American Journal of Bioscience and Clinical Integrity
https://biojournals.us/index.php/AJBCI
ISSN: 2997-7347

Synthesis and Characterization of New Imidazole Derivatives and Evaluation of Biological Efficacy

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Received: 2025, 15, Jan
Accepted: 2025, 21, Feb
Published: 2025, 07, Mar

Annotation: The present research involves the synthesis of new imidazole derivatives, known for their good biological activity, prepared by the reaction of Schiff bases with the amino acid glycine in the presence of absolute ethanol in a conventional manner. Physical and spectroscopic techniques, including FT-IR spectroscopy, proton and carbon nuclear magnetic resonance spectroscopy (NMR)-[1H NMR]-[13C], and the determination of the produced compounds' melting point, were used to confirm the structures. The effect of some of the prepared compounds on the growth of two types of bacterial isolates, one of which is Gram-negative (G-), i.e., E. coli, and the other Gram-positive (G+) Staphylococcus aureus, was studied using the antibiotic amoxicillin as a control sample. Some prepared compounds showed good inhibitory activity against the bacterial species used.

Keywords: Heterocyclic, Imidazole, biological activity.

1. Introduction

Heterocyclic compounds such as nitrogen, sulfur, or oxygen have different atoms organized in rings. These chemicals are widely distributed in nature. They are valuable and significant in many fields, including as industry and medicine [1]. The chemical, as mentioned earlier, contains one heteroatom. Heterocyclic compounds can contain several heteroatoms and are classified according to the ring's kind and number of atoms [2]. **Imidazole** One of the most important nitrogen-containing five-membered heterocyclic structures, imidazole rings are present in many pharmacological and natural compounds. Furthermore, imidazole heterocyclic molecules have a critical role in medicinal chemistry and the treatment of some illnesses. Around the world, a lot of activity is going on to produce new medical compounds [3]. It is favorable for the imidazole group to bind to different receptors and enzymes in biological systems through various weak interactions, showing a range of biological activities because of the imidazole structure's distinctive features and electron-rich qualities[4]. Many imidazole-containing compounds with great medical promise are currently being utilized extensively as clinical medications to treat a variety of illnesses, including antibacterial [5], antifungal [6], and anti-inflammatory [7] conditions. Researchers have discovered that imidazole-based compounds have antiviral [8], antiparasitic [9], and anticancer properties [10] due to their crucial pharmacological or biological actions and enormous medical potential.

2. Materials and Methods:

2.1. Chemicals used: Chemicals produced by BDH Thomas, Fluka, Merck, and Aldrich were utilized.

2.2. Preparation of imidazole

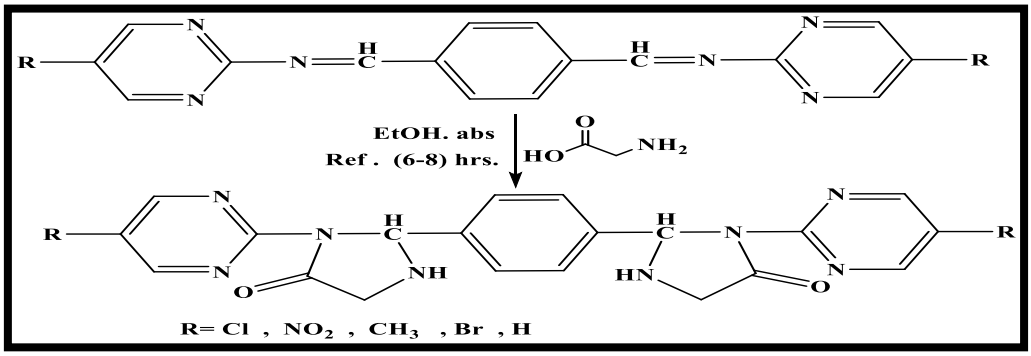
(0.001 mol) of the prepared Schiff bases were mixed in (15 ml) of absolute ethanol with (0.001 mol, 0.9 gm) of glycine dissolved in (10 ml) of absolute ethanol, and the mixture was elevated for (6-8 hours). The completion of the reaction was confirmed using the TLC technique. The mixture was cooled to room temperature and filtered, then washed and recrystallized with ethanol [11,12]. As shown in **Table** (1).

Table (1): Some physical properties of for Prepared compounds (S11-S15).

Comp. No.	R	Molecular formula	m.p. °C	Yield%	Color
S11	4-Cl	$C_{20}H_{16}Cl_2N_8O_2$	223-225	76	Light Yellow
S12	4-NO2	$C_{20}H_{16}N_{10}O_6$	245-247	71	Brown
S13	4-CH_3	$C_{22}H_{22}N_8O_2$	232-234	78	Yellow
S14	4-Br	$C_{20}H_{16}Br_2N_8O_2$	219-221	69	Red
S15	4-H	$C_{20}H_{18}N_8O_2$	247-249	73	Blue

.2.4. study of Biological activity

The pathology laboratories at Tikrit University provided two isolates containing antibiotic-resistant bacteria, the first was a strain of Escherichia coli and the second was a strain of Staphylococcus aureus. Agar medium No. 2 was used, prepared according to the manufacturer's instructions [13,14]. Agar-Well diffusion method was used to evaluate the antibacterial activity of he tested chemical compounds against the growth of any pathogenic bacteria. The medium was prepared and sterilized in an autoclave and poured into Petri dishes to solidify [15,16]. The bacterial suspension was then poured onto the surface. Three holes were punched in each dish using a cork punch and different concentrations of the previously prepared compounds were introduced into these holes [17,18]. The dishes were then incubated at 37 degrees after 24 hours, approximately one day, and the results were read the next day using an inhibition diameter. The solutions were prepared at three concentrations for each substance (0.01, 0.001, 0.0001) mg/ml [19,20].



Scheme (1): Path of the Ready Compounds (S11-S15)

3. Results and discussions

3.1. Characterization of imidazole.

The FT-IR spectrum showed a band at (3210-3165) cm^{-1} for (NH), a band at (1672-1659) cm^{-1} for (C=O), a band at (1247-1211) cm^{-1} for (C-N), two bands at (2997-2916 & 2943-2856) cm^{-1} for aliphatic (CH), two bands for (Ar-C=C) at (1566-1518 & 1487-1471) cm^{-1}, a band for aromatic (CH) at (3062-3022) cm^{-1}[21,22], as in Table 2 and Figures 1 and 2.

Table (2): FT-IR absorption results for Prepared compounds (S11-S15)

Comp. No	R	ν(N-H)	ν(C-H) Arom.	(C-H) Aliph.	(C-O)	(C-N)	(C=C) Arom.	Others
S11	4-Cl	3194	3022	2916 2856	1664	1247	1518 1479	ν (C-F) 717
S12	4-NO2	3187	3043	2943 2879	1672	1225	1532 1481	ν(N-O) as sy15276. Sy1322
S13	4-CH_3	3179	3062	2940 2871	1659	1233	1547 1471	ν (C-F)953
S14	4-Br	3165	3049	2997 2943	1670	1211	1566 1487	ν (C-Br) 555
S15	4-H	3210	3051	2929 2883	1668	1234	1531 1477	--

The ^{1}H-NMR spectrum of compound S11 showed two signals at (7.99, 7.74) ppm for (Ar-CH), a signals at (7.17) ppm for (NH), a signals at (6.77) ppm for (CH), and a signals at (3.95) ppm for (CH_2)[23]. As in Figure 3

The ^{1}H-NMR spectrum of compound S13 showed two signals at (7.80, 7.37) ppm for (Ar-CH), a signals at (6.98) ppm for (NH), a signals at (6.17) ppm for (CH), a signals at (4.06) ppm for (CH_2), and a signals at (2.22) ppm for (CH_3). As in Figure 3

The ^{13}C-NMR spectrum of compound S13 showed a signal at (161.21) for (C=O), signals at (153.23-129.59) for (Ar-C=C), a signal at (65.51) for (CH), and a signal at (33.97) for (CH_2). As in Figure 5

The ^{13}C-NMR spectrum of compound S13 showed a signal at (169.64) for (C=O), signals at (153.89-127.46) for (Ar-C=C), a signal at (63.83) for (CH), a signals at (44.32) ppm for (CH_2), and a signal at (30.87) for (CH_3). As in Figure 6

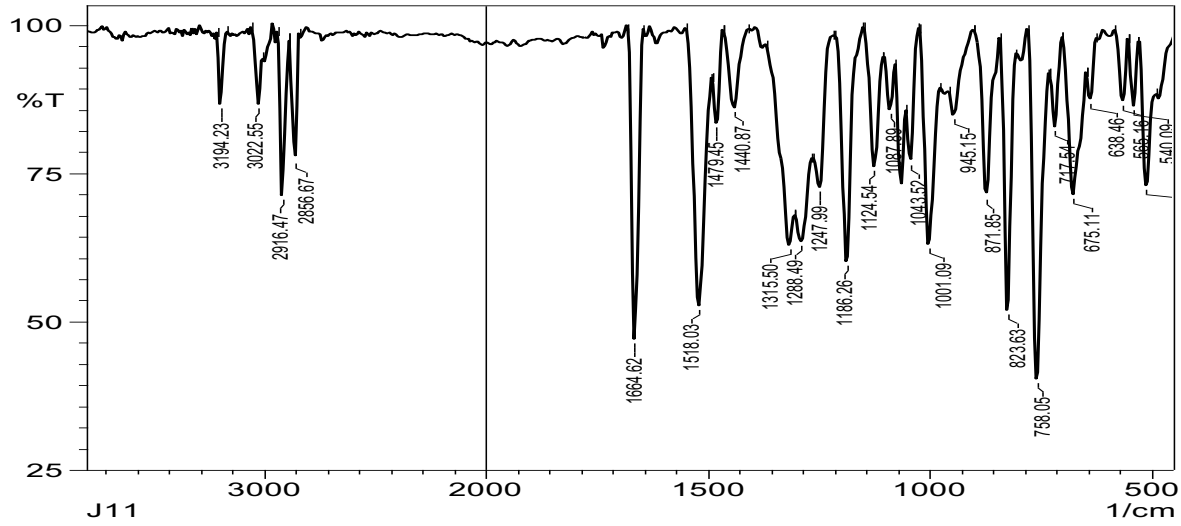


Figure (1): The compound's FT-IR spectra (S11).

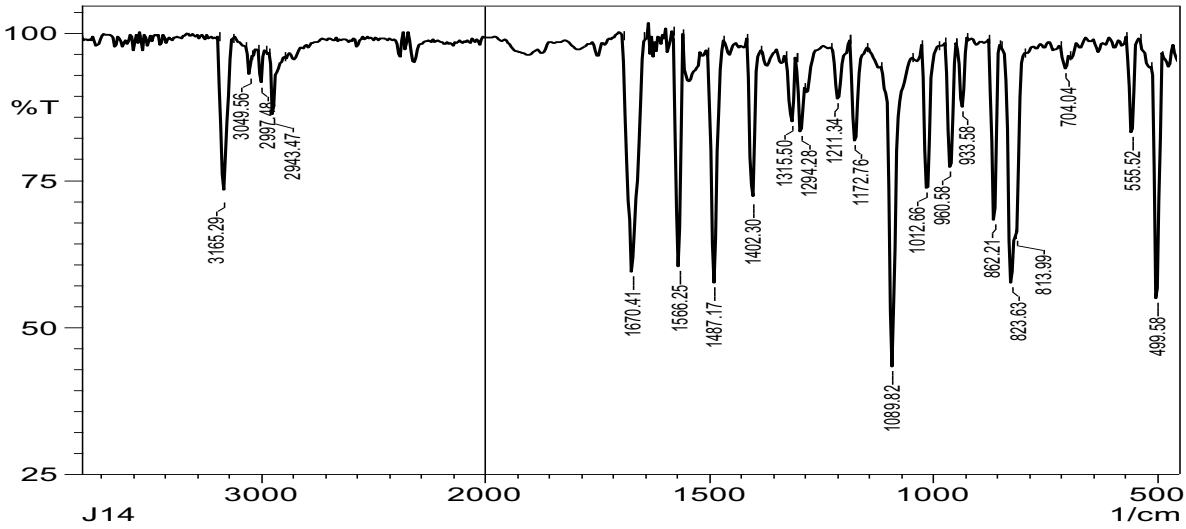


Figure (2): The compound's FT-IR spectra (S14).

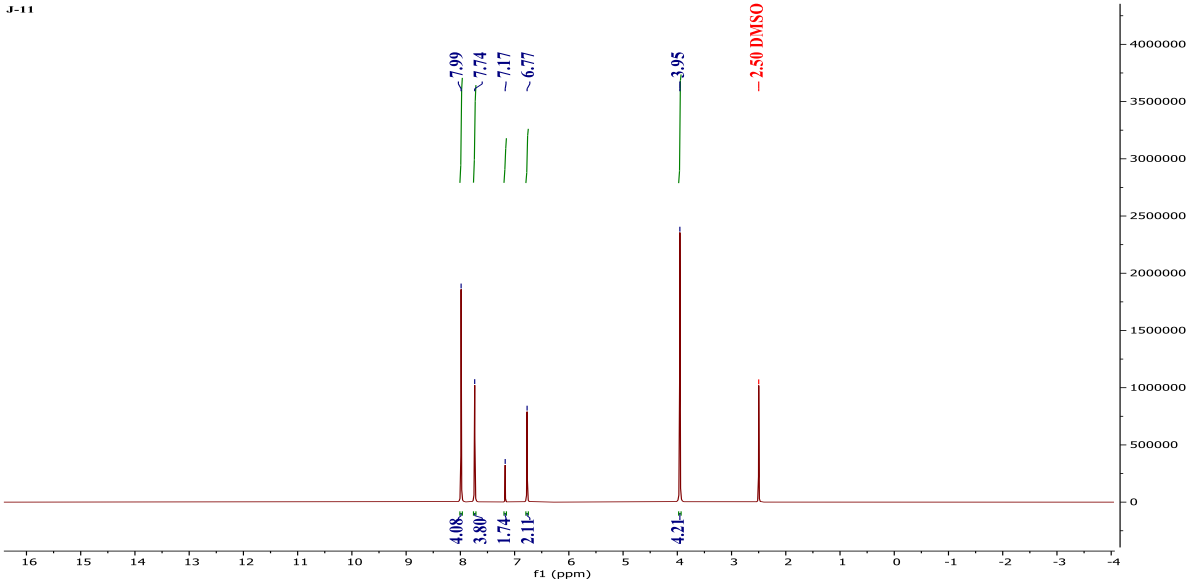


Figure (3): 1-H NMR spectra of the substance (S11).

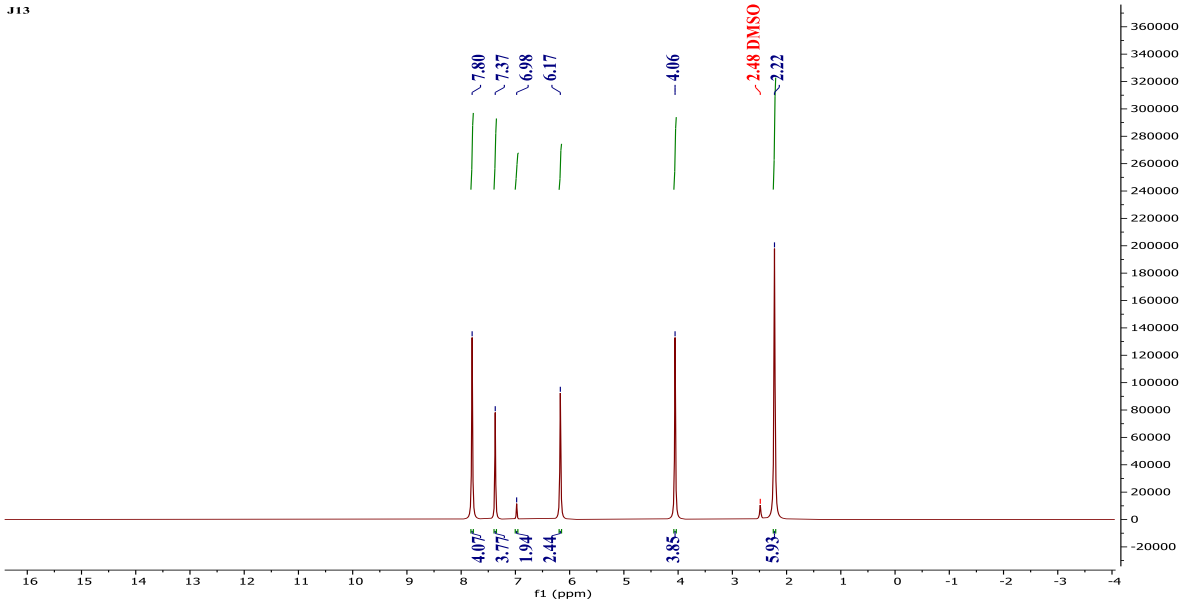


Figure (4): 1-H NMR spectra of the substance (S13).

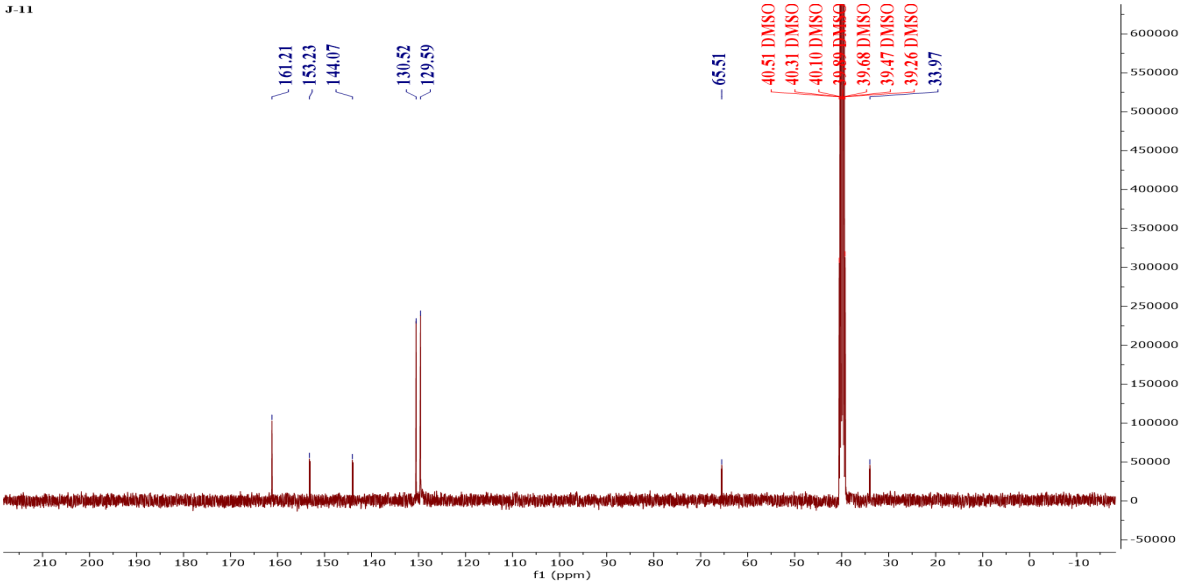


Figure (5): ^{13}C-NMR spectra of the substance (S11).

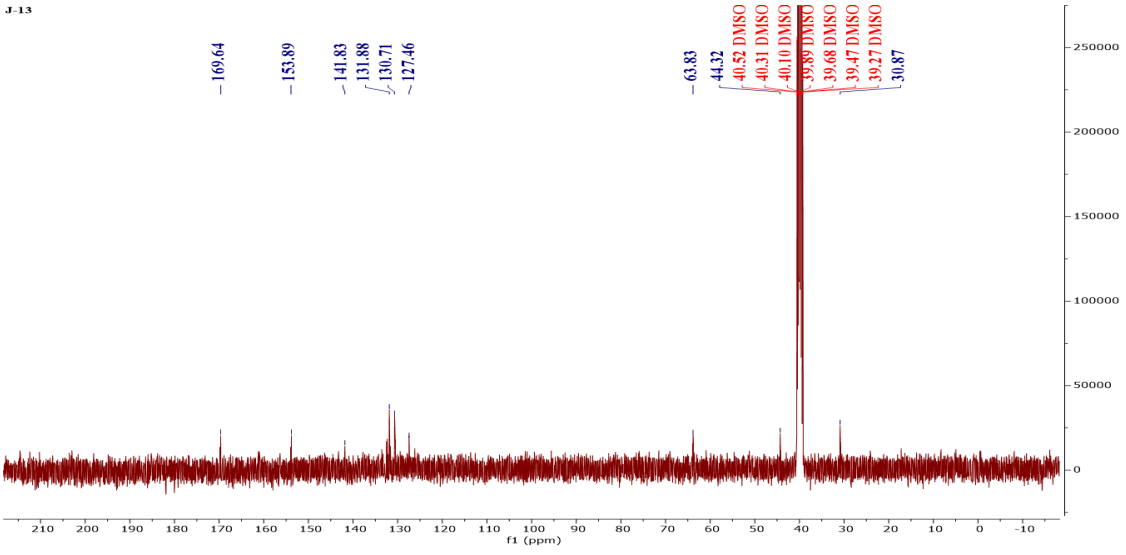
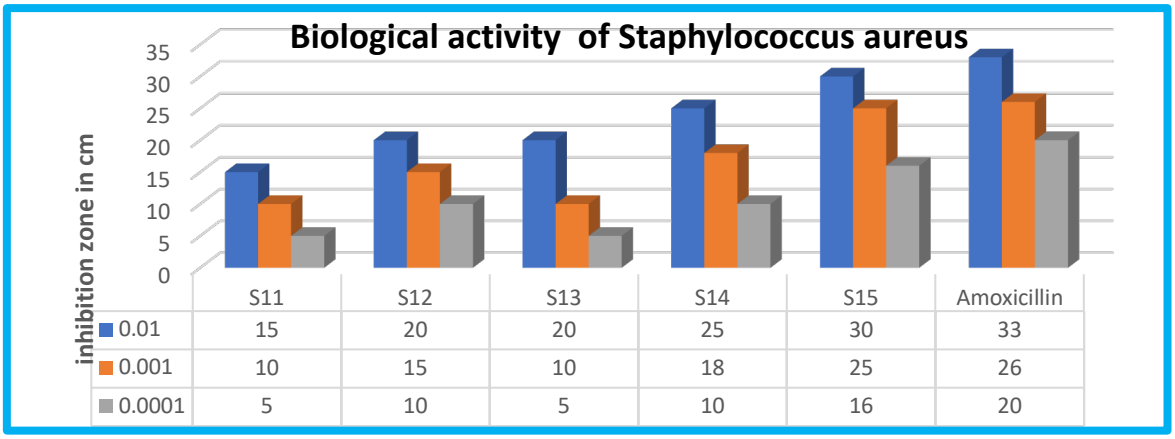


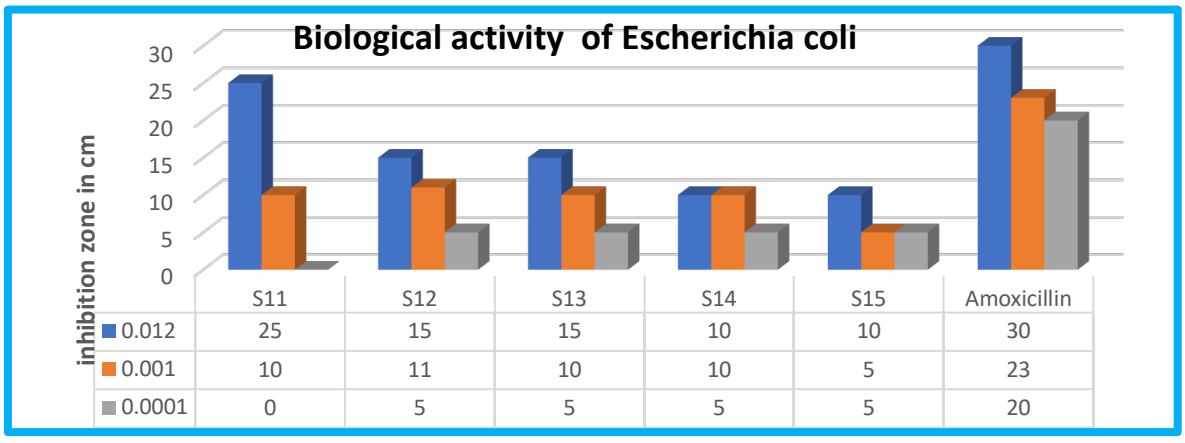
Figure (6): 13C-NMR spectra of the substance (S13).

3.2. Evaluation of the Biological Activity of Prepared Compounds

Gram-positive Staphylococcus aureus and Gram-negative Escherichia coli were the two types of bacteria that were tested against a couple of the compounds produced in this study. The test was carried out on Petri plates using the diffusion technique [24,25]. The inhibitory zone width of several of the generated compounds was evaluated at dosages of 0.1, 0.01, and 0.001 mg/ml using Mueller-Hinton medium.The outcomes were compared with those of conventional antibiotics [26,27]. It was observed that some of these produced compounds clearly affected the first kind of bacteria in comparison to the first type of bacteria, while others clearly affected the second type of bacteria in comparison to the first type of bacteria [28,29]. Another kind Where compounds (S14, S15) showed the highest inhibition rate against Staphylococcus aureus with a diameter of (30, 25) mm, respectively. As for Escherichia coli bacteria, compound (S11) showed the highest inhibition at a rate of (25) mm. It is noted that the inhibition increases with increasing concentration, as the compounds showed the highest inhibition at a concentration of 0.01 mg/ml[30,31] . as shown in Table (3), Scheme (2), (3), Figures (6), (7).



Scheme (2): Inhibitory activity of (S11-S15) for Staphylococcus aureus



Scheme (3): Inhibitory activity of (S11-S15) for Escherichia coli

Table (3): Biological efficacy of produced substances and control methods (measured in millimeters of inhibition).

Comp. No.	E. Coil Conc. mg/ml			Staph. Aureus Conc. mg/ml		
	0.01	0.001	0.0001	0.01	0.001	0.0001
S11	25	10	0	15	10	5
S12	15	11	5	20	15	10
S13	15	10	5	20	10	5

S14	10	10	5	25	18	10
S15	10	5	5	30	25	16
Amoxicillin	30	23	20	33	26	20

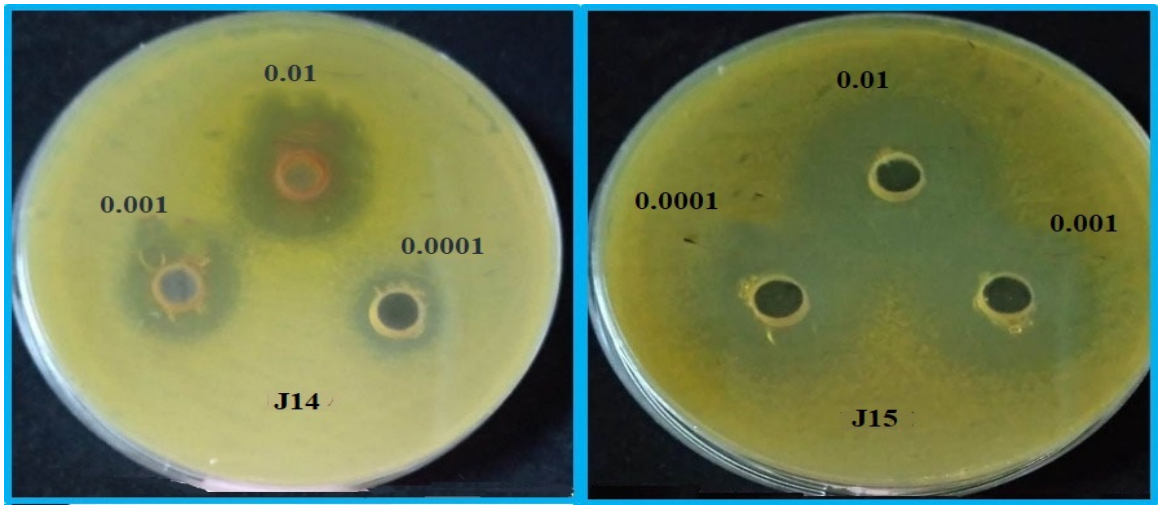


Figure 6: Biological effectiveness of the compound S14,S15 against becteral Staph.aureus

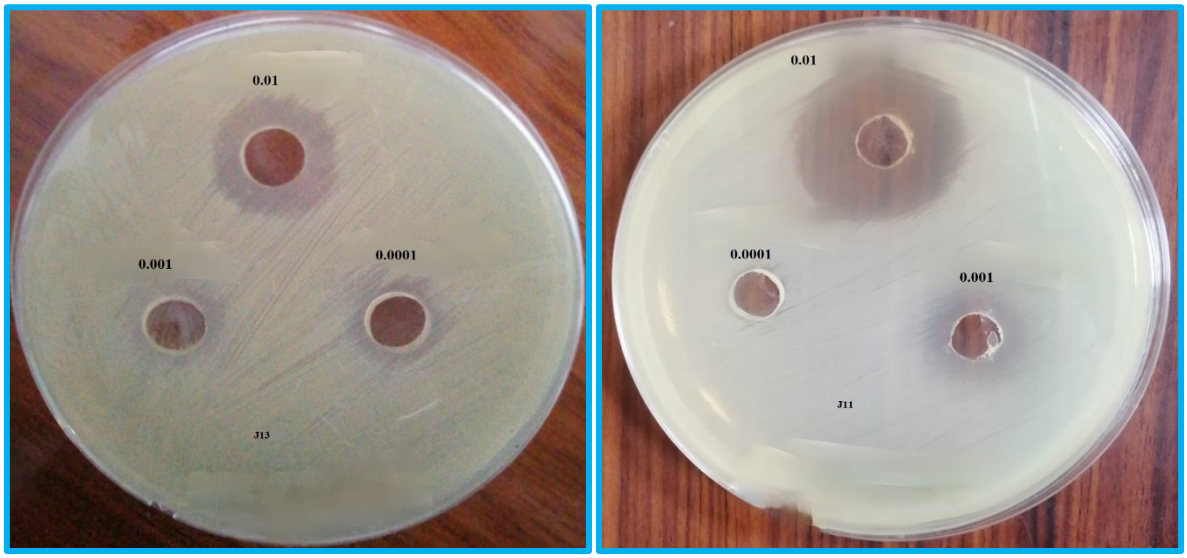


Figure7: Biological effectiveness of the compound S11,S13 against becteral E.COLI

4. Conclusions

Five-membered imidazole rings are produced when amino acids like glycine react with the (C=N) group of hydrazone or Schiff bases. Since the produced chemicals demonstrated great purity and a good product percentage, their authenticity was verified by spectroscopic tests such as nuclear magnetic resonance and infrared spectroscopy. In comparison to the antibiotic used as a control sample, these compounds also shown strong activity against the two kinds of bacteria utilized.

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