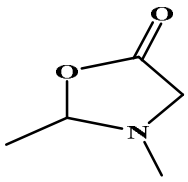
Preparation and characterization of some oxazolidine-5-one derivatives and evaluation of their biological activity

Abstract: The research included the preparation of new compounds of oxazolidinone-5-one from the reaction of prepared Schiff bases with chloroacetic acid in the presence of dioxane as a solvent. The sublimation method was used for the preparation, and the reaction was monitored and described by determining the melting point, yield and color. The completeness of the reaction was confirmed using thin layer chromatography (T.L.C.), infrared spectroscopy (FT-IR), proton and carbon nuclear magnetic resonance (^{1}H&^{13}C-NMR) and quantitative elemental analysis (C.H.N.). The biological sensitivity of the prepared compounds was evaluated by examining their effect on the growth of two antibiotic-resistant bacterial isolates: Gram-negative (***K. pneumoniae***) and Gram-positive (***Staph. epidermidis***). The antibiotic ***ampicillin*** was used as a control sample.
Keywords: Heterocyclic , oxazolidinone-5-one , Biological activity.

1. Introduction

Heterocyclic chemistry is one of the most interesting scientific fields and has excellent practical and One of the most fascinating scientific disciplines, heterocyclic chemistry has great theoretical and practical applications. As a result, it makes up a significant portion of chemistry and chemical science research. Common in nature, heterocyclic molecules possess biological characteristics. One broad and expanding area of chemistry is heterocyclic chemistry. This is due to the evident importance of molecules generated from heterocyclic compounds in plastics, polymers, medicine, agriculture, and other sectors. Heterocyclic compounds are used to treat infectious disorders due to their biological features. [1-3].Oxazolidinones are a new class of antibiotics; this synthetic chemical is effective against various Gram-positive bacteria, including vancomycin-resistant staphylococci and penicillin-resistant pneumococcus. The creation and biological properties of oxazolidin-5-ones are important in medicinal chemistry and chemical biology[4]. Oxazolidin-5-ones substituted with polyhydroxylidin-2-phenyl and their derivatives have a variety of pharmacological and biological properties. Oxazolidin-5-one derivatives are important types of chemical compounds with heterocyclic structure. Many aryl-oxazolidinone compounds have diverse biological properties, including hypoglycemic and strong antibiotic effects against various bacteria. However, Figure 1 shows the general ring structure of oxazolidin-5-one compounds[5]. Many 5-substituted-1,3-oxazolidindione derivatives with different substituents have been generated and their anti-inflammatory capabilities have been evaluated [6,7].



To sum up, the purpose of this work is to create new five-ring compounds from oxazolidinone-5-one by reacting prepared Schiff bases with chloroacetic acid while dioxane is present as a solvent. The biological activity of these compounds against two different kinds of Gram-positive and Gram-negative bacteria will be assessed.

2. Materials and Methods:

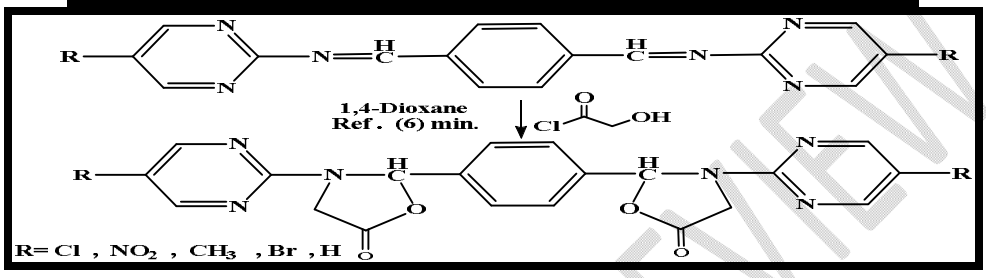
2.1.Chemicals used: Chemicals prepared by Aldrich, BDH Thomas, Fluka, and Merck were used.

2.2. Preparation of 1,3-oxazolidinone-5-onederivatives (J1-J5):

(0.001) mol of the previously prepared Schiff bases and (0.002) mol of chloroacetic acid were combined in a round-bottomed flask with dioxane acting as a solvent. The components were recrystallized from ethanol after the mixture was raised for six hours in a water bath[8,9]. The reaction was followed by TLC, as shown in Table 1.

Table (1): Some Physical Properties of the 1,3-oxazolidinone-5-onederivatives (J1-J5)

Comp. No.	R	Molecular Formula	Color	M.P. □	Y. %
J 1	4-Cl	$C_{20}H_{14}Cl_2N_6O_4$	Yellow	231-233	76
J 2	4-NO_2	$C_{20}H_{14}N_8O_8$	Light Brown	245-247	71
J 3	4-CH_3	$C_{22}H_{20}N_6O_4$	Light yellow	217-219	85
J 4	4-Br	$C_{20}H_{14}Br_2N_6O_4$	Orange	265-267	64
J 5	4-H	$C_{20}H_{16}N_6O_4$	White	206-208	83



Scheme 1: Prepared compounds (J1-J5)

2.3. Biological activity study: The synthesized compounds were evaluated for antibacterial activity using the disk diffusion technique. Two bacterial strains - Gram-positive (***Staphylococcus epidermidis***) and Gram-negative (***Klebsiella pneumoniae***) - were used to evaluate the amount of chemicals produced[9-12]. The antibiotic ampicillin was chosen as a control. Filter paper discs with a diameter of 5 mm were steam sterilized for 15 min at 121 °C[13,14]. All compounds were evaluated after impregnating the sterile discs with 100 µg/disc. Each microorganism examined was cultured and added to the surface of the disc (100 µl). To allow sound diffusion, the impregnated discs were incubated for 1 h at 5 °C and then for 24 h at 37 °C. The area of inhibition of the tested drugs against the bacteria was measured[15-16].

3. Results and discussions

3.1. Characterization of 1,3-oxazolidinone-5-onederivatives (J1-J5)

When studying the FT-IR spectrum of the disordered compounds, a band was observed at (3082-3029) cm-1 for the aromatic (CH), two bands at (2981-2918&2904-2848) cm-1 for the aliphatic (CH), a band at (1704-1693) for (C=O), two bands at (1541-1513&1508-1479) cm-1 for the aromatic (C=C), a band at (1373-1330) cm-1 for (C-O), and a band at (1096-1076) cm-1 for (N-N)[17,18]. As in Table 2

Table (2): FT-IR absorption results for Prepared compounds (J1-J5)

Comp.	R	νCHArom.	ν(CH)Aliph.	ν(C=O)	ν(C=C)Arom.	ν(C-O)	ν(N-N)	Others
J 1	4-Cl	3082	2918, 2848	1693	1541, 1491	1373	1091	ν(C-Cl) 790
J 2	4-NO_2	3048	2981, 2932	1696	1533, 1482	1361	1096	ν(NO) 1506, 1324
J 3	4-CH_3	3029	2937, 2911	1699	1523, 1479	1357	1090	--
J 4	4-Br	3074	2974, 2904	1701	1531, 1508	1330	1076	ν(C-Br) 686
J 5	4-H	3041	2939, 2889	1704	1513, 1489	1369	1084	--

When studying the 1H-NMR spectrum of compound J1, it was found that there are two signals at (7.69, 7.47)ppm for the protons of the aromatic rings, a signal at (5.16)ppm for the (CH) proton, and a signal at (3.76)ppm for the (CH_2) protons[19,20]. As in Fig. 3

The 1H-NMR spectrum of compound J1 showed two signals at (7.64, 7.28) for the aromatic ring protons, a signal at (5.66) for the (CH) proton, a signal at (3.45) for the (CH_2) protons, And a signal at (2.10) for the (CH_3) protons. As in Fig.4

When studying the 13C-NMR spectrum of compound J1, it was found that there was a signal at (169.72) for (C=O), signals in the range (127.06-161.27) for the carbons of the aromatic rings, a signal at (73.40) for (CH), and a signal at (44.01) for (CH_2). as in Fig. 5

The 13C-NMR spectrum of compound J3 showed a signal at (172.31) for (C=O), signals in the range (129.81-159.22) for aromatic ring carbons, a signal at (94.73) for (CH), a signal at (43.57) for (CH2).and a signal at (33.96) for (CH_3). as in Fig. 6

3.2. Elemental Analysis (C.H.N.O.) Measurement

To confirm the correctness and precision of the synthesized compounds' structural composition, elemental analysis (C.H.N.O.) was carried out. The obtained elemental ratios validated the structures of the produced compounds by being either consistent with or extremely near to the calculated values [21,22], as shown in Table (3).

Table (3): Results of elemental analysis (C.H.N.O) of manufactured compounds

Comp No.	Molecular Formula	Calculated				Found			
		C%	H%	N%	O%	C%	H%	N%	O%
J 1	$C_{20}H_{14}Cl_2N_6O_4$	50.76	2.98	17.76	13.52	50.60	3.05	17.83	13.32
J 2	$C_{20}H_{14}N_8O_8$	48.59	2.85	22.67	25.89	48.36	2.72	22.48	25.81
J 3	$C_{22}H_{20}N_6O_4$	61.10	4.66	19.43	14.80	60.43	4.57	19.31	14.65
J 4	$C_{20}H_{14}Br_2N_6O_4$	42.73	2.51	14.95	11.38	42.63	2.39	15.07	11.14
J 5	$C_{20}H_{16}N_6O_4$	59.40	3.99	20.78	15.83	59.49	4.10	20.65	15.76

3.3. Evaluation of the Biological Activity of Prepared Compounds

The biological activity of the compounds was tested in vitro against Gram-negative bacteria, ***K. pneumoniae***, and Gram-positive ***Staph. epidermidis*** by agar diffusion test [23–26]; a sterile cotton swab was dipped in the prepared suspension, and its surface was wiped homogeneously on a Mueller-Hinton agar plate. Three wells of 7 mm diameter were made on the agar gel at 20 mm intervals, and 100 µl of the prepared dilution concentrations (0.01, 0.001, 0.0001) were added to each well [27–30]. Dimethyl sulfoxide was used as a solvent. One of the wells was filled with dimethyl sulfoxide or ethanol to observe the solvent effect. Plates were incubated for 24 h at 37 °C (without transfer), growth was observed, and growth inhibition was measured in mm [31, 33], with compound A5 showing the highest inhibition against K. pneumoniae with a diameter of 15 mm, while compound A6 showed the highest inhibition against Staph. epidermidis with a diameter of inhibition of 33 mm [34, 36]. As shown in Table 4 and Scheme 2.

Table (4): Antibacterial activity of the synthesized compounds (inhibition zone in mm).

Comp. No.	*K. pneumoniae* mg/ml			*Staph. epidermidis* mg/ml		
	0.01	0.001	0.0001	0.01	0.001	0.0001
J 1	15	10	10	23	18	15
J 2	13	11	5	33	27	15
J 3	15	5	0	20	15	10
J 4	11	8	5	26	26	15
J 5	10	10	10	21	16	5
Ampicillin.	25	20	15	35	30	25

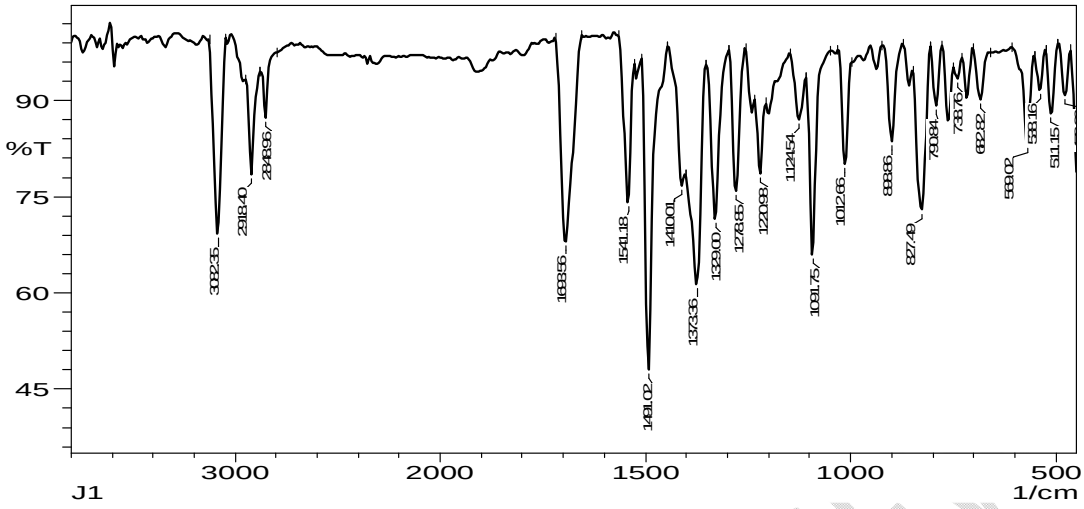
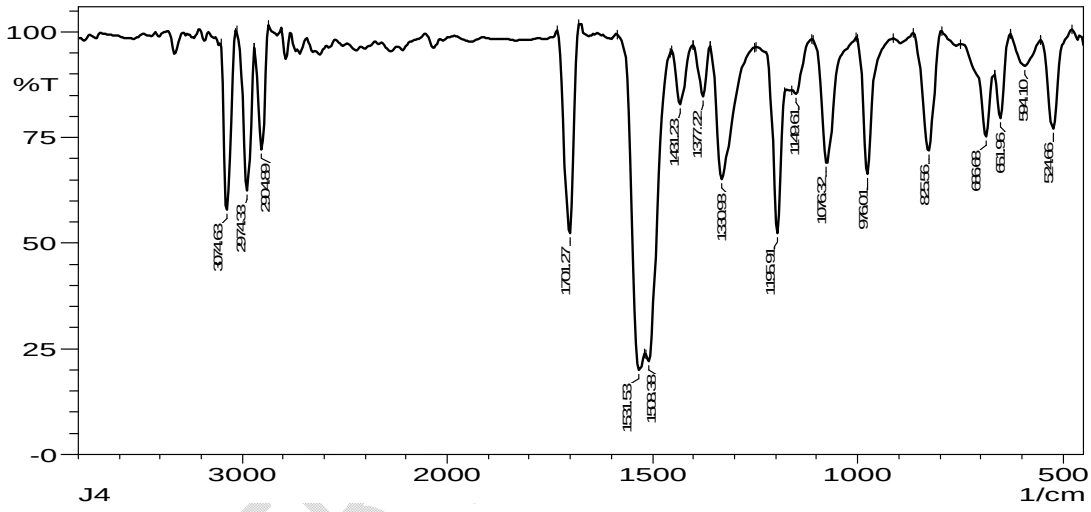
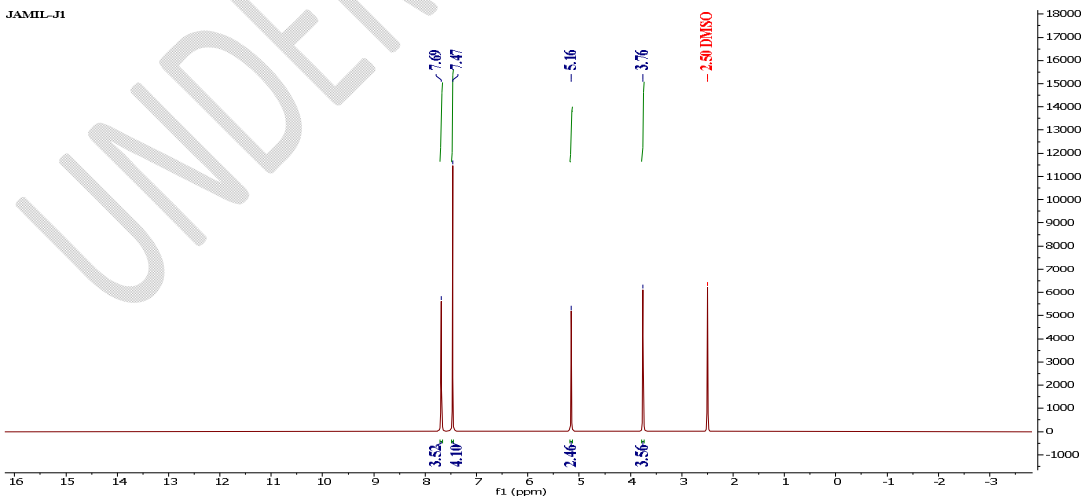


Figure (1): The compound's FT-IR spectra (J1).





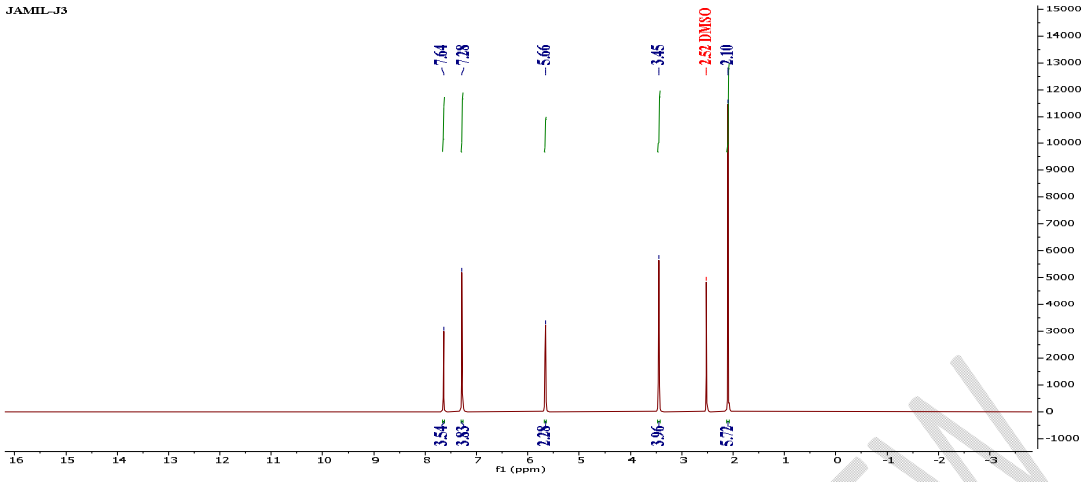


Figure (4): 1H-NMR spectra of the substance (J3).

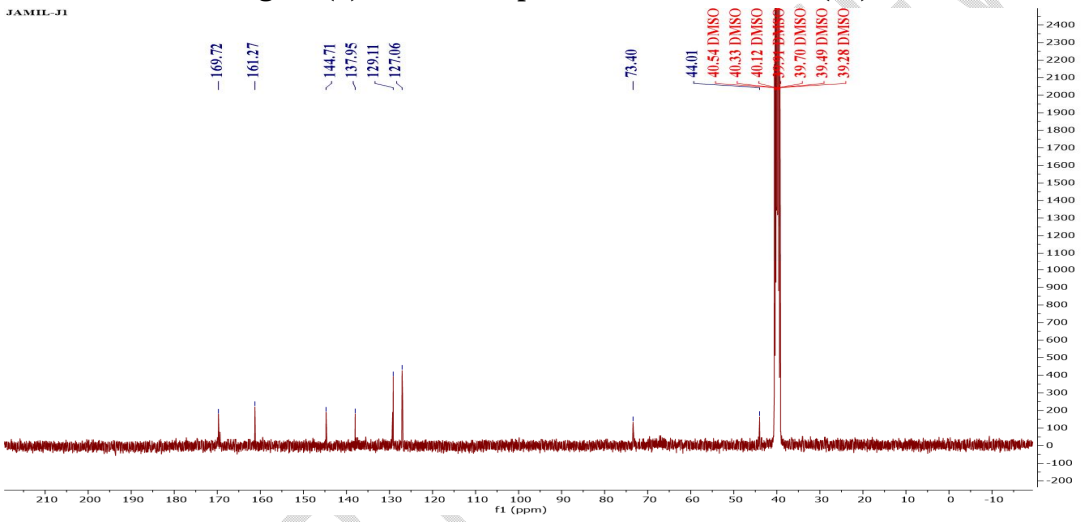


Figure (5): 13C-NMR spectra of the substance (J1).

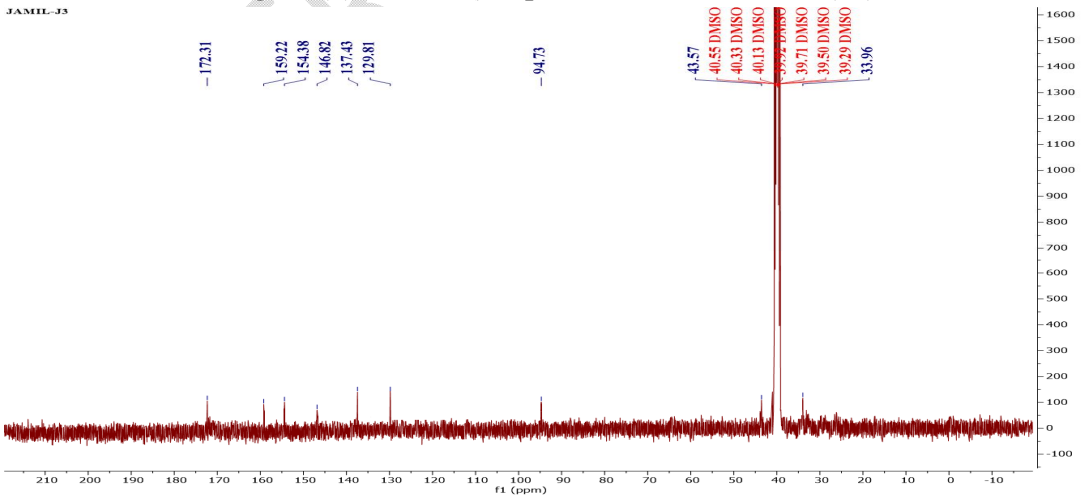
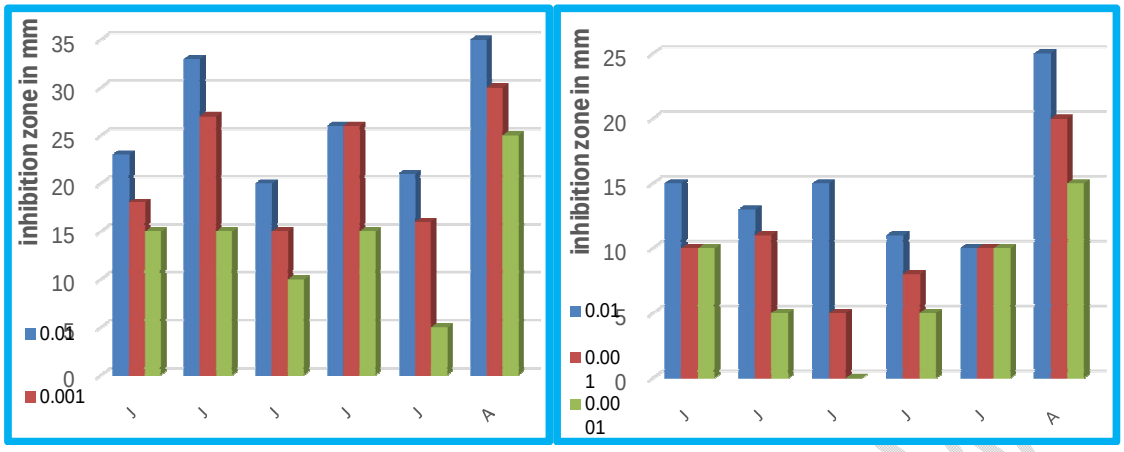


Figure (6): 13C-NMR spectra of the substance (J3).



Scheme (2): Inhibitory activity of (J1-J5) for Staph. epidermidis & K. pneumoniae

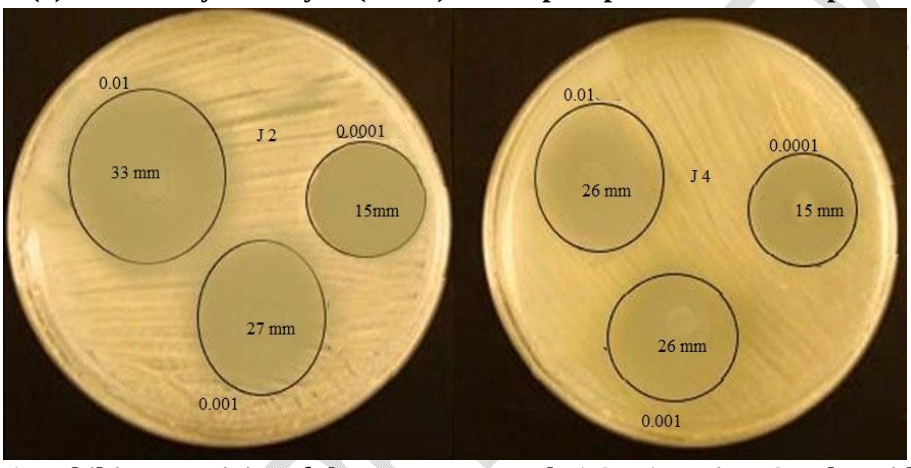


Figure (7): Inhibitory activity of the two compounds (J2,J4) against Staph. epidermidis

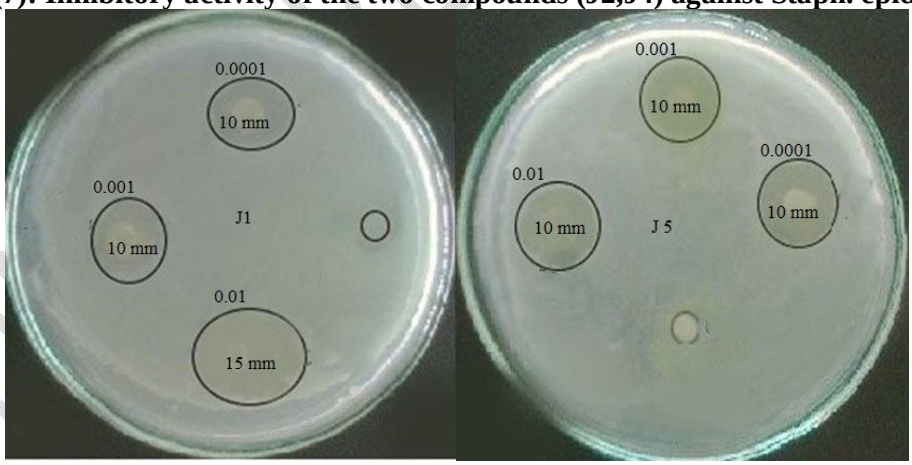


Figure (8): Inhibitory activity of the two compounds (J1,J5) against *K. pneumoniae*

4. Conclusions: Schiff base derivatives frequently react to form five-membered heterocyclic rings with substances that have appropriate functional groups. The synthesised compounds' accuracy and precision have been proven by spectroscopic measurements. According to biological research, the produced chemicals can stop bacteria from growing and have antibacterial properties. The biological activity of these compounds is greater than that of the parent material.

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