Anadolu Üniversitesi Bilim ve Teknoloji Dergisi C – Yaşam Bilimleri ve Biyoteknoloji
Anadolu University Journal of Science and Technology C – Life Sciences and Biotechnology
Cilt: 4 Sayı: 1 - 2015
Sayfa: 31 - 39
DOI: 10.18036/btdc.57492

ARAŞTIRMA MAKALESİ / **RESEARCH ARTICLE**

Esra BAŞYİĞİT[1], Ulviye ACAR[1], Yusuf ÖZKAY [1]*, Hülya KARACA GENÇER[2], Ümit UÇUCU[1]

SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF SOME NOVEL QUINOXALINE HYDRAZONES

ABSTRACT

A new class of 10 novel quinoxaline hydrazones was synthesized to examine their antimicrobial activity. The structures of the compounds were confirmed by IR, ^{1}H-NMR, and MS spectral data and elemental analyses. Antimicrobial activity of the compounds was evaluated against 3 fungal and 7 bacterial strains by Micro-broth dilution assay. All of the synthesized compounds showed significant antibacterial activity against *Pseudomonas aeruginosa*. Furthermore, antibacterial activity of the 2,4-difluoro substituted compound **4b** displayed two fold better activity than chloramphenicol against this bacterial strain.

Keywords: Quinoxaline, Hydrazone, Antimicrobial activity, Micro-broth dilution, *Pseudomonas aeruginosa*

BAZI YENİ KİNOKSALİN HİDRAZONLARIN SENTEZİ ve ANTİMİKROBİYAL AKTİVİTELERİ

ÖZ

10 yeni kinoksalin hidrazondan oluşan yeni bir grup aktimikrobiyal aktivitesi incelenmek üzere sentezlenmiştir. Bileşiklerin yapıları IR, 1H-NMR, MS spektral ve elemental analiz ile aydınlatılmıştır. Bileşiklerin antimikrobiyal aktiviteleri Mikro-broth dilüsyon yöntemi ile 3 fungus ve 7 bakteri türüne karşı değerlendirilmiştir. Sentezlenen bütün bileşikler Pseudomonas aeruginosa' ya karşı önemli antibakteriyal aktivite göstermiştir. Ayrıca, 2,4-difloro yapısı içeren 4b bileşiği Pseudomonas aeruginosa' ya karşı kloramfenikolden 2 kat daha iyi antibakteriyal aktivite göstermiştir.

Anahtar Kelimeler: Kinoksalin, Hidrazon, Antimikrobiyal aktivite, Mikro-broth dilüsyon, Pseudomonas aeruginosa

[1]Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, 26470 Eskişehir, Turkey
* Corresponding Author: E-mail: yozkay@anadolu.edu.tr Tel: +902223350580/3779
[2]Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, 26470, Eskişehir, Turkey
Received: 24 December 2015 **Accepted:** 28 December 2015

1. INTRODUCTION

Since 1942, when the commercial solvents corporation launched penicillin, invented by Alexander Fleming, a considerable reduce in the number of deaths caused by bacterial infections has been declared. Optimists have even noticed an end to the era of bacterial diseases. However, too frequent, and frequently improper, applications of antibiotics have resulted in the formation of drug resistant bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin- resistant *Enterococci* (VRE) and vancomycin-resistant *Staphylococcus aureus* (VRSA) and the world has begun to face another problem; that of treating nosocomial infections (Ishikawa et al., 2013). In recent decades, resistant bacteria have increased and the interval between the appearances of novel and the multi-drug resistant species have formed in short periods of time. These conditions have created an urgent public health issues that they compromise the efficacy of antimicrobial agents and thus the weal of the population (Vieira et al., 2014). To overcome these problems, lots of new molecules have been discovered and introduced for the treatment of infectious diseases. However, resistance problem is still not been solved and thus there is still a need to screen new compounds for the development of new antimicrobial agents with better effectiveness (El-Sabbagh et al., 2009).

Nitrogen-containing heterocycles form the main component of many indispensable biomolecules, from DNA and RNA to coenzymes. They are thought to have high biocompatibility, and have been improved for clinical use. Among the different classes of heterocyclic units, the quinoxaline ring that is also known as benzo[*b*][1,4]diazine has frequently been used as a component of various antibiotic molecules, such as hinomycin, echinomycin, leromycin, levomycin and actindeutin, which restrict the growth of Gram-positive bacteria and are active against various transplantable tumours (Khaksar et al., 2014; Kotharkar and Shinde 2006; Ramalingam et al., 2010; Ishikawa et al., 2012). Moreover, many reports describe a chemotherapeutic importance of quinoxaline derivatives as antibacterial (Nagaraj et al., 2015), antifungal (El-Faham et al., 2002), antiviral (Kamal et al., 2014), antimalarial (Sıngh et al., 2011), antihelmintic (Carta et al., 2002) antiprotozoal (Ishikawa et al., 2013). Therefore, the quinoxaline ring is an important class of nitrogen-containing heterocycles in pharmaceutical field (Soliman and Amer 2012).

Hydrazones constitute one of the most biologically effective classes in medicinal chemistry (Narasimhan et al. 2010). Hydrazone moiety can easily interact with biomolecules and forms a conjugate and it is a useful linkage in pH-dependent release of drugs from polymer-drug conjugates (Ulbrich and Subr 2004). Thus, one of the most studied areas of hydrazone derivatives is antimicrobial chemistry. In many works hydrazone compounds have been claimed to possess antibacterial (Wu et al., 2012) and antifungal (Backes et al., 2014) activities.

Looking at the antimicrobial importance of hydrazone moiety and quinoxaline compounds it would be valuable to synthesize some new quinoxaline derivatives including hydrazone group and to investigate their antibacterial and antifungal activities. Thus, in the present study we synthesized 10 new quinoxaline-hydrazone derivatives and investigated their antimicrobial activities so as to obtain new biologically active compounds.

2. MATERIALS and METHODS

2.1. Chemistry

The chemicals used in syntheses were purchased from Merck (Germany), Acros (Belgium), or Sigma-Aldrich (Germany) companies. Melting points determinations were performed on an Electrothermal 9001 Digital Melting Point Apparatus and were uncorrected. IR, ^{1}H-NMR and MS spectra were recorded on Shimadzu 8400 FTIR spectrometer, BrukerUltrashield 500 MHz spectrometer and Agilent 1100 Series LC/MSD Trap VL&SL spectrometer, respectively. Elemental analyses (C, H, and N) were determined on a Leco CHNS-932 analyser.

Microwave-assisted synthesis of quinoxaline-2(1H)-one (1)

1,2-phenylenediamine (4.32 g, 0.04 mol) and ethyl glyoxalate (5 mL) in ethanol (10 mL) were put into a vial (30 mL) of microwave synthesis reactor (Anton-Paar Monowave 300). The reaction mixture was kept under the conditions of 200 ^{o}C and 25 bar for 15 min. After cooling, ethanol was evaporated, the residue was washed with water, dried and

recrystallized from ethanol. Yield: 94 %. m.p. 269 ºC (ref. 267.2-268.5 ºC) (Yan-Yan 2010).

Synthesis of 2-chloroquinoxaline (2)

Quinoxaline-2(1*H*)-one **1** (5.11g, 0.035 mol) in $POCl_3$ (100 mL) was refluxed for 3h. After cooling, excessive of $POCl_3$ was evaporated and crude product was held for further reaction without recrystallization. Yield: 86 %. m.p. 49 ºC (ref. 47-50 ºC) (Becker 2008).

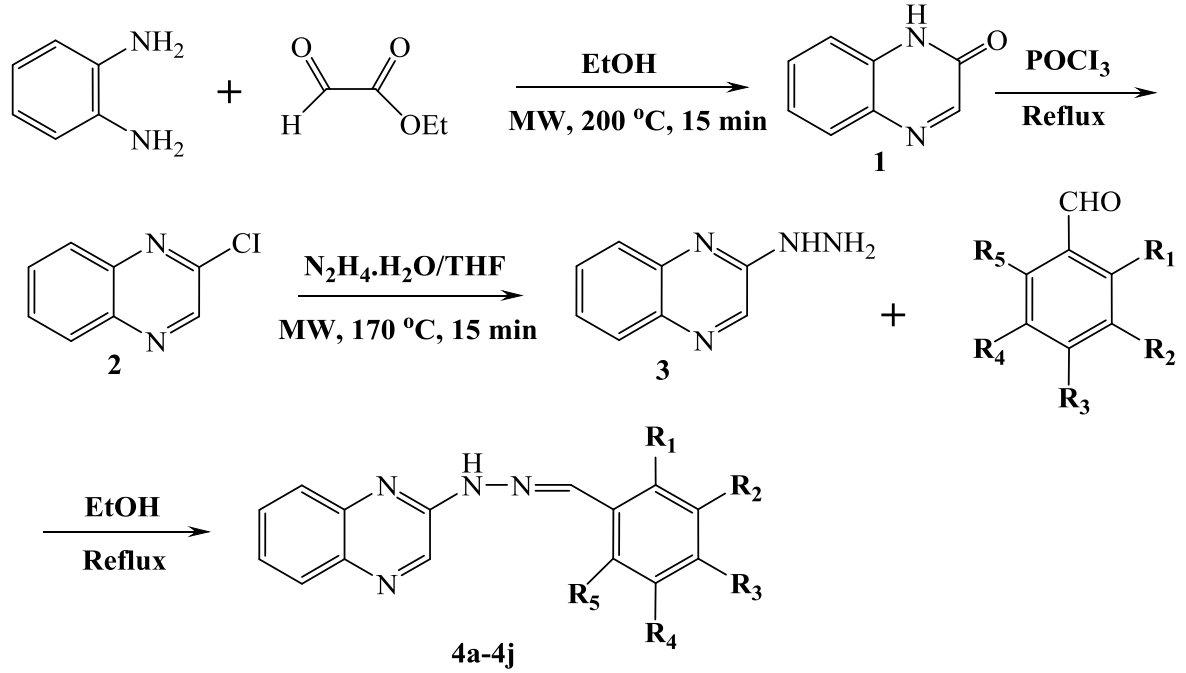
Microwave-assisted synthesis of quinoxaline-2-hydrazine (3)

In a vial (30mL) of microwave synthesis reactor (Anton-Paar Monowave 300) 2-chloroquinoxaline **2** (4.1g, 0,025 mol) in tetrahydrofuran (THF) (10 mL) and hydrazine hydrate (3 mL) were irradiated at 170 ºC and 10 bar for 15 min. In the end of reaction, the solvent and excessive of hydrazine hydrate were evaporated, the residue was washed with water, dried and recrystallized from ethanol. Yield: 91 %. m.p. 168 ºC (ref. 167 ºC) (Chen et al. 2008).

General Synthesis of N-(4-substitutedbenzylidene)-N'-quinoxalin-2-yl-hydrazine Derivatives (4a-4j)

Quinoxaline-2-hydrazine **3** (0.32g, 0.002 mol) and appropriate benzaldehyde derivatives in ethanol (10 mL) were refluxed for 1h with catalytic amount of acetic acid. The precipitate was filtered, dried and recrystallized from ethanol (**Scheme 1).**

Scheme 1. The synthesis of the compounds



N-(4-trifluoromethylbenzylidene)-N'-quinoxalin-2-yl-hydrazine (4a)

Yield: 76%. m.p. 278ºC. IR ν_{max}(cm^{-1}): 3161 (N-H), 1581-1425 (C=C and C=N). ^{1}H-NMR (500 MHz) (DMSO-d_6) δ(ppm): 7.5-8.1 (9H, m, Ar-H), 9.1 (H, s, N=CH), 11.9 (H, s, NH-N=). Es-Ms (m/z): M+1: 317.28. Anal. calcd. for $C_{16}H_{11}F_3N_4$: C, 60.76; H, 3.51; N, 17.71. Found: C, 60.72; H, 3.47; N, 17.65.

N-(2,4-difluorobenzylidene)-N'-quinoxalin-2-yl-hydrazine (4b)

Yield: 77%. m.p. 261ºC. IR ν_{max}(cm^{-1}): 3219 (N-H), 1571-1422 (C=C and C=N). ^{1}H-NMR (500 MHz) (DMSO-d_6) δ(ppm): 7.2-8.3 (8H, m, Ar-H), 9.1 (H, s, N=CH), 11.8 (H, s, NH-N=). Es-Ms (m/z): M+1: 285.26. Anal. calcd. for $C_{15}H_{10}F_2N_4$: C, 63.38; H, 3.55; N, 19.71. Found: C, 63.44; H, 3.58; N, 19.76.

N-(2,4-dimethylbenzylidene)-N'-quinoxalin-2-yl-hydrazine (4c)

Yield: 79%. m.p. 186ºC. IR ν_{max}(cm^{-1}): 3201 (N-H), 1581-1417 (C=C and C=N). ^{1}H-NMR (500 MHz) (DMSO-d_6) δ(ppm): 2.3 (3H, s, CH_3), 2.4 (3H, s, CH_3), 7.0-8.4 (8H, m, Ar-H), 9.0 (H, s, N=CH), 11.6 (H, s, NH-N=). Es-Ms (m/z): M+1: 277.34. Anal. calcd. for $C_{17}H_{16}N_4$: C, 73.89; H, 5.84; N, 20.27. Found: C, 73.95; H, 5.88; N, 20.31.

N-(3,5-dimethoxybenzylidene)-N'-quinoxalin-2-yl-hydrazine (4d)

Yield: 84%. m.p. 219ºC. IR ν_{max}(cm^{-1}): 3188 (N-H), 1581-1409 (C=C and C=N). ^{1}H-NMR (500 MHz) (DMSO-d_6) δ(ppm): 3.8 (6H, s, 2 x OCH_3), 6.5-8.0 (8H, m, Ar-H), 9.1 (H, s, N=CH), 11.8 (H, s, NH-N=). Es-Ms (m/z): M+1: 309.33. Anal. calcd. for $C_{17}H_{16}N_4O_2$: C, 66.22; H, 5.23; N, 18.17. Found: C, 66.24; H, 5.22; N, 18.19.

N-(3-Hydroxy-4-methoxybenzylidene)-N'-quinoxalin-2-yl-hydrazine (4e)

Yield: 76%. m.p. 267ºC. IR ν_{max}(cm^{-1}): 3172 (N-H), 1583-1417 (C=C and C=N). ^{1}H-NMR (500 MHz) (DMSO-d_6) δ(ppm): 3.8 (3H, s, OCH_3), 7.0-8.0 (8H, m, Ar-H), 9.0 (H, s, N=CH), 9.3 (H, s, OH), 11.5 (H, s, NH-N=). Es-Ms (m/z): M+1: 295.31. Anal. calcd. for $C_{16}H_{14}N_4O_2$: C, 65.30; H, 4.79; N, 19.04. Found: C, 65.35; H, 4.84; N, 19.10.

N-(3,5-Dimethoxy-4-hydroxybenzylidene)-N'-quinoxalin-2-yl-hydrazine (4f)

Yield: 80%. m.p. 214ºC. IR ν_{max}(cm^{-1}): 3196 (N-H), 1587-1417 (C=C and C=N). ^{1}H-NMR (500 MHz) (DMSO-d_6) δ(ppm): 3.9 (6H, s, 2 x OCH_3), 7.0-8.0 (8H, m, Ar-H), 8.8 (H, s, N=CH), 9.1 (H,s, OH), 11.5 (H, s, NH-N=). Es-Ms (m/z): M+1: 325.33. Anal. calcd. for $C_{17}H_{16}N_4O_3$: C, 62.95; H, 4.97; N, 17.27. Found: C, 62.94; H, 4.90; N, 17.22.

N-(2,4,6-trimethylbenzylidene-N'-quinoxalin-2-yl-hydrazine (4g)

Yield: 74%. m.p. 173ºC. IR ν_{max}(cm^{-1}): 3127 (N-H), 1581-1427 (C=C and C=N). ^{1}H-NMR (500 MHz) (DMSO-d_6) δ(ppm): 2.3 (3H, s, CH_3), 2.5 (6H, s, 2 x CH_3), 6.9-8.5 (7H, m, Ar-H), 9.0 (H, s, N=CH), 11.6 (H, s, NH-N=). Es-Ms (m/z): M+1: 291.36. Anal. calcd. for $C_{18}H_{18}N_4$: C, 74.46; H, 6.25; N, 19.29. Found: C, 74.52; H, 6.30; N, 19.36.

N-(4-dimethylaminobenzylidene)-N'-quinoxalin-2-yl-hydrazine (4h)

Yield: 79%. m.p. 272ºC. IR ν_{max}(cm^{-1}): 3221 (N-H), 1577-1425 (C=C and C=N). ^{1}H-NMR (500 MHz) (DMSO-d_6) δ(ppm): 3.0 (6H, 2xCH_3), 6.8-8.0 (9H, m, Ar- H), 9.0 (H, s, N=CH), 11.4 (H, s, NH-N=). Es-Ms (m/z): M+1: 292.35. Anal. calcd. for $C_{17}H_{17}N_5$: C, 70.08; H, 5.88; N, 24.04. Found: C, 70.11; H, 5.93; N, 24.13.

N-(4-Acetaminobenzylidene)-N'-quinoxalin-2-yl-hydrazine (4ı)

Yield: 78%. m.p. 196°C. IR ν_{max}(cm^{-1}): 3228 (N-H), 1604 (C=O), 1577-1404 (C=C and C=N). ^{1}H-NMR (500 MHz) (DMSO-d_6) δ(ppm): 2.0 (3H, s, CH_3), 7.5-8.1 (9H, m, Ar- H), 9.1 (H, s, N=CH), 10.0 (H, s, NHCO), 11.6 (H, s, NH-N=). Es-Ms (m/z): M+1: 306.33. Anal. calcd. for $C_{17}H_{15}N_5O$: C, 66.87; H, 4.95; N, 22.94. Found: C, 66.82; H, 4.90; N, 22.88.

N-(4-diethylaminobenzylidene)-N'-quinoxalin-2-yl-hydrazine (4j)

Yield: 82%. m.p. 287°C. IR ν_{max}(cm^{-1}): 3221 (N-H), 1581-1408 (C=C and C=N). ^{1}H-NMR (500 MHz) (DMSO-d_6) δ(ppm): 1.0 (6H, t, 2xCH_3), 3,4 (4H, q, 2 x CH_2), 6.7-8.0 (9H, m, Ar-H), 9.0 (H, s, N=CH), 11.4 (H, s, NH-N=). Es-Ms (m/z): M+1: 320.40. Anal. calcd. for $C_{19}H_{21}N_5$: C, 71.45; H, 6.63; N, 21.93. Found: C, 71.48; H, 6.70; N, 21.99.

Biological test

Antimicrobial activity

The study was designed to compare MICs obtained by the CLSI reference M7–A7 broth microdilution method for antibacterial activity (CLSI, 2006). Anticandidal activity test was performed according to CLSI reference M27-A3 broth microdilution method (Wayne, 2008). MIC readings were performed twice for each chemical agent. Final products were tested for their *in vitro* growth inhibitory activity against human pathogenic *Salmonella typhimuirium* NRRL B-4420, *Listeria monocytogenes* (ATCC 7644), *Enterococcus faecalis* (ATCC 29212), *Pseudomonas aeruginosa* (ATCC 27853), *Klebsiella pneumoniae* (ATCC 700603), *Escherichia coli* (ATCC 35218), *Escherichia coli* (ATCC 25922) and yeast as *Candida albicans* (ATCC 90028), *Candida glabrata* (ATCC 90030) and *Candida krusei* (ATCC 6258). Chloramphenicol and ketoconazole were used as control drugs.

Broth Microdilution Assay

The cultures were obtained from Mueller–Hinton broth (Difco) for the bacterial strains after overnight incubation at 35 ± 1 °C. The yeasts were maintained in Sabouraud dextrose broth (Difco) after overnight incubation 35 ± 1 °C. The inocula of test microorganisms adjusted to match the turbidity of a Mac Farland 0.5 standard tube as determined with a spectrophotometer and the final inoculum size was 0.5-2.5 × 10^5 cfu/mL for antibacterial and antifungal assays. Testing was carried out in Mueller–Hinton broth and Sabouraud dextrose broth (Difco) at pH 7 and the two-fold serial dilutions technique was applied. The last well on the microplates containing only inoculated broth was kept as controls and the last well with no growth of microorganism was recorded to represent the MIC expressed in μg/mL. For both the antibacterial and antifungal assays the compounds were dissolved in DMSO. Further dilutions of the compounds and standard drugs in test medium were prepared at the required quantities of 800, 400, 200, 100, 50, 25, 12.5, 6.25, 3.13 and 1.63 μg/mL concentrations with Mueller–Hinton broth and Sabouraud dextrose broth (Yurttaş et al.2013). Each experiment in the antimicrobial assays was replicated twice in order to define the MIC values given in **Table 2**.

3. RESULTS and DISCUSSION

Chemistry

In the present work, the reaction sequence outlined in **Scheme 1** was followed for the synthesis of *N*-(4-substitutedbenzyl)-*N'*-quinoxalin-2-yl-hydrazine derivatives **(4a-4j).** Initially, microwave supported synthesis of quinoxaline-2(1*H*)-one **(1)** was performed in ethanol. In the second step, quinoxaline-2(1*H*)-one **(1)** in phosphoryl chloride was refluxed to obtain 2-chloroquinoxaline **(2).** In the third step, 2-chloroquinoxaline **(2)** in tetrahydrofuran (THF) was reacted with hydrazine hydrate to gain quinoxaline-2-hydrazine **(3),** which was then reacted with appropriate benzaldehyde derivatives in ethanol with catalytic amount of acetic acid to obtain target compounds (**4a**–**4j)**. Some physicochemical properties of the final compounds **4a**–**4j** were presented in the **Table 1.**

Table 1

Some characteristics of the synthesized compounds

Comp.	R_1	R_2	R_3	R_4	R_5	Yield (%)	M.p. (°C)	Molecular formula	Molecular weight
4a	H	H	CF_3	H	H	76	278	$C_{16}H_{11}F_3N_4$	316.28
4b	H	H	F	H	F	77	261	$C_{15}H_{10}F_2N_4$	284.26
4c	H	H	CH_3	H	CH_3	79	186	$C_{17}H_{16}N_4$	276.34
4d	H	OCH_3	H	OCH_3	H	84	219	$C_{17}H_{16}N_4O_2$	308.33
4e	H	OH	OCH_3	H	H	76	267	$C_{16}H_{14}N_4O_2$	295.31
4f	H	OCH_3	OH	OCH_3	H	80	214	$C_{17}H_{16}N_4O_3$	324.33
4g	CH_3	H	CH_3	H	CH_3	74	173	$C_{18}H_{18}N_4$	290.36
4h	H	H	$N(CH_3)_2$	H	H	79	272	$C_{17}H_{17}N_5$	291.35
4ı	H	H	$NHCOCH_3$	H	H	78	196	$C_{17}H_{15}N_5O$	305.33
4j	H	H	$N(C_2H_5)_2$	H	H	82	287	$C_{19}H_{21}N_5$	319.40

Table 2

Antimicrobial activities of the compounds (μg/mL)

Compounds	A	B	C	D	E	F	G	H	I	J
4a	100	50	100	200	200	200	200	50*	100	200
4b	100	50	100	200	200	200	200	25**	100	200
4c	50	50	100	200	200	200	200	50*	200	200
4d	50	50	100	100	200	200	200	50*	400	200
4e	100	50	100	200	200	200	200	50*	200	200
4f	50	100	200	200	200	200	200	50*	200	100
4g	100	100	100	200	200	200	200	50*	200	200
4h	100	200	200	200	200	200	200	50*	200	100
4ı	100	100	100	200	200	200	200	50*	200	200
4j	100	100	200	200	200	200	200	50*	200	200
Ref 1	25	25	25	-	-	-	-	-	-	-
Ref 2	-	-	-	12.5	25	25	12.5	50	50	12.5

A: *Candida crusei* (ATCC 6258), **B:** *Candida glabrata* (ATCC 90030), **C:** *Candida albicans* (ATCC 90028), **D:** *Listeria monocytogenes* (ATCC 7644), **E:** *Escherichia coli* (ATCC 35218), **F:** *Klebsiella pneumoniae* (ATCC 700603), **G:** *Salmonella typhimurium* NRRL B-4420, **H:** *4g-4t* (ATCC 27853), **I:** *Escherichia coli* (ATCC *25922*), **J:** *Enterococcus faecalis* (ATCC 29212), **Ref-1:** Ketoconazole **Ref-2**: Chloramphenicol. * MIC values equal to the reference drug ** MIC values lower than the reference drug

The chemical structures of the compounds (**4a**–**4j**) were confirmed by IR, ^{1}H NMR, and mass spectral data and elemental analyses. Characteristic stretching absorption of N-H groups were observed at 3127-3305 cm^{-1} as expected. The stretching absorption at about 1606-1404 cm^{-1} were recorded for C=C and C=N double bonds respectively. In the ^{1}H-NMR spectra, all of the aromatic and aliphatic protons were observed at estimated areas. Aromatic protons were resonated a large area between 6.3-8.5 ppm as multiplet and amine protons were determined at about 11.4-12.1 ppm as singlet peaks. The azomethine protons of hydrazone recorded at 8.8-9.2 ppm as a singlet. The mass spectra (Es-Ms) of compounds showed [M+1] peaks, in agreement with their molecular formula. All compounds gave satisfactory elemental analyses results.

Antimicrobial activity

The synthesized 10 novel quinoxaline hydrazones were tested against 3 fungal and 7 bacterial species**.** MIC values of the synthesized compounds are given in the **Table 2**.

Candida glabrata was the most sensitive fungal strain against tested compounds. The compounds **4a**-**4e** indicated moderate antifungal activity with a MIC value of 50 µg/mL. The MIC value of the reference drug ketoconazole was 25 µg/mL against Candida species. All of the synthesized compounds in the series were found to be inactive against *Candida albicans*.The compounds **4c**, **4d** and **4f** displayed half potency of reference against *Candida crusei*. Antifungal activity of the other compounds were not comparable with that of reference against *Candida crusei.*

The synthesized compounds showed poor antibacterial activity against *Salmonella typhimuirium, Listeria monocytogenes, Enterococcus faecalis, Klebsiella pneumoniae, Escherichia coli* strains when compared with reference chloramphenicol. On the other hand, all of the compounds in the series showed remarkable antibacterial activity against *Pseudomonas aeruginosa*. The compounds **4a** and **4c**-**4j** exhibited the same antibacterial potency with reference against *Pseudomonas aeruginosa*. Moreover, MIC value (25 µg/mL) of the **4b** was two-fold lower than that of chloramphenicol (50 µg/mL). The activity results showed that 2,4-diflorobenzylidene moieties in compound **4b** enhance the antibacterial effect against *Pseudomonas aeruginosa*.

In spite of narrow antibacterial effect spectrum observed in the present study, the active compound **4b** against *Pseudomonas aeruginosa* possess an antibacterial importance. *Pseudomonas aeruginosa* lives nearly everywhere as in water, in soil and on plants. This pathogenic bacteria can also be exist in tap water found in patient rooms and adapt to a wide range of conditions. Thus, it can be responsible for numerous kinds of nosocomial infections with increasingly limited therapeutic options owing to multi drug resistance resulting in higher mortality and morbidity. Infections caused by *Pseudomonas aeruginosa* are critical because it is inherently resistant to many antibiotics. A limited class of drugs is effective against this bacteria, including the carboxypenicillins, quinolones (ciprofloxacin, levofloxacin), the antipseudomonal cephalosporin, and aminoglycosides (Khan et al. 2014; Akhand et al. 2014; Poole 2014; Veerappa et al. 2014). On that account the compound **4b** may be essential for the prevention of the infections caused by *Pseudomonas aeruginosa*.

4. CONCLUSIONS

In this study, we synthesized some quinoxaline hydrazones in order to examine their antimicrobial effects against various bacterial and fungal strains. Some compounds in the series exhibited moderate anticandidal effects. Although most of the bacterial strains were resistant to synthesized compounds, *Pseudomonas aeruginosa* displayed sensitivity to entire tested compounds. Compound **4b** bearing 2,4-diflorobenzylidene moiety showed better antibacterial activity than the reference agent against *P. aeruginosa.* In conclusion, result of this work may have a good impact on medicinal chemists to synthesize similar and more potent antimicrobial compounds.

Declaration of Interest

The authors report no conflicts of interest.

Acknowledgement

This work was financially supported by Anadolu University Scientific Projects Fund. Project Number: 1505S407

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