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Article

Preparation and Characterization of New Imidazole Derivatives Derived From Hydrazones and Study of their Biological and Laser Efficacy

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Abstract: This research aims to synthesize and characterize imidazole derivatives from the reaction of hydrazones with amino acids (glycine and alanine) using conventional methods. The validity of the synthesized compounds was confirmed through physical measurements such as melting point and color, as well as spectroscopic methods such as infrared spectroscopy and proton nuclear magnetic resonance spectroscopy. The research methods included testing the biological effectiveness of the compounds against two types of bacteria: Gram-positive Staphylococcus epidermidis and Gram-negative Klebsiella pneumoniae. The compounds (M11-M15) were also irradiated using a neodymium nanosecond laser system (Nd laser) with a wavelength of 808 nm and a frequency of 5 Hz. Changes in melting point and color were measured after irradiation. The results showed that the synthesized compounds exhibited significant antibacterial activity against both types of bacteria. Additionally, some compounds demonstrated high stability under laser irradiation, while others experienced changes in melting point and color, indicating alterations in bond structures.

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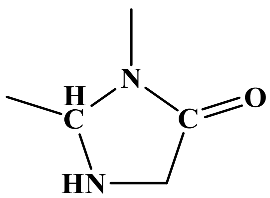
1. Introduction

Imidazole is a pentagonal ring containing two nitrogen atoms, two carbon atoms, and a carbon group.



Imidazole rings are among the most significant nitrogen-containing heterocyclic scaffolds and are present in many natural products and pharmaceutical compounds[1]. Furthermore, heterocyclic imidazole compounds are crucial to medicinal chemistry and are used extensively in the treatment of a wide range of illnesses [2]. Worldwide, there is a strong push to produce new pharmaceutical derivatives [3]. It is favorable for the imidazole group to bind to different receptors and enzymes in biological systems through a range of weak contacts, showing a diversity of biological activities, because of the distinct electron-rich structural characteristics of the imidazole scaffold [4–5]. Currently, a wide range of imidazole-containing substances with excellent clinical medical potential are being utilized extensively to treat a variety of illnesses, including anti-inflammatory, antioxidant, and antibacterial conditions [6-8]. Laser It is the amplification of light by stimulated emission of radiation or the amplification of microwaves by stimulated emission of radiation. The word laser is an abbreviation for light amplification of stimulated emission of radiation because these rays are in the form of very narrow lines. a light. Lasers are an unusual source of light because they produce beams of light with different wavelengths, for example blue light is shorter than red light. Very small spot of light. Lasers have been used in many different fields and technologies [9].

2. Materials and Methods

Chemicals Used

Chemical prepared by Aldrich, BDH Thomas, Fluka and Merck

Instruments used

A thermometer 9300, a KBr disk with a 400–4000 cm–1 scale, an FT-IR 8400S Shimadzu spectrophotometer, and 1H– and 13C–NMR spectra from Bruker apparatus running at 400 MHz are used to determine the melting point. Using Fluka silica gel plates with a thickness of 0.2 mm, thin-layer chromatography (TLC) was examined.

Preparation of Imidazole derivatives (M6-M10).[10]

Add (0.01) mole of Hydrazone to (25) ml of ethanol, and stir well with (0.01) mole of amino acids (glycine, alanine) and a few drops of triethylamine (Et3N), and stir in the opposite direction (13-14) hour after cooling: The solid product is collected, recrystallized with ethanol, and TLC technology is used to ensure the reaction is complete. The physical properties appear in Table (1).

Tabel 1. Some Physical Properties of for Prepared Compound (M6-M15)

Comp. No.	R	Molecular formula	m.p. °C	Yield%	Color
M6	4-NO2	$C_{16}H_{16}N_6O_5S_2$	204-206	75	Orange
M7	4-Cl	$C_{16}H_{16}ClN_5O_3S_2$	216-218	73	Brown
M8	4-CH3	$C_{17}H_{19}N_5O_3S_2$	232-234	67	Brown
M9	4-Br	$C_{16}H_{16}BrN_5O_3S_2$	241-243	58	White
M10	4-H	$C_{16}H_{17}N_5O_3S_2$	219-221	71	Orange
M11	4-NO2	$C_{17}H_{18}N_6O_5S_2$	238-240	64	White
M12	4-Cl	$C_{17}H_{18}ClN_5O_3S_2$	209-211	69	Blue
M13	4-CH3	$C_{18}H_{21}N_5O_3S_2$	225-227	78	Orange
M14	4-Br	$C_{17}H_{18}BrN_5O_3S_2$	253-255	61	Brown
M15	4-H	$C_{17}H_{19}N_5O_3S_2$	230-232	70	Yellow

Biological activity study

Two types of bacteria, Gram-Negative Klebsiella pneumoniae and Gram-positive Staphylococcus epidermidis, were used. Then, DMSO was used as a solvent to prepare chemical solutions of the compounds prepared at concentrations of (0.001, 0.01, and 0.1) mg/ml for each solid derivative. After that, prepare Mueller-Hinton agar medium according to the manufacturer's instructions to study its biological activity. The medium powder (38 g) is dissolved in (1) liter of distilled water in a conical flask and the solution is heated until it dissolves.[11,12] After dissolving the culture medium, the solution is placed in an autoclave and sterilized. For (15) minutes at a temperature of 121 degrees

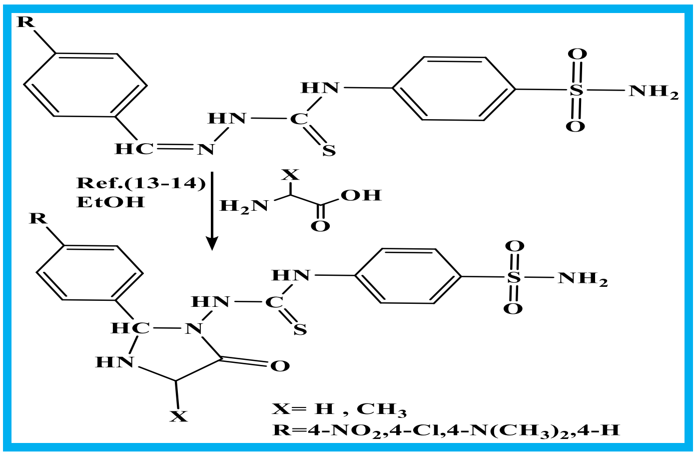
Celsius and a pressure of (1.5 bar) until the culture medium cools and then sterilizes it [13,14]. Pour into a plate and cook until done. Place the bacteria in the culture medium, then use a cork drill to make holes in these Petri dishes, sterilize the holes with alcohol, and use a fine pipette to put the prepared solution into the holes. After placing (24) hours in the incubator at a temperature of: 37 degrees Celsius, the diameter of the inhibition zone of the compound under study was measured using a centimeter ruler [15,16].

Study the effect of laser radiation. [17]

The compounds (M11-M15) are irradiated by a neodymium nanosecond laser system (Nd:YAG laser), which generates pulsed nanosecond laser light with wavelength (808 nm) and frequency (5 Hz) to the irradiated compound. The duration is (10) seconds, and the distance between the light source and the sample is (5 cm). The laser radiation falls perpendicular to the sample using a concave quartz lens with a focal length of (100 mm).

3. Results and Discussion

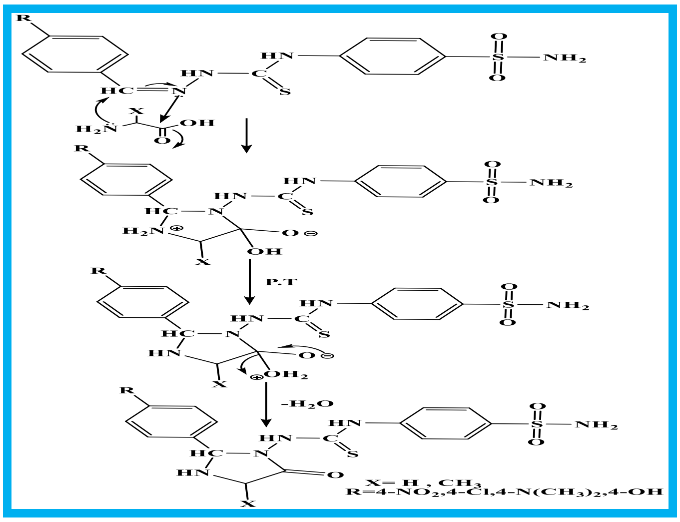
Scheme 1 shows the compounds formed by the reaction of hydrazone with amino acids.



Scheme (1): Path of the Ready Compounds (M6-M15)

Characterization of Imidazole Derivatives (M6-M15)

The mechanism of imidazole preparation can be explained according to the following diagram.



Scheme 2: Explains the mechanism of preparing imidazole (M6-M15)

When studying FT-IR, it was found that the absorption band appeared at (3313-3217) cm-1, which is usually used to stretch imidazole (NH) conjugates. The band is traced to the aromatic stretching (=CH) in the range (3023-3080) cm-1, The two absorption bands are located in the range (2963-2906) cm-1 and (2900-2823) cm-1, usually for aliphatic bonds (CH), and an absorption band usually to the (C=O) bond in the range (1656-1627) cm-1, there are two absorption bands at (1526-1568) cm-1 and (1466-1508) cm-1, which are usually aromatic bonds (C=C), and a band at (1265-1220) usually linked to a bond (C-N).[18] As in Table 2 and Figures 1,2,3.

Table (2): FT-IR absorption results for Prepared compounds (M6-M15)

Comp. No.	R	ν(C-H) Arom.	ν(C-H) Aliph.	ν(N-H)	ν(C=O)	ν(C=C) Arom.	Others
M6	4-NO2	3047	2918,2860	3232	1627	1545,1479	ν(N-O) 1357
M7	4-Cl	3023	2951,2871	3231	1638	1560,1484	ν (C-Cl)716
M8	4-CH3	3069	2941,2900	3295	1649	1549,1466	--
M9	4-Br	3038	2938,2841	3243	1639	1554,1467	ν (C-Br) 589
M10	4-H	3032	2929,2850	3224	1656	1536,1486	--
M11	4-NO2	3045	2906,2875	3276	1641	1541,1478	ν(N-O) 1341
M12	4-Cl	3080	2918,2848	3217	1645	1562,1475	ν (C-Cl)707
M13	4-CH3	3075	2954,2895	3313	1643	1568,1502	--
M14	4-Br	3064	2963,2876	3302	1635	1526,1489	ν (C-Br) 638
M15	4-H	3063	2914,2823	3223	1637	1541,1508	--

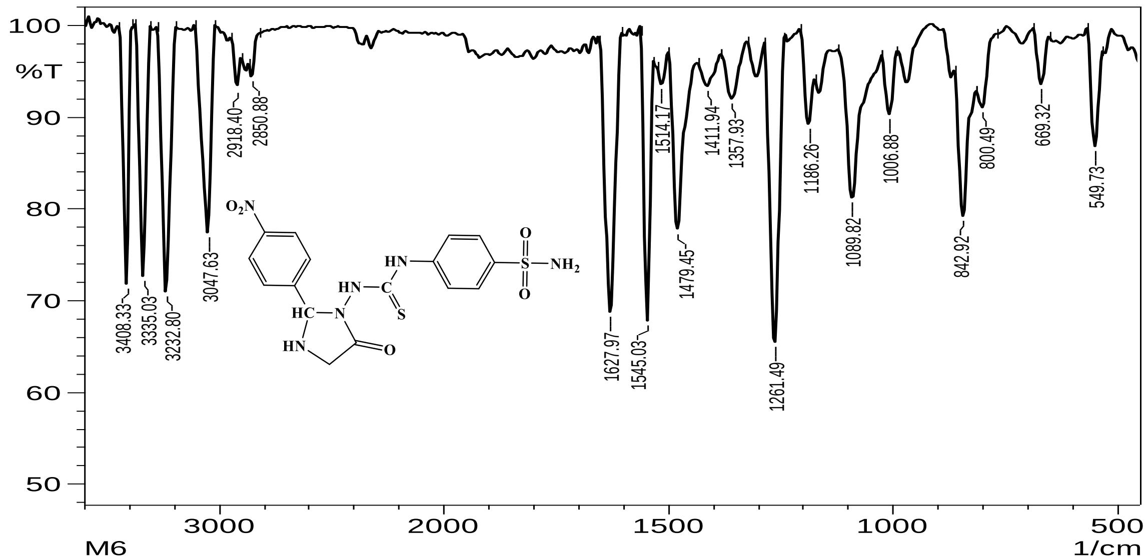


Figure (1): The compound's FT-IR spectra (M6).

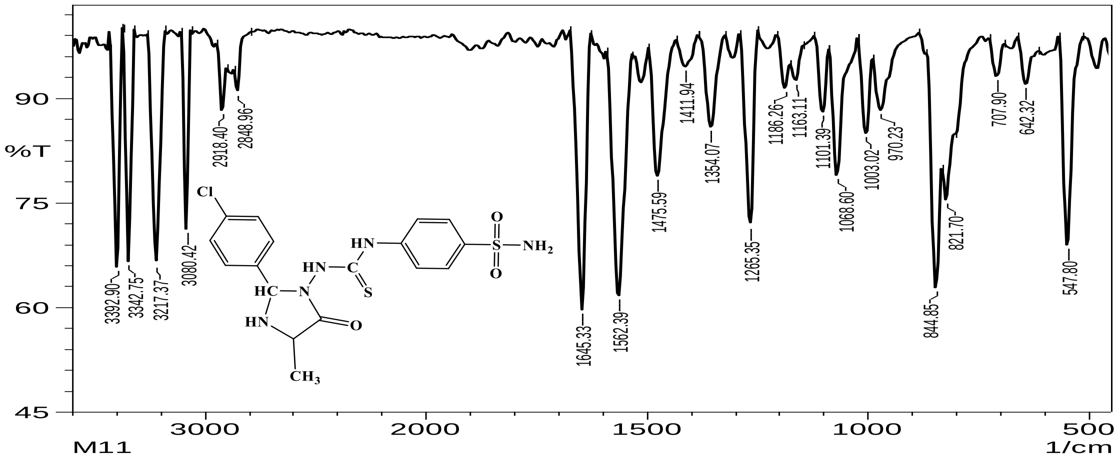


Figure (2): The compound's FT-IR spectra (M11).

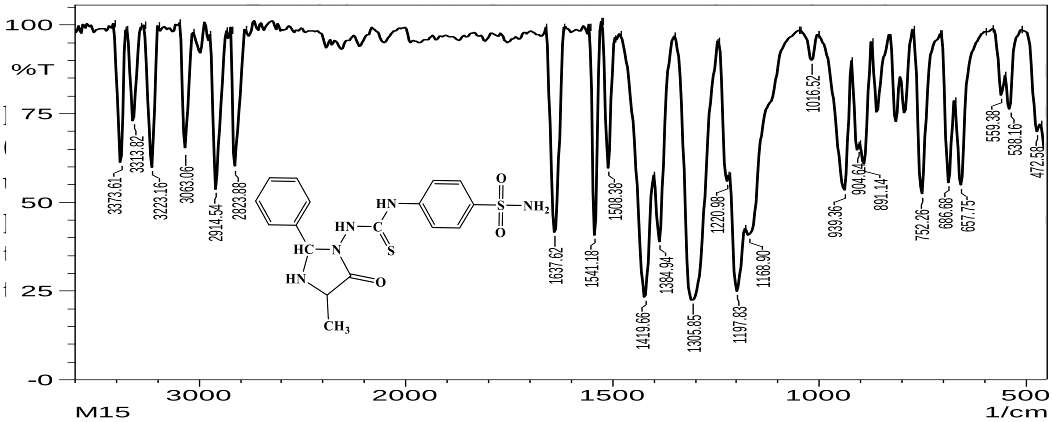


Figure (3): The compound's FT-IR spectra (M15).

When studying 1H-NMR of compound M6, the signal observed at position (3.19) ppm is usually a proton (CH2) of the pentameric ring, and the signal observed at position (4.60) ppm is usually the (CH) group of the pentagram, indicating A signal at (5.68 ppm) usually indicates a proton (NH2), multiple symbols in the range (6.60-7.51) ppm indicate protons of the benzene ring, and a single symbol at (8.78) ppm indicates protons (NH) of the ring The pentagon, and the two symbols in (10.03-11.00)ppm return the sum outside the loop

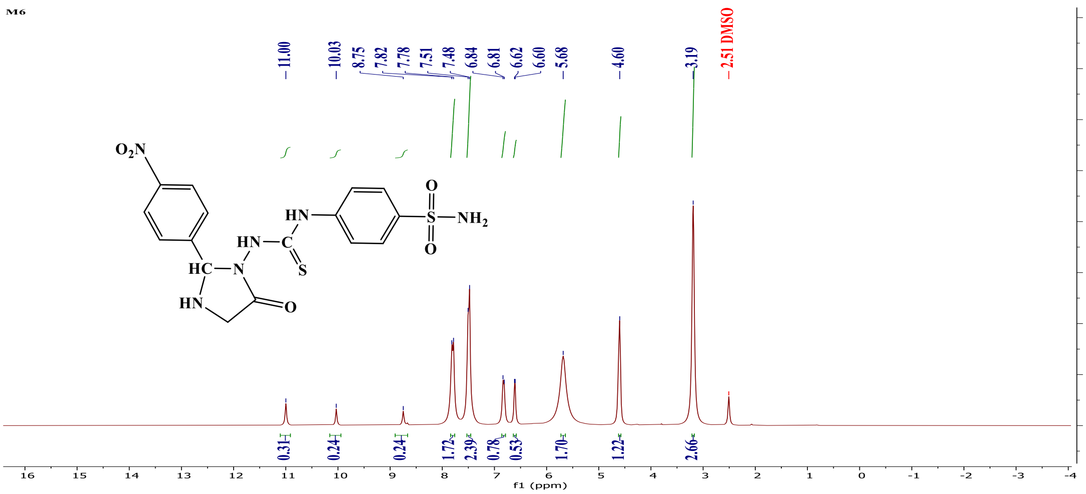


Figure (4): 1-H NMR spectra of the substance (M6).

When studying 1H-NMR of compound M7, the signal observed at position (3.66) ppm is usually a proton (CH2) of the penta ring, and the signal observed at position (4.26) ppm is usually the (CH) group of the penta ring, indicating A signal at (5.75) ppm usually indicates a proton (NH2), multiple number in the range (6.87-7.88) ppm usually indicate protons of the benzene ring, and a single number at (8.63) ppm indicates protons (NH) of the ring The pentagon, and the two symbols in (9.82-10.23)ppm return the sum outside the loop (NH). As shown in Figure 5

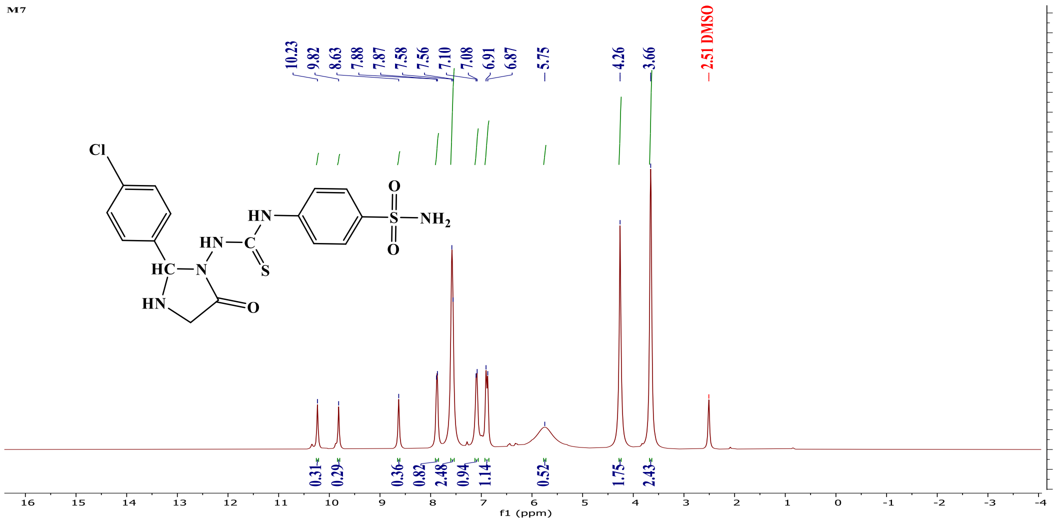


Figure (5): 1-H NMR spectra of the substance (M7).

When studying 1H-NMR of compound M14, the double signal observed at the position (1.85,1.88) ppm is usually a proton (CH3) attached to the pentameric ring, and the quadruple signal observed in the range (3.62-3.69) ppm is usually a group (CH) of the pentagonal ring, the signal at (6.46 ppm) usually indicates a proton (NH2), the multiple signal in the range (6.91-7.84) ppm usually indicates protons of the benzene ring, and the two signals at (8.78) ppm Denotes protons (NH) from the pentagonal ring, and the two symbols in (9.64-10.33) ppm return the sum outside the ring (NH). As shown in Figure 6

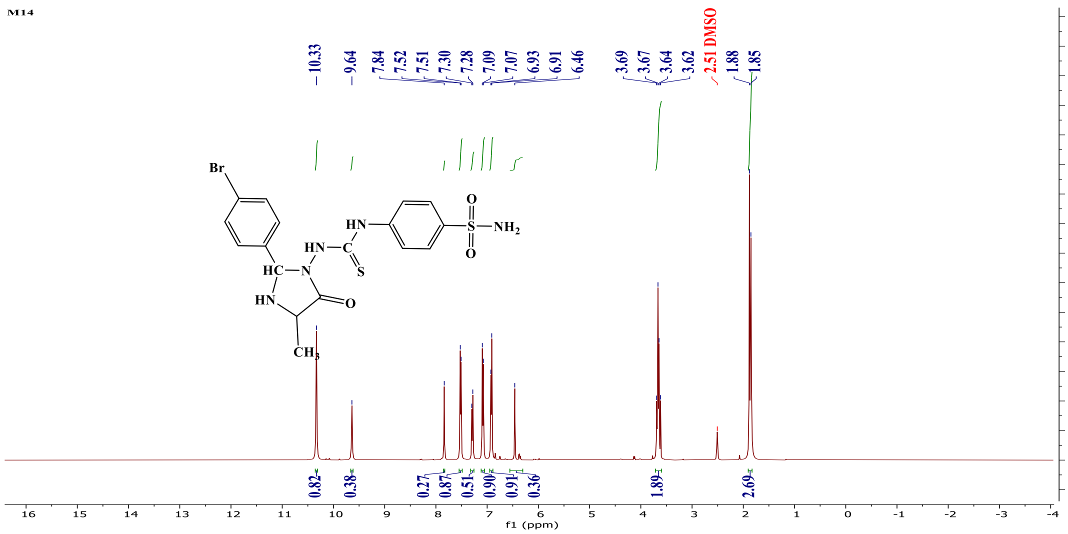


Figure (6): 1-H NMR spectra of the substance (M14).

When studying 1H-NMR of compound M15, the double signal observed at the position (2.28,2.30) ppm is usually a proton (CH3) attached to the penta ring, and the quadruple signal observed in the range (4.18-4.24) ppm is usually a group (CH) of the pentagonal ring, the signal at (5.96) ppm usually indicates a proton (NH2), the multiple signals in the range (6.45-7.98) ppm usually indicates protons of the benzene ring, and the two signals at (8.50) ppm Denotes protons (NH) from the pentagonal ring, and the two symbols in (9.57-10.29) ppm return the sum outside the ring (NH). As shown in Figure 7

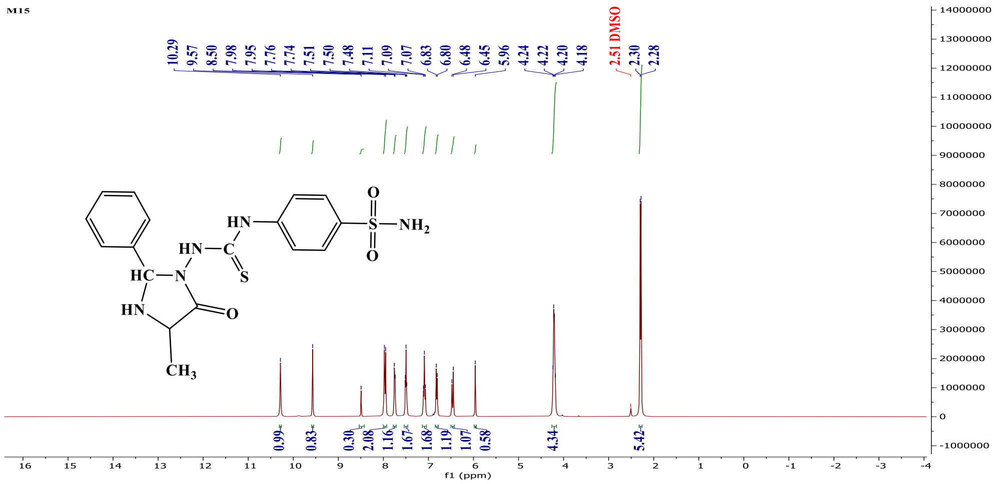
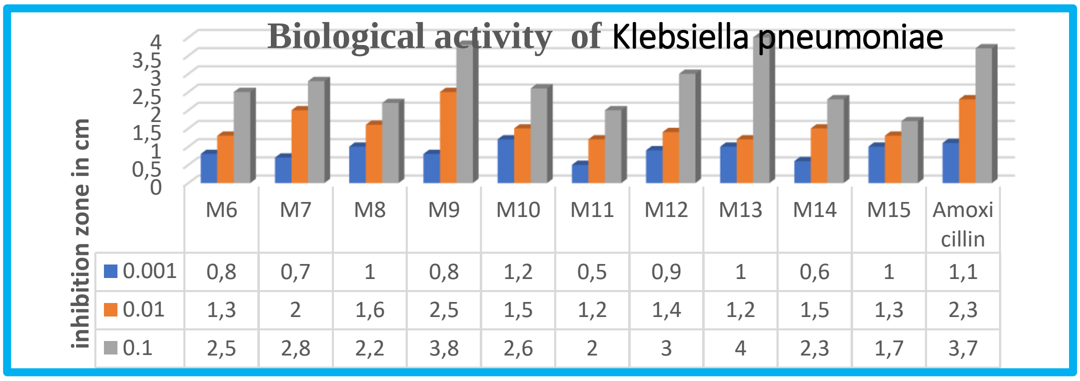


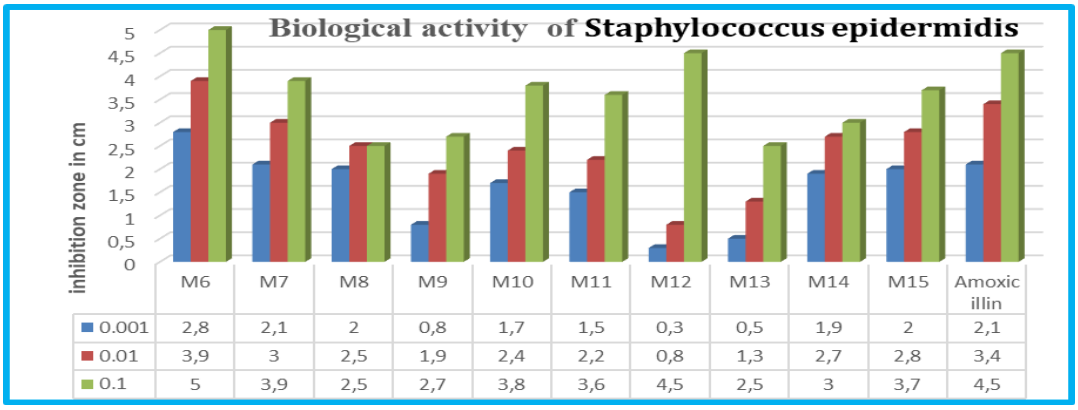
Figure (7): 1-H NMR spectra of the substance (M15).

Evaluation of the Biological Activity of Prepared Compounds

These bacteria were chosen for their medical importance, as they cause many diseases. In addition, they differ in their resistance to antibiotics[19,20]. The bioavailability of some of the prepared compounds was evaluated using the etching method (130) and measuring the antibiotic levels[21]. The results showed that the prepared compounds could inhibit the growth of bacteria with different proportions of Gram-positive and negative stains, and the antibiotic amoxicillin was used as a control gene, based on what. It is used in Ministry of Health laboratories and based on World Health Organization tests[22,23]. As in Schemes 3 and 4 and Figures 8 and 9



Scheme (3): Inhibitory activity of (M6-M15) for K. Pneumonia



Scheme (4): Inhibitory activity of (M6-M15) for S. epidermidis.

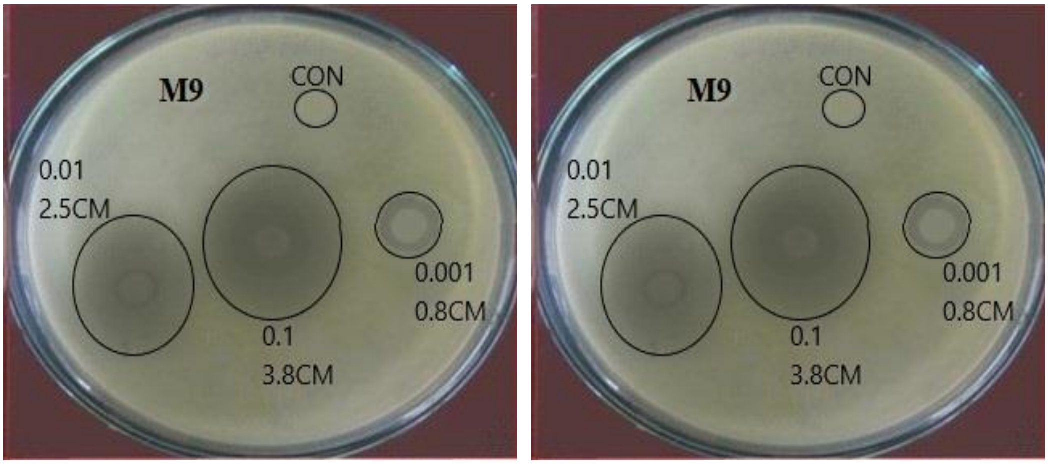


Figure 8: Biological Effectiveness of the Compound M9, M13 against Becteral K.Pneumoniae

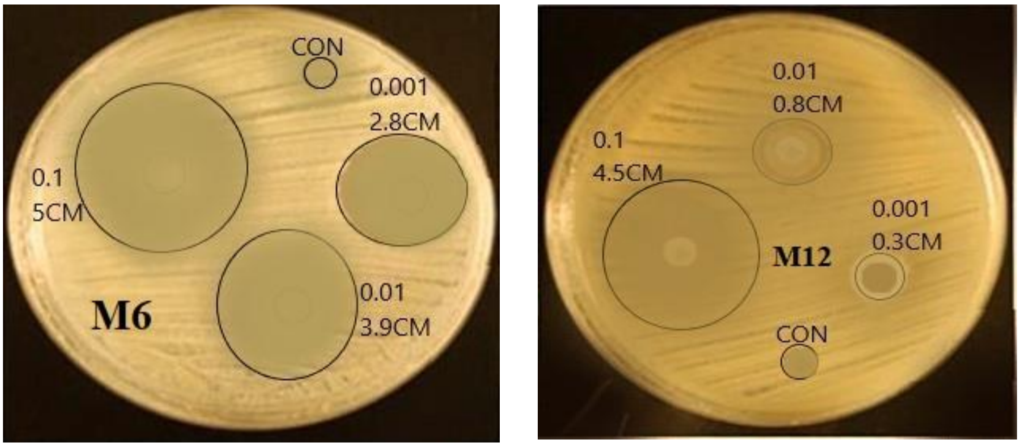


Figure 9: Biological Effectiveness of the Compound M6, M12 against Becteral S.epidermidis

The effect of laser beams on some prepared compounds [24]:

The needimium Pak (Nd:YAG) pulsed laser device was used with a wavelength (532 nm) in continuous waves with an energy (800 mJ) and a frequency (5 Hz), the distance between the sample and the laser (10 cm) and the irradiation time (30 sec).Five solid samples were selected (M11,M12,M13,M14, M15) bombarded with pulsed nedymium buck (Nd:YAG) lasers, and it was noted that some of the compounds under study experienced slight changes in melting points and color, while some were not affected by laser radiation, through measurements of melting points before and after being bombarded with a laser, and Table (4): the effect of laser beams on some prepared compounds.

Table 4. The Effect of Laser Beams on Some Prepared Compounds (M11-M15)

Comp. No.	Before Irradiation		After Irradiation	
	M.P. ^{0}C	Color	M.P. ^{0}C	Color
M11	238-240	White	238-240	White
M12	209-211	Blue	205-209	Light green
M13	225-227	Orange	243-246	Light yellow
M14	253-255	Brown	253-255	Brown
M15	230-232	Yellow	211-214	White

4. Conclusion

The research successfully synthesized imidazole derivatives through the reaction of amino acids with hydrazones, resulting in compounds with high purity as evidenced by nuclear magnetic resonance spectroscopy. These imidazole derivatives exhibited significant antibacterial activity, comparable to the effectiveness of the antibiotic amoxicillin. Additionally, the study examined the impact of laser irradiation using a neodymium nanosecond laser on the compounds. It was found that certain compounds, specifically M11 and M14, demonstrated high stability when exposed to laser radiation, while others showed changes in melting points and color due to alterations in their bonds

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