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3-Aril-4-(benzensulfoniloksi)-benzilidenamino-4,5-dihiro-1*H*-1,2,4-triazol-5-on Bileşiklerinin Antimikrobiyal Aktiviteleri

Antimicrobial Activities of 3-Aryl-4-(benzenesulfonyloxy)-benzylideneamino-4,5-dihyro-1*H*-1,2,4-triazol-5-one Compounds

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Geliş Tarihi
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Öz

Çalışmanın sentez bölümünde, ilk olarak 3 adet 3-aril-4-amino-4,5-dihidro-1*H*-1,2,4-triazol-5-on bileşiğinin bir benzaldehid türevi olan 3-etoksi-4-hidroksibenzaldehidin trietilamin varlığında benzensulfonil klorür ile muamelesinden sentezlenen 3-etoksi-4-(benzensulfoniloksi)-benzaldehid ile ayrı ayrı muamelesinden karşın olan 3 adet 3-aril-4-(benzensulfoniloksi)-benzilidenamino-4,5-dihiro-1*H*-1,2,4-triazol-5-on bileşiği elde edilmiştir. 3 Adet 1,2,4-triazol türevli Schiff bazı bileşikleri olan 3-aril-4-[3-etoksi-4-(benzensulfoniloksi)-benzilidenamino]-4,5-dihidro-1*H*-1,2,4-triazol-5-on'ların *Klebsiella pneumoniae, Pseudomonas aeruginosa, Echerichia coli, Staphylococcus aureus, Entercoccus faecalis* bakterileri üzerindeki antimikrobiyal etkileri disk difüzyon yöntemi ile araştırılmıştır. Yapılan araştırma sonucunda 3-*p*-klorobenzil-4-[3-etoksi-4-(benzensulfoniloksi)-benzilidenamino]-4,5-dihidro-1*H*-1,2,4-triazol-5-on'un *E. coli ve K. pneumoniae* üzerinde antimikrobiyal etki gösterdiği, 3-*m*-klorobenzil-4-[3-etoksi-4-(benzensulfoniloksi) benzilidenamino]-4,5-dihidro-1*H*-1,2,4-triazol-5-on'un da yalnızca *K. pneumoniae* üzerinde etkili olduğu belirlenmiştir.

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Abstract

In the synthesis section, three 3-aril-4-amino-4,5-dihydro-1*H*-1,2,4-triazol-5-one compounds were obtained through the reaction of 3-ethoxy-4-hydroxybenzaldehyde, a derivative of benzaldehyde, with benzenesulfonyl chloride in the presence of triethylamine. Subsequent reactions with these compounds yielded three distinct 3-aril-4-(benzenesulfonoxy)-benzylideneamino-4,5-dihydro-1*H*-1,2,4-triazol-5-one derivatives. The antimicrobial effects of three 1,2,4-triazole derivative Schiff base compounds, which are 3-aryl-4-[3-ethoxy-4-(benzenesulfonyloxy)benzylideneamino]-4,5-dihydro-1*H*-1,2,4-triazol-5-ones, were investigated against *Klebsiella pneumoniae, Pseudomonas aeruginosa, Escherichia coli, Staphylococcus aureus*, and *Enterococcus faecalis* using the disk diffusion method. Results revealed that 3-p-chlorobenzyl-4-[3-ethoxy-4-(benzenesulfonyloxy)benzylideneamino]-4,5-dihydro-1*H*-1,2,4-triazol-5-one displayed antimicrobial activity against *E. coli* and *K. pneumoniae*, while 3-m-chlorobenzyl-4-[3-ethoxy-4-(benzenesulfonyloxy) benzylideneamino]-4,5-dihydro-1*H*-1,2,4-triazol-5-one was effective only against *K. pneumoniae*.

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1. INTRODUCTION

Schiff bases were first synthesized by the German chemist Hugo Schiff, who was awarded the Nobel Prize in the 1860s. Due to their stability and ease of synthesis, Schiff bases have become widely used and studied compounds (Blagus et al., 2010; Karaca, 2018; Aydınlı Esen, 2006). There are numerous areas where Schiff bases are effectively utilized. In the paint industry, Schiff base metal complexes are employed (Aydınlı Esen, 2006). Compounds containing aromatic rings and metal complexes are also used as catalysts (Pişkin, 2011). Schiff bases have been utilized as ligands to coordinate metal ions and to coordinate anions (Blagus et al., 2010). They have been observed to play a regulatory role in plant growth and to affect growth hormones in roots (Pişkin, 2011). Additionally, they exhibit herbicidal properties (Karaca, 2018) and have been found to show toxicity against insects (Pişkin, 2011). Schiff bases are used in the treatment of diabetes and AIDS (Karaca, 2018). Similar to important coordination compounds in the human body such as hemoglobin and in plants such as chlorophyll, Schiff bases are used as ligands and play a role in the oxidation of biologically significant molecules such as free oxygen and ascorbic acid (Aydınlı Esen, 2006). Due to their antitumor and anticancer properties, Schiff bases hold an important place in cancer drugs (Özsen, 2010; Değirmencioğlu, 2010). In recent years, numerous *in silico, in vitro,* and *in vivo* studies regarding Schiff bases have gained significant importance (Koç et al., 2020; Beytur and Avinca, 2021; Beytur and Uğurlu, 2020; Kardaş et al., 2016; Yüksek et al., 2018; Turhan Irak and Beytur, 2019; Gürsoy Kol et al., 2020). Many studies on Schiff bases have observed their antiviral, antifungal, and antibacterial properties (Bahçeci et al., 2017; Beytur et al., 2019; Karaca, 2018; Aydınlı Esen, 2006; Özsen, 2010; Değirmencioğlu, 2010; Pişkin, 2011; Kayapa, 2018; Zeydan, 2009).

Microorganisms have numerous beneficial applications in foods, such as kefir, yogurt, vinegar, bread fermentation, alcohol and acetone production, as well as biological wastewater treatment and use as biological fertilizer. However, they can also cause diseases and fatalities in humans, animals, and plants, in addition to economic losses resulting from food spoilage. The emergence of antibiotic resistance among bacteria has become a significant problem in modern times, increasing the importance of alternative treatment methods to antibiotics. Therefore, the production of effective drugs against harmful microorganisms is important and valuable (Arda, 2006).

S. aureus is a staphylococcal bacterium capable of causing food poisoning and pyogenic infections in humans and warm-blooded animals. It is commonly found in nature and is a significant cause of mastitis. It can contaminate milk and dairy products from carrier cows. Infections caused by S. aureus typically manifest as skin and mucosal infections, such as abscesses, furuncles, impetigo, carbuncles, panaris, hidradenitis, blepharitis, tonsillitis, pharyngitis, and peritonsillar abscess. S. aureus can also lead to conditions like sepsis, endocarditis, pneumonia, food poisoning, and enteritis. (Akan, 2006). *E. faecalis*, on the other hand, is a fecal bacterium found in human and animal feces. Enterococci can cause diseases such as peritonitis, bacteremia, and endocarditis. The presence of a high level of enterococci in water samples indicates the presence of fecal contamination (Akan, 2006; Murray vd.,2016). *P. aeruginosa* is commonly found in nature and can survive for long periods in organic matter and water. It is a component of the intestinal flora in humans and animals and typically causes suppurative and sometimes acute systemic infections. Diseases caused by *P. aeruginosa* include respiratory tract infections, urinary tract infections, skin and soft tissue infections, ear and eye infections, bacteremia, and endocarditis (Tuncer ve Akova, 1997; Murray vd., 2016; Esendal, 2006). *E. coli*, a normal flora of the intestine, becomes an opportunistic pathogen when the host's defense mechanisms are compromised. It can cause diseases such as urinary tract infections, gallbladder and bile duct infections, meningitis, peritonitis, sepsis, sinusitis, and wound infections (Murray vd., 2016). *E. coli* is a major cause of gastroenteritis and can also lead to intestinal diseases, urogenital infections, mastitis, lung inflammations, and wound infections in domestic animals (İzgür, 2006). Klebsiella species, including *K. pneumoniae* and *K. oxytoca*, can cause community or hospital-acquired primary lobar pneumonia (Murray vd., 2016). *K. pneumoniae* is an opportunistic pathogen found in the upper respiratory tract and fecal flora, including in domestic animals. It synergistically causes metritis in horses with *Streptococcus zooepidemicus*. Isolates from dogs have been associated with cystitis, mastitis, and metritis. In pigs, they are responsible for agalactia syndrome (Akan, 2006).

The increasing prevalence of resistance in bacteria has led to a growing importance of anti-infective models in modern medicine and biotechnology. Numerous studies have demonstrated that Schiff bases, which exhibit antimicrobial activity, are among the prominent options in this field. The utilization of Schiff bases as therapeutic agents is considered a

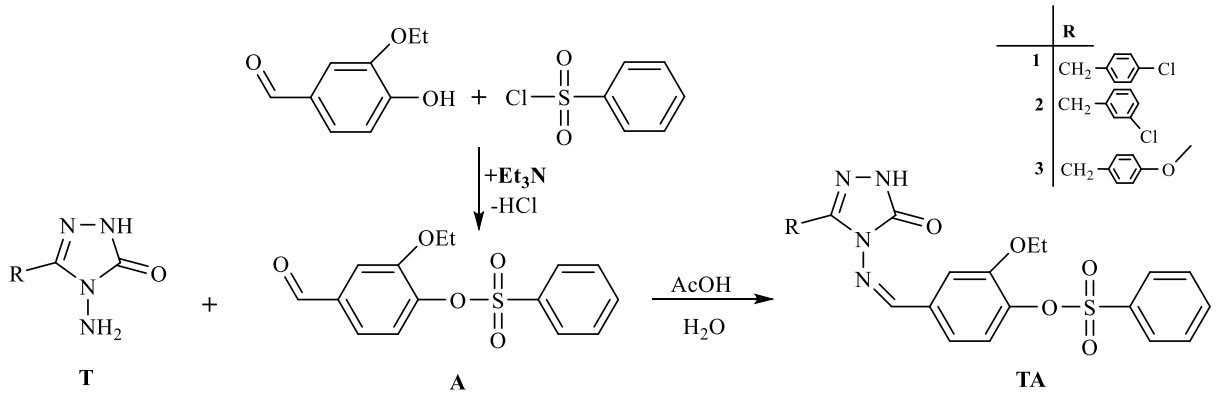
potential treatment approach for the control of pathogenic bacteria. In this study, the efficacy of newly synthesized Schiff bases in controlling certain pathogens crucial for human and animal health has been investigated.

2. MATERIALS AND METHODS

The chemicals utilized in the synthesis of the Schiff bases were procured from Merck, Fluka, and Aldrich companies. The necessary solvents were obtained from domestic or international sources. The melting points of the synthesized compounds were determined using a Stuart SMP30 brand melting point determination apparatus within the scope of the study. The IR spectra of newly synthesized compounds were recorded at the Department of Organic Chemistry Research Laboratory, Faculty of Science and Literature, Kafkas University, using the ALPHA-P BRUKER FT-IR spectrometer. The ^{1}H-NMR and ^{13}C-NMR spectra were acquired at Mersin University Advanced Technology Education, Research, and Application Center, using a BRUKER ULTRASHIELD PLUS BIOSPIN 400 MHz NMR spectrometer.

2.1. Method

In the synthesis section of the study, three new 3-aryl-4-amino-4,5-dihydro-1*H*-1,2,4-triazol-5-one compounds were obtained from the treatment of a benzaldehyde derivative, namely 3-ethoxy-4-hydroxybenzaldehyde, with benzene sulfonyl chloride in the presence of triethylamine. These compounds were synthesized separately from the treatment of 3-ethoxy-4-(benzenesulfonyloxy)benzaldehyde, which was obtained through the aforementioned reaction, resulting in three novel 3-aryl-4-(benzenesulfonyloxy)benzylideneamino-4,5-dihydro-1*H*-1,2,4-triazol-5-one compounds. (Özdemir, 2016).



Scheme 1. Synthesis of Schiff Base Compounds (Özdemir, 2016)

2.2. Synthesis of 3-Aryl-4-[3-ethoxy-4-(benzenesulfonyloxy)benzylideneamino]-4,5-dihydro-1*H*-1,2,4-triazol-5-one (TA) Compounds

After dissolving three 3-aryl-4-amino-4,5-dihydro-1*H*-1,2,4-triazol-5-one (T) compounds in acetic acid, 0.01 mol of 3-ethoxy-4-(benzenesulfonyloxy)benzaldehyde (A) was added, and the mixture was refluxed under a cooling condenser for 1.5 hours. The resulting mixtures were left overnight in a refrigerator, and the precipitated crude product was filtered, washed with distilled water, dried under vacuum over $CaCl_2$ in a desiccator, and recrystallized from ethanol.

2.2.1. 3-p-Chlorobenzyl-4-[3-ethoxy-4-(benzenesulfonyloxy) benzylidene-amino]-4,5-dihydro-1H-1,2,4-triazol-5-one (TA1): Productivity 96%, mp. 172°C. IR (KBr) cm^{-1}: 3169 (NH), 1704 (C=O), 1587 (C=N), 1370 ve 1174 (SO_2), 845 (1,4- Disubstitute benzenoid ring), 752 ve 687 (monosubstitue benzenoid ring) ^{1}H NMR (200 MHz, DMSO-d_6): δ 11.12 (t, 3H, OCH_2CH_3; *J*=7.20 Hz), 3.79 (q, 2H, OCH_2CH_3; *J*=7.20 Hz), 4.07 (s, 2H, CH_2Ph), 7.29 (d, 1H, ArH), 7.34-7.40 (m, 6H, ArH), 7.67 (t, 2H, ArH; *J*=8.00 Hz), 7.81-7.85 (m, 3H, ArH), 9.64 (s, 1H, N=CH), 12.03 (s, 1H, NH). ^{13}C NMR (50Mz, DMSO-d_6): δ 14.04 ($OCH_2\underline{CH_3}$), 30.48 (CH_2Ph), 63.98 ($O\underline{CH_2}CH_3$), 111.99, 120.53, 124.26, 128.14 (2C), 128.36 (2C), 129.46 (2C), 130.56 (2C), 131.37, 133.68, 134.82 (2C), 135.12, 139.53, 151.12 (ArC), 145.80 (Triazole C_3), 150.82 (N=CH), 151.97 (Triazole C_5).

2.2.2. 3-m-Chlorobenzyl-4-[3-ethoxy-4-(benzenesulfonyloxy) benzylidene-amino]-4,5-dihydro-1H-1,2,4-triazol-5-one (TA2) Productivity 97%, mp. 179°C. IR (KBr) cm^{-1}: 3166 (NH), 1705 (C=O), 1576 (C=N), 1350 ve 1194 (SO_2), 817 ve 701 (1,3-disubstitue benzenoid ring), 754 ve 691 (monosubstitue benzenoid ring). ^{1}H NMR (200 MHz, DMSO-d_6): δ 1.11 (t, 3H, OCH_2CH_3; *J*=7.20 Hz), 3.81 (q, 2H, OCH_2CH_3; *J*=6.80 Hz), 4.09 (s, 2H, CH_2Ph), 7.25-7.33 (m, 4H, ArH), 7.37-7,39 (m, 2H, ArH), 7.66 (t, 2H, ArH; *J*=8.00 Hz), 7.80-7.84 (m, 3H, ArH), 9.64 (s, 1H, N=CH), 12.04 (s, 1H, NH). ^{13}C NMR (50Mz, DMSO-d_6): δ 14.04 ($OCH_2\underline{CH_3}$), 30.70 (CH_2Ph), 64.00 ($O\underline{CH_2}CH_3$), 111.84, 120.68, 124.23, 126.74, 127.41, 128.14 (2C), 128.73, 129.47 (2C), 130.26, 132.94, 133.67, 134.85, 135.10, 138.26, 139.55, 151.09 (ArC), 145.65 (Triazole C_3), 150.85 (N=CH), 151.97 (Triazole C_5).

2.2.3. 3-p-Methoxybenzyl-4-[3-ethoxy-4-(benzenesulfonyloxy) benzylidene-amino]-4,5-dihydro-1H-1,2,4-triazol-5-one (TA3): Productivity 95%, mp. 174°C. IR (KBr) cm^{-1}: 3209 (NH), 1696 (C=O), 1595 (C=N), 1366 ve 1174 (SO_2), 856 (1,4-disubstitue benzenoid ring), 755 ve 685 (monosubstitue benzenoid ring). ^{1}H NMR (200 MHz, DMSO-d_6): δ 1.12 (t, 3H, OCH_2CH_3; *J*=7.20 Hz), 3.71 (s, 3H, OCH_3), 3.82 (q, 2H, OCH_2CH_3; *J*=7.20 Hz), 3.98 (s, 2H, CH_2Ph), 6.85 (d, 2H, ArH; *J*=8.80 Hz), 7.22 (d, 2H, ArH; *J*=8.80 Hz), 7.30 (d, 1H, ArH; *J*=8.00 Hz), 7.39 (s, 1H, ArH), 7.42 (m, 1H, ArH), 7.66 (t, 2H, ArH; *J*=8.00 Hz), 7.81-7.85 (m, 3H, ArH), 9.64 (s, 1H, N=CH), 11.98 (s, 1H, NH). ^{13}C NMR (50Mz, DMSO-d_6): δ 14.03 ($OCH_2\underline{CH_3}$), 30.29 (CH_2Ph), 55.01 (OCH_3), 63.99 ($O\underline{CH_2}CH_3$), 112.05, 113.85 (2C), 120.47, 124.27, 127.57, 128.14 (2C), 129.47 (2C), 129.72 (2C), 133.76, 134.83, 135.14, 139.50, 151.15, 158.06 (ArC), 146.46 (Triazole C_3), 150.83 (N=CH), 151.87 (Triazole C_5).

2.3. Test Bacteria

The bacterial strains *S. aureus* (ATCC 25923), *E. faecalis* (ATCC 29212), *K. pneumoniae* (ATCC 700603), *E. coli* (ATCC 25922), and *P. aeruginosa* (ATCC 27853) utilized in the study were obtained from the Department of Microbiology, Faculty of Medicine, Kafkas University.

2.2.1. Bacterial Culture Media

To activate the bacteria, Nutrient Broth (Oxoid) was utilized, while for antimicrobial studies, Muller Hinton Agar (Oxoid) was employed.

2.4. *Preparation of Schiff Base Solutions*

The stock solutions of Schiff bases, whose antimicrobial effect will be determined, were prepared by dissolving them in DMSO at concentrations of 10 mg/ml and 4 mg/ml. Subsequently, the 4 mg/ml stock solution was diluted each time to prepare dilutions of 2 mg/ml, 1 mg/ml, and 0.5 mg/ml.

2.5. *Disc Diffusion Method*

The test bacteria were inoculated into Nutrient Broth and left to incubate overnight. Following incubation, the turbidity was adjusted to 0.5 McFarland. Subsequently, 100 µl of each bacterial solution was spread onto Muller Hinton Agar using a Drigalski spatula. After inoculation, the petri dishes were allowed to air dry at room temperature for 10 minutes. Three 6mm sterile discs were impregnated with dilutions of Schiff base at concentrations of 10 µl/ml, 4 µl/ml, 2 µl/ml, 1 µl/ml, and 0.5 µl/ml, and then placed onto the surface of the dried petri dishes. Dimethyl sulfoxide (DMSO) was used as the negative control, while ampicillin/sulbactam, tigecycline, and amoxicillin/clavulanic acid were used as positive controls. The petri dishes were then incubated at 37°C for 24 hours. By measuring the inhibition zone diameters formed after incubation, Schiff bases that formed a zone diameter of 5 mm and above were evaluated as effective (Aydınlı Esen, 2006).

3. RESULTS AND DISCUSSION

The antimicrobial effect of Schiff bases was evaluated, revealing that TA1 (3-p-Chlorobenzyl-4-[3-ethoxy-4-(benzenesulfonyloxy)benzylideneamino]-4,5-dihydro-1*H*-1,2,4-triazol-5-one) Schiff base exhibited antimicrobial activity against both *E. coli* and *K. pneumoniae*, while TA2 (3-m-Chlorobenzyl-4-[3-ethoxy-4-(benzenesulfonyloxy)benzylideneamino]-4,5-dihydro-1*H*-1,2,4-triazol-5-one) Schiff base showed antimicrobial activity only against *K. pneumoniae*. Both TA1 and TA2 Schiff bases exhibited inhibitory effects at a concentration of 10 mg/ml. However, TA3 (3-p-Methoxybenzyl-4-[3-ethoxy-4-(benzenesulfonyloxy)benzylideneamino]-4,5-dihydro-1*H*-1,2,4-triazol-5-one) Schiff base showed no significant effect on the test bacteria at any concentration tested. Additionally, concentrations below 10 mg/ml of the Schiff bases did not exhibit any inhibitory effects on *E. coli, S. aureus, E. faecalis, K.*

pneumoniae, or *P. aeruginosa*. Figure 2 shows the inhibition zones of Schiff bases against the test bacteria.

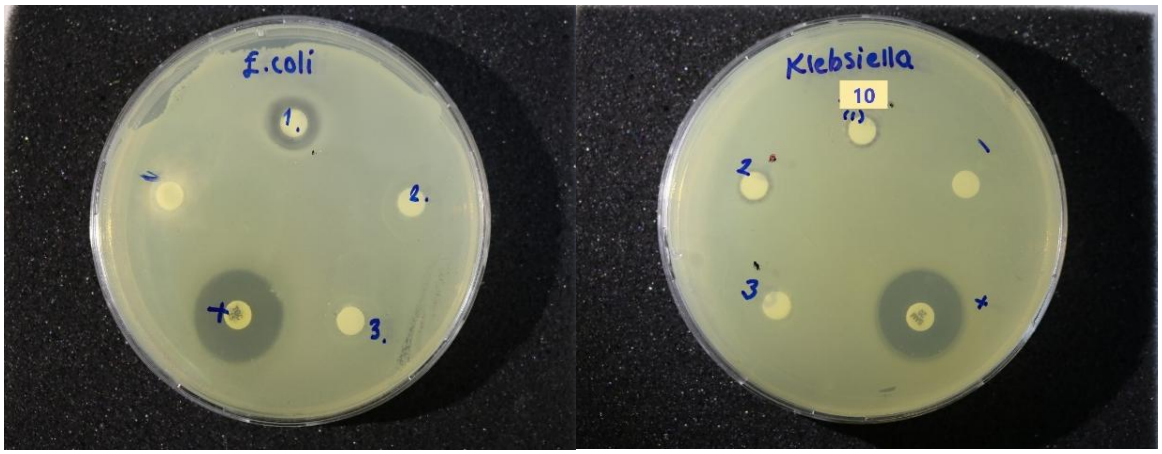


Figure 1. The inhibition zones formed by Schiff base No.1 against *E.coli* at a dose of 10 mg/ml, and the inhibition zones formed by Schiff base No.2 against *K.pneumoniae* at a dose of 10 mg/ml

Table 1. Inhibition zone diameters of utilized Schiff bases

No	Schiff base	Inhibition zone (mm)				
		S. aureus	*E. faecalis*	*K.pneumoniae*	*E.coli*	*P. aeruginosa*
1	TA1	≤6	≤6	8	11	≤6
2	TA2	≤6	≤6	8	≤6	≤6
3	TA3	≤6	≤6	≤6	≤6	≤6

Tablo 2. Effect Dosages of Schiff Bases

No	Schiff base	Testing Bacteria				
		S. aureus	*E. faecalis*	*K.pneumoniae*	*E.coli*	*P. aeruginosa*
1	TA1	-	-	10	10*	-
2	TA2	-	-	10	-	-
3	TA3	-	-	-	-	-

*mg/ml

When reviewing studies similar to the research conducted with triazole derivative Schiff bases, similarities in results have been observed. Generally, it has been reported that simple Schiff bases exhibit insignificant activity in these studies, whereas substances coordinated with vanadium (IV) metal demonstrate higher activity (Chohan vd., 2010). In the study conducted by Bagihalli and colleagues, it was determined that triazole derivatives of

Schiff bases exhibited varying degrees of effectiveness against *E. coli, S. aureus, S. pyogenes, P. aeruginosa,* and *S. typhi* at various doses (Bagihalli vd., 2008). Bayrak and colleagues have determined that newly synthesized triazole derivative Schiff bases exhibit either good or moderate inhibitory effects on test bacteria (Bayrak vd., 2009). In another study, the effects of 1,2,4-triazole-3-thione-imidazole 1 derivative on *E. coli, S. aureus, B. subtilis, S. typhi,* and *S. dysentrae* bacteria were investigated. It was observed that compounds 1b, 1d, and 1f exhibited similar characteristics to tetracycline (inhibition zone: 14-17 mm) (Ghasemzadeh vd., 2018). Yüksek et al. investigated the effects of 9 synthesized triazole-derived Schiff bases on various bacterial strains including *B. subtilis, B. cereus, Y. enterocolitica, S. aureus, E. coli, P. multocida*, and *K. pneumoniae* using the agar well diffusion method. The study revealed that all tested Schiff bases were effective against all investigated bacteria except for *P. multocida* and *K. pneumoniae*. Specifically, it was observed that 4 out of the 9 Schiff bases did not exhibit efficacy against *P. multocida*, while 2 of them were ineffective against *K. pneumoniae* (Yüksek vd., 2017). Zeydan determined the Minimum Inhibitory Concentration (MIC) values of 10 Triazol Schiff bases against *S. aureus, S. epidermidis*, *E. coli, K. pneumoniae*, and *P. aeruginosa*. While none of the substances were effective against *K. pneumoniae*, nine of them exhibited effectiveness against *S. aureus*, with MIC values ranging between 156 mg/ml and 612 mg/ml (Zeydan, 2009). In some studies, 1,2,4-triazole-pyrazole derivatives have shown weak to moderate antibacterial activity (MIC: 62.5-250µg/mL) against various bacteria including *E. coli, S. typhi, S. pneumoniae, B. subtilis,* and *C. tetani* (Prasad et al., 2018). Similarly, 1,2,4-triazole-thiazole derivatives exhibited antimicrobial activity (MIC: 1.95–62.5µg/mL) against two Gram-positive bacteria (*L. monocytogenes* and *S. aureus*) and three Gram-negative bacteria (*E.coli, S. typhimurium*, and *P. aeruginosa*) (Nastasa et al., 2018). Additionally, it has been observed that some triazolothiadiazole-pyrimidone derivatives exhibited inhibitory properties ranging from 44% to 92% at 25µg/mL against *B. amiloliquefaciens, S. aureus,* and *B. subtilis* (Cui et al., 2017).

In numerous studies, the antimicrobial, antifungal, and antiviral effects of Schiff bases have been evaluated. The majority of obtained results support the potential of Schiff bases as alternatives to antibiotics. Some studies have even found Schiff bases to exhibit more effective activity than antibiotics. In our conducted research, it was observed that two newly

synthesized Schiff bases demonstrated antimicrobial activity. It is anticipated that these effective Schiff bases could be utilized in combating sensitive bacterial species

4. CONCLUSION

This study investigated the antimicrobial properties of Schiff base derivatives of 3-aryl-4-(benzenesulfonyloxy) benzylideneamino-4,5-dihydro-1*H*-1,2,4-triazol-5-one. The findings of our experiments revealed that one specific compound, namely 3-p-chlorobenzyl-4-[3-ethoxy-4-(benzenesulfonyloxy) benzylideneamino]-4,5-dihydro-1*H*-1,2,4-triazol-5-one, exhibited remarkable efficacy against both *E. coli* and *K. pneumoniae*.

This promising antimicrobial activity underscores the potential of these synthesized compounds as effective agents in combating bacterial infections. The observed effectiveness against such clinically relevant bacteria highlights the importance of further investigations, including *in vivo* studies and toxicity assessments, to validate their therapeutic potential and safety profile. Additionally, exploring the mechanisms underlying their antimicrobial action could provide valuable insights for the development of novel antimicrobial agents to address the growing challenge of antibiotic resistance.

In conclusion, the results of this study suggest that Schiff base derivatives of 3-aryl-4-(benzenesulfonyloxy) benzylideneamino-4,5-dihydro-1*H*-1,2,4-triazol-5-one hold promise as potential candidates for the development of new antimicrobial drugs, emphasizing the need for continued research in this area to address the pressing global health threat posed by antibiotic-resistant bacteria.

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This study has been conducted based on the Master's thesis carried out at the Institute of Science, Kafkas University.

Conflict of Interest

There are no conflicts of interest among the authors.

Author Contributions

The research was conceived and written by E. Koc, antimicrobial analyses and data evaluation were conducted by S.G. Talay, N. Mutlu, synthesis of chemicals used in the study was performed by G. Özdemir Toraman, M. Beytur and characterization was carried out by H. Yuksek.

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