli* (RCMB 010052), *Pseudomonas aeurginosa* (RCMB 010043), and Gram-positive bacteria; *Bacillus subtilis* (RCMB 010067), *Staphylococcus aureus* (RCMB 010028) and unicellular fungi; *Candida albicans* (RCMB 05031), *Geotricum candidum* (RCMB 05097) and filamentous fungi; *Aspergillus fumigatus* (RCMB 02568), *Syncephalastrum racemosum* (RCMB 05922) were obtained from the Regional Center for Mycology and Biotechnology, Al-Azhar University, Cairo, Egypt and used as test organisms.

3.0 Results and Discussion

3.1 Chemistry

Reaction of anthranilic acid with 4-nitro benzoyl chloride in methylene chloride in the presence of triethylamine, as an acid scavenger, affords the corresponding *N*-acylanthranilic acid (36-40). The later compound was cyclized by boiling with acetic anhydride to produce the benzoxazin-4-one derivative. Previous studies mentioned that the reaction of aliphatic amines with this lactone afforded the open diamide and not the 3-substituted quinazolin-4-one compounds usually obtained when the same reaction conditions were applied with aromatic amines.

Our trials to obtain 3-amino-6-iodo-2-methyl-3(H)-quinazolin-4-one, with considerable yield and purity, have failed in this study. The reaction was tried by prolonged heating in ethanol, pyridine, and *n*-butanol. In all of these cases, the separated solid proved to be a mixture consisting of different ratios from both the 3-amino and the diamide derivatives (41-46). However, boiling the 3*H*-benzoxazin-4-one with 100% hydrazine without solvent afforded the required 3-amino derivative with almost 85 % yield. The IR spectrum of this compound indicated the presence of a doublet band corresponding to the NH_2 absorption band at 3287, 3251 cm^{-1}. The NMR spectrum showed the NH_2 protons at δ 5.6 ppm and the carbonyl carbon at 160.5 ppm.

Reaction of the obtained amine with certain aromatic aldehydes afforded the corresponding arylidenes derivatives (1-13), and their structure was confirmed by elemental analyses and spectral data. Generally, the spectra of these compounds showed the absence of an NH absorption band from the IR spectra. The ^{1}H NMR spectra showed the olefenic proton at δ value between 10.0-11.0 ppm. The ^{13}C spectra showed the exact number of carbon atoms at the expected

Table 1: Antimicrobial activities of compounds 6-18

Test Organism	**Diameter of inhibition zone (mm)**													
	6	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**Standard Antibiotic**
Bacteria: Gram-Negative *Escherichia coli*	00.0	11.1± 0.44	00.0	12.6± 0.44	18.1± 0.28	00.0	00.0	13.9± 0.25	00.0	14.0± 0.25	13.1± 0.23	12.6± 0.44	14.2± 0.63	Gentamicin 22.3± 0.18
Pseudomonas aeurginosa	00.0	00.0	00.0	00.0	00.0	00.0	00.0	00.0	00.0	00.0	00.0	00.0	00.0	17.3± 0.15
Gram-Positive *Bacillus subtilis*	00.0	13.4± 0.44	00.0	15.7± 0.63	21.4± 0.63	00.0	00.0	16.3± 0.44	12.3± 0.58	19.9± 0.58	18.3± 0.53	15.7± 0.63	18.9± 0.37	Ampicillin 32.4±0.10
Staphylococcus aureus	00.0	11.2± 0.25	00.0	12.6± 0.58	20.3± 0.37	00.0	00.0	14.2± 0.58	10.2± 0.44	17.2± 0.37	14.7± 0.44	13.2± 0.58	16.2±0 .58	27.4± 0.18
Fungi: Unicellular *Candida albicans*	00.0	00.0	00.0	00.0	00.0	00.0	00.0	00.0	00.0	00.0	00.0	00.0	00.0	Amphotericin B 19.8± 0.20
Geotricum candidum	00.0	12.5± 0.37	00.0	00.0	18.3± 0.25	00.0	00.0	13.4± 0.58	00.0	14.6± 0.44	14.3± 0.53	00.0	15.9±0 .44	28.7± 0.20
Filamentous *Aspergillus fumigatus*	00.0	10.6± 0.37	00.0	00.0	16.3± 0.25	00.0	00.0	11.9± 0.37	00.0	11.3± 0.44	12.6± 0.53	00.0	13.1±0 .25	23.7± 0.10
Syncephalastrum racemosum	00.0	00.0	00.0	00.0	00.0	00.0	00.0	00.0	00.0	00.0	00.0	00.0	00.0	19.7± 0.20

Table 2: The Minimum inhibitory concentration (MIC) of compounds **7, 10, 13, 15, 16** and **18**

Test Organism	**Minimum Inhibitory Concentration (µg/mL)**						
	7	**10**	**13**	**15**	**16**	**18**	**Standard Antibiotics**
Bacteria: Gram-Negative *Escherichia coli*	500.00	015.63	500.00	500.00	500.00	125.00	Gentamicin 000.98
Pseudomonas aeurginosa	000.00	000.00	000.00	000.00	000.00	000.00	031.25
Gram-Positive *Bacillus subtilis*	125.00	001.95	062.50	003.90	015.63	007.81	Ampicillin 00.007
Staphylococcus aureus	500.00	003.90	125.00	031.25	125.00	062.50	000.06
Fungi: Unicellular *Candida albicans*	000.00	000.00	000.00	000.00	000.00	000.00	Amphotericin B 003.90
Geotricum candidum	500.00	015.63	500.00	125.00	125.00	062.50	000.03
Filamentous *Aspergillus fumigatus*	500.00	062.50	500.00	500.00	500.00	500.00	000.24
Syncephalastrum racemosum	000.00	000.00	000.00	000.00	000.00	000.00	003.90

δ values, that were in agreement with the proposed structures (47-50).

3.2. Antimicrobial Testing

The antimicrobial activities of the current series showed that 9 out of 13 compounds have remarkable activities against the investigated test organisms (Table 1). However, six compounds, namely **7**, **10**, **13**, **15**, **16**, and **18** showed antibacterial and antifungal activities, while **9**, **14** and **17** showed only antibacterial activity. The best activity (21.4±063) (19.9±0.58) was obtained against *Bacillus subtilis* by compounds **10** and **15**, respectively. On the other hand, compounds **6**, **8**, **11, and 12**, showed no activity (32-34).

On the other hand, the best minimum inhibitory concentrations (1.90 µg/ml) and (3.9 µg/ml) were obtained by compound **10** against *Bacillus subtilis* and *Staphylococcus aureus*, respectively (Table 2). Also, compound **10** showed the best MICs (15.63 and 62.50 µg/ml) against the filamentous fungi; *Aspergillus fumigatus* and *Syncephalastrum racemosum*, respectively.

4.0 Conclusion

We synthesized certain focused series of new 6-iodoquinazoline-based Schiff's bases by simple chemical procedures. The obtained compounds were evaluated for their growth inhibitory activity against four selected fungal strains, two gram-positive bacterial strains and two gram-negative bacterial strains. Most of the synthesized compounds were promising as useful backbones for further derivatization and developing more effective antimicrobial and antifungal small molecules.

A**uthorship contribution statement**

AMA: synthesised the intermediate and final compounds and wrote the manuscript draft, **KA:** provided the facilities, supervised and analysed the biological tests, **MEZ:** assisted in the synthesis of compounds and manuscript writing, **SS:** edited the manuscript**.**

Acknowledgment

The authors would like to thank Department of Microbiology, Faculty of Science, Al-Azhar University for their technical support.

Conflict of Interest

The authors declare that there are no conflicts of interest.

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