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Synthesis and Characterization of the New Imidazole-Derivative Salts' Nanoparticles and Studying of Its Biological Activity

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Heterocyclic compounds have great importance in the medical and industrial fields. Imidazole compounds and salts are the most widespread and effective of these compounds. Therefore, in this research, we prepare a number of mono- and di-substituted derivatives of imidazole and its salts. The prepared compounds are characterized using ^{1}H-NMR, ^{13}C-NMR, SEM, and IR techniques. In addition, the biological activity against *Escherichia coli* and *Staphylococcus aureus* bacteria is studied for the prepared compounds. As revealed, the prepared salts are more biologically effective.

Гетероциклічні сполуки мають велике значення в медичній і промисловодослідній сферах. Імідазольні сполуки та солі є найбільш поширеними й ефективними з цих сполук. Тому в даному дослідженні ми готуємо ряд моно- і ди-заміщених похідних імідазолу та його солей. Одержані сполуки характеризуються методами ^{1}Н-ЯМР, ^{13}С-ЯМР, СЕМ, ІЧ-спектроскопії. Крім того, для приготованих сполук вивчається біологічна активність щодо бактерій *Escherichia coli* та *Staphylococcus aureus*. Як з'ясувалося, приготовані солі більш біологічно ефективні.

Key words: imidazole derivatives, heterocyclic compounds, imidazole salts, pharmacological applications, biological activity.

Ключові слова: похідні імідазолу, гетероциклічні сполуки, солі імідазолу, фармакологічні застосування, біологічна активність.

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1. INTRODUCTION

Imidazole is a five-membered heterocyclic compound containing two nitrogen atoms in the 1,3 positions, which is widely used as a building block for the synthesis of a variety of biologically active compounds. Alkylation of imidazole at the N-1 or N-2 position with alkyl halides or sulfonate esters can introduce lipophilic substituents into the imidazole ring, which can modify the physicochemical and biological properties of the resulting compounds. Overall, imidazole is an important and versatile compound with a wide range of applications in various fields of science and technology [1–4].

Alkylated derivatives of imidazole [5] have been extensively studied for their biological activities, including antifungal [6–8], antidiabetic [9], antiparasitic, antibacterial [10–13], antioxidant [14], antituberculosis [15], anti-inflammatory [16–18], antitumor [19–21], antimalarial, anticancer [22–24], antihypertensive, antidepressant, anxiolytic. The nature and position of the alkyl substituent can significantly affect the biological activity of the imidazole derivatives. For example, the introduction of bulky alkyl groups, such as tert-butyl or isopropyl, at the N-1 position of imidazole can enhance the antifungal activity of the compounds, while adding the longer alkyl chains, such as octyl or dodecyl, at the same position can improve the antibacterial activity.

In addition to their biological activities, alkylated imidazoles have also been used as ligands in coordination chemistry and as catalysts in organic reactions. For example, 1-methylimidazole is a common ligand in metal-organic frameworks [25], while 2-alkylimidazoles have been used as phase transfer catalysts and as catalysts in the synthesis of organic compounds. Methylimidazole has a wide range of applications in various fields. It is used as a building block in organic synthesis. It has also been shown to exhibit biological activities. For example, methylimidazole derivatives have been synthesized and evaluated as potential antifungal agents against various fungal pathogens, including *Candida albicans* and *Aspergillus fumigatus*. Methylimidazole derivatives have also been evaluated for their antitumor activity against various cancer cell lines.

Octylimidazole has been shown to exhibit antimicrobial, antifungal, and antibiofilm activities. For example, octylimidazole derivatives have been synthesized and evaluated as potential antibacterial agents against various gram-positive and gram-negative bacteria, including *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa*. Octylimidazole derivatives have also been evaluated for their antifungal activity against *Candida albicans* and *Aspergillus fumigatus*. Overall, octylimidazole is a versatile compound with diverse biological and chemical properties, and it continues to be an active area of research in medicinal chemistry and organic synthesis.

Isopropylimidazole is used as a building block in organic synthesis and as a ligand in coordination chemistry. It has been shown to exhibit antifungal, antibacterial, and antitumor activities. For example, isopropylimidazole derivatives have been synthesized and evaluated as potential antifungal agents against various fungal pathogens, including *Candida albicans*, *Cryptococcus neoformans*, and *Aspergillus fumigatus*. Isopropylimidazole derivatives have also been evaluated for their antibacterial activity against gram-positive and gram-negative bacteria.

Overall, isopropylimidazole is a versatile compound with diverse biological and chemical properties, and it continues to be an active area of research in medicinal chemistry and organic synthesis.

In addition to its biological activities, imidazole derivatives have been used as ligands in coordination chemistry and as a catalyst in organic reactions, including the aldol condensation, Michael addition, and Mannich reaction.

Overall, alkylated derivatives of imidazole are a versatile class of compounds with diverse biological and chemical properties, and they continue to be an active area of research in medicinal chemistry, materials science, and organic synthesis.

Imidazole derivatives such as clotrimazole, miconazole, and ketoconazole are used to treat fungal infections of the skin, nails, and mucous membranes.

Clotrimazole 1-[(2-chlorophenyl) (diphenyl)methyl]-1H-imidazole [26] (Fig. 1) is an antifungal used to treat a variety of fungal infections. It belongs to the class of drugs known as imidazole antifungals and works by inhibiting the growth of the fungus, and used to treat infections of the skin. It is also treat yeast infections of the mouth (oral thrush) and the vagina (vaginal candidiasis) [27].

Azelastine [28], levocetirizine [29], and desloratadine [30] (Fig. 2) are examples of imidazole derivatives used to treat allergic conditions such as hay fever, hives, and allergic rhinitis.

Imidazole derivatives such as etodolac and ketorolac [31] are nonsteroidal anti-inflammatory drugs (NSAIDs) used to treat pain and inflammation associated with arthritis, menstrual cramps, and oth-

er conditions.

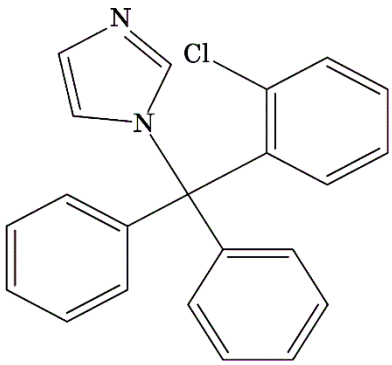

Fig. 1. Chemical structure of clotrimazole [26].

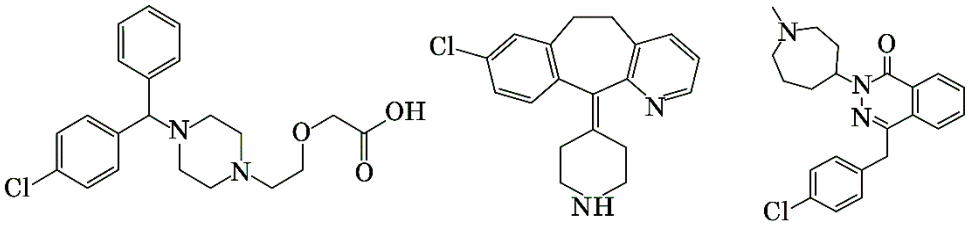

Fig. 2. Chemical structure of azelastine, levocetirizine, and desloratadine.

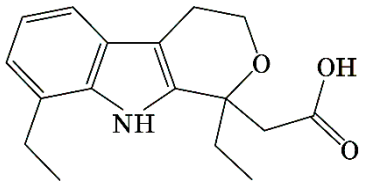

Fig. 3. Chemical structure of etodolac.

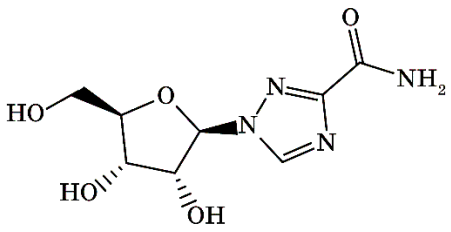

Fig. 4. Chemical structure of ribavirin.

Etodolac (Fig. 3) is a nonsteroidal anti-inflammatory drug (NSAID) used to treat pain and inflammation associated with arthritis, menstrual cramps, and other conditions. It works by reducing the levels of prostaglandins, which are chemicals responsible for pain and inflammation [32], and is available in various forms, including tablets and capsules. The medication is usually taken orally, with or without food, as directed by your healthcare provider Etodolac is generally well tolerated, but some people may experience side effects such as stomach upset, nausea, vomiting, diarrhoea, headache, dizziness, and drowsiness. Serious side effects such as stomach bleeding, liver damage and allergic reactions are rare but can occur. If you experience symptoms like severe stomach pain, dark urine, yellowing of the skin or eyes, or difficulty breathing, seek immediate medical attention.

Ribavirin (Fig. 4) is an antiviral used to treat a variety of viral infections. It is a synthetic nucleoside analogue that acts by inhibiting the replication of viral genetic material, is commonly used to treat hepatitis C, a viral infection that can cause liver disease, and respiratory syncytial virus (RSV), a common viral infection that can cause respiratory illness in infants, young children, and elderly adults.

In other hands, imidazolium-salt (which is the focus of our attention) and ionic liquids have shown wide-ranging applications in medicinal chemistry due to their unique properties such as ionic nature, solubility, and lipid affinity [33, 34].

In other usage, imidazolium salts are used to extract metal ions from aqueous solutions and metal nanoparticles coating, offering antimicrobial action and creating oriented liquid crystals [35, 36]. In bioactive applications, imidazole is used as imidazolium hydrogels, antiarrhythmics, and antimetastatic agents. Imidazolium salts have potential activity of antimicrobial [37].

This research aims to prepare several new imidazole compounds and some imidazolium salts and study their biological activity.

2. EXPERIMENTAL

2.1. Apparatus

NMR spectra were recorded on a Brucker instrument (400 MHz) spectrometer. Chemical shifts were reported in (δ) [ppm] relative to tetramethylsilane (TMS).

Data were reported as follows: chemical shift, multiplicity, coupling constant [Hz], integration, and assignment. FTIR spectra (ν [cm^{-1}]) were recorded on a JASCO Spectrum (FTIR 4100) spectrometer using KBr pellets.

2.2. Materials and General Procedure

The imidazole, 1,3-dibromopropane, 1,4-dibromobutane, 1,3-bis(chloromethyl)benzene were procured from Aldrich chemical company. Potassium carbonate, magnesium sulphate, THF, and petroleum ether were purchased from Fisher scientific. All reactions were carried out under argon atmosphere.

Reagents and solvents used without further purification. The reaction and purity of the synthesized compounds were monitored by TLC using aluminium plates precoated with silica gel with F254 nm manufactured by Merck Company.

2.3. Synthesis of Imidazolium Salts

Figure 5 provides the reaction sequences used in the synthesis of imidazole derivatives and their salts.

2.3.1. Synthesis of 1-(3-Bromopropyl)-1H-Imidazole (A1)

In a clean three-necked round bottom flask 100 mL equipped with a magnetic stir bar under argon gas flowing and reflux condenser, imidazole (0.1 g (1.5 mmol)) and 15 mL of dry THF were gradually added into the flask and stirred for 1 h at 65°C. 1,3-dibromopropane (0.303 g (1.5 mmol)) dissolved in 10 mL THF was added into the flask, after 10 min of stirring (0.02 g, 0.2 mmol) of K_2CO_3 was added to the flask. The resulting mixture was stirred for 24 h at 65°C temperature. After 24 h, the mixture was filtrated. The resulting solution was then transferred into 125 mL separator funnel and extracted with (ethanol-ethylacetate). After drying, the

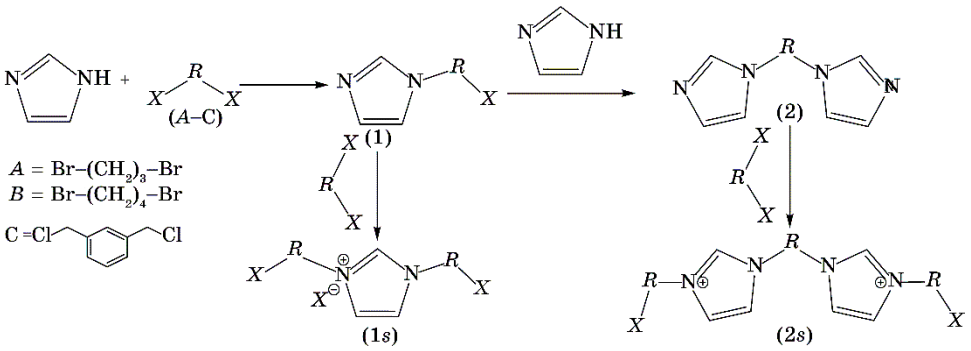

Fig. 5. General reaction scheme for synthesizing imidazole derivatives and their salts.

product was extracted three times with the diethyl ether and the diethyl ether extracted layers were combined and dried overnight using anhydrous magnesium sulphate. The mixture was filtered and the filtrate was collected. The filtrate was concentrated by rotary evaporation to obtain a white precipitate product. The yield of the product was found to be 76.6%.

Like the same procedure for producing (A1), we used 1,4-dibromobutane (0.323 g (1.5 mmol)) to produce 1-(4-bromobutyl)-1H-imidazole (B1) with 69.4% yield, 1,3-bis(chloromethyl)benzene (0.262 g (1.5 mmol)) to produce 1-(3-(chloromethyl)benzyl)-1H-imidazole (C1) with 61.7% yield.

2.3.2. Synthesis of 1,3-Bis(3-Bromopropyl)-1H-Imidazol-3-Ium Bromide (*A*1*S*)

As the previous reaction conditions, in a clean three-necked round bottom flask 100 mL equipped with a magnetic stir bar under argon gas flowing and reflux condenser, 1-(3-bromopropyl)-1H-imidazole (*A*1) (0.283 g (1.5 mmol)) and 20 mL of dry THF were gradually added into the flask and stirred for 1 h at 65°C. 1,3-dibromopropane (0.303 g (1.5 mmol)) dissolved in 10 mL THF was added into the flask. The resulting mixture was stirred for 6 h at 65°C temperature. After 6 h, a yellowish precipitate appeared. The yield of the product was found to be 57%.

The same procedure for producing (*A*1*S*) has been repeated, we used (*B*1) (0.304 g (1.5 mmol)) and 1,4-dibromobutane (*B*) (0.323 g (1.5 mmol)) to produce 1,3-bis(4-bromobutyl)-1H-imidazol-3-ium Bromide (*B*1*S*) with 59.8% yield, and 1-(3-(chloromethyl)benzyl)-1H-imidazole (0.31 g (1.5 mmol)) (*C*1) and 1,3-bis(chloromethyl)benzene (0.262 g (1.5 mmol)) to produce 1,3-bis(3-(chloromethyl)benzyl)-1H-imidazol-3-ium chloride (*C*1*S*) with 55.3% yield.

2.3.3. Synthesis of 1,3-DI(1H-Imidazol-1-Yl) Propane (A2):

In a clean three-necked round bottom flask 100 mL equipped with a magnetic stir bar under argon gas flowing and reflux condenser, imidazole (0.1 g (1.5 mmol)) and 15 mL of dry THF were gradually added into the flask and stirred for 1 h at 65°C 1-(3-bromopropyl)-1H-imidazole (*A*1) (0.283 g (1.5 mmol)) dissolved in 15 mL THF was added into the flask, after 10 min of stirring (0.02 gr, 0.2 mmol) of K_2CO_3 was added to the flask. The resulting mixture was stirred for 24 h at 65°C temperature. After 24 h, the mixture was filtrated. The resulting solution was then transferred into 125 mL separator

funnel and extracted with (ethanol-ethylacetate). After drying, the product was extracted three times with the diethyl ether and the diethyl ether extracted layers were combined and dried overnight using anhydrous magnesium sulphate. The mixture was filtered and the filtrate was collected. The filtrate was concentrated by rotary evaporation to obtain a yellowish precipitate product. The yield of the product was found to be 85.4%.

For producing 1,4-di(1H-imidazol-1-yl)butane (*B*2), we used 1-(4-bromobutyl)-1H-imidazole (*B*1) (0.304 g (1.5 mmol)) with imidazole (0.1 g (1.5 mmol)), the product yield was 73.1%, and imidazole (0.1 g (1.5 mmol)) with 1-(3-(chloromethyl) benzyl)-1H-imidazole (*C*1) (0.31 g (1.5 mmol)) to produce 1,3-bis((1H-imidazol-1-yl)methyl) benzene (*C*2) with 64.8% yield.

2.3.4. Synthesis of 1,3-Bis(3-Bromopropyl)-1H-Imidazol-3-Ium Bromide (A2S)

As the previous reaction conditions, in a clean three-necked round bottom flask 100 mL equipped with a magnetic stir bar under argon gas flowing and reflux condenser, 1,3-di(1H-imidazol-1-yl)propane (*A*2) (0.264 g (1.5 mmol)) and 20 mL of dry THF were gradually added into the flask and stirred for 1 h at 65°C. 1,3-dibromopropane (0.606 gr (3 mmol)) dissolved in 20 mL THF was added into the flask. The resulting mixture was stirred for 6 h at 65°C temperature. After 6 h, a yellowish precipitate formed with 51.2% yield.

The last procedure has been repeated to produce 1,1′-(butane-1,4-diyl)bis(3-(4-bromobutyl)-1H-imidazol-3-ium)bromide (*B*2*S*) with yield 53.4% by reacting (0.285 g (1.5 mmol)) of (*B*2) with (0.647 g (3 mmol)) of (*B*), and reacting (0.357 g (1.5mmol)) with (0.525 g (3 mmol)) of (*C*) for producing phenylenebis (methylene))bis(3-(3-(chloromethyl)benzyl)-1H-imidazol-3-ium)chloride (*C*2*S*) with yield 49.6%.

All the products were characterized by IR, ^{1}H-NMR, ^{13}C-NMR and SEM.

3. RESULTS AND DISCUSSION

The compounds entitled (1 and 2) were prepared through the alkylation reaction between alkyl halides and imidazole (Fig. 1), these compounds were. The characterized using IR, ^{1}H-NMR and ^{13}C-NMR, where the IR spectra showed the disappearance of the absorption band at 3125 cm^{-1} belongs to N–H bond of the imidazole, which confirmed the reaction between the imidazole and the alkyl halide

has occurred.

^{1}H-NMR spectroscopy confirmed this result through the disappearance of the protonic signal at (1.602 ppm) of the imidazole proton (N−H), and the appearance of new protonic signals corresponding to the used alkyl halides compounds, in addition to the clear shifts in the protonic signals of the imidazole ring.

The C-NMR spectrum showed the emergence of three carbon signals that characterize the imidazole ring, in addition to the emergence of new carbon signals indicating the binding of the alkyl compound to the imidazole ring.

The prepared imidazolium salts, labelled with the symbol (*S*), were prepared by adding alkyl halides to the alkyl imidazole compounds prepared in a previous step. These compounds have been characterized using the same techniques mentioned previously. We did not obtain, through IR spectra, distinct bands confirming the occurrence of the reaction (absorption bands have been shifted in general); the structure of the compounds was proven through the H-, C-NMR techniques, whose results were consistent with the structure of the prepared compounds in terms of the number of signals, their shifts, and their integrations.

Table 1 shows the physical properties and yields of prepared compounds.

TABLE 1. The yield and physical statues of produced compounds.

Entry	IUPAC name	State of precipitate	Yield, %
*A*1	1-(3-bromopropyl)-1H-imidazole	white	76.6
*A*1*S*	1,3-bis(3-bromopropyl)-1H-imidazol-3-ium bromide	yellowish	57
*A*2	1,3-di(1H-imidazol-1-yl)propane	yellowish	85.4
*A*2*S*	1,1′-(propane-1,3-diyl)bis(3-(3-bromopropyl)-1H-imidazol-3-ium)bromide	yellowish	51.2
*B*1	1-(4-bromobutyl)-1H-imidazole	yellowish	69.4
*B*1*S*	1,3-bis(4-bromobutyl)-1H-imidazol-3-ium	brownish	59.8
*B*2	1,4-di(1H-imidazol-1-yl)butane	yellowish	73.1
*B*2*S*	1,1′-(butane-1,4-diyl)bis(3-(4-bromobutyl)-1H-imidazol-3-ium)	brownish	53.4
*C*1	1-(3-(chloromethyl)benzyl)-1H-imidazole	yellowish	61.7
*C*1*S*	1,3-bis(3-(chloromethyl)benzyl)-1H-imidazol-3-ium	yellowish	55.3
*C*2	1,3-bis((1H-imidazol-1-yl)methyl)benzene	yellowish	64.8
*C*2*S*	phenylenebis(methylene))bis(3-(3-(chloromethyl)benzyl)-1H-imidazol-3-ium)	yellowish	49.6

3.1. Characterization

(*A*1): (76.6%) was obtained as a white precipitate. ^{1}H-NMR (400 MHz, CDCl3) δ 2.19 (*m*, 2H), 3.42 (*t*, $J = 3.6$ Hz, 2H), 4.07 (*t*, $J = 3.6$ Hz, 2H), 6.96 (*dd*, $J_1 = 1.2$ Hz, $J_2 = 3.2$ Hz, 1H), 7.26 (*dd*, $J_1 = 1.2$ Hz, $J_2 = 3.2$ Hz, 1H), 7.67(*t*, $J = 3.2$ Hz, 1H) ppm; ^{13}C-NMR (125 MHz, CDCl3): δ 30.52, 33.24, 47.11, 118.87, 129.57, and 137.65 ppm.
(*A*1*S*): (57%) was obtained as a yellowish precipitate. ^{1}H-NMR (400 MHz, CDCl3) δ 2.18 (*m*, 2H), 2.59 (*m*, 2H), 3.41 (*t*, $J = 3.6$ Hz, 2H), 3.58 (*t*, $J = 4.4$Hz, 2H), 4.14 (*t*, $J = 3.6$ Hz, 2H), 4.67 (*t*, $J = 4$ Hz, 2H), 7.47 (*dd*, $J_1 = 1.2$ Hz, $J_2 = 2.8$ Hz, 1H), 7.82 (*dd*, $J_1 = 1.2$ Hz, $J_2 = 2.8$ Hz, 1H), 10.25 (*t*, $J = 1.2$ Hz, 1H) ppm; ^{13}C-NMR (125 MHz, CDCl3): δ 30.39, 30.67, 32.94, 33.42, 48.59, 49.06, 121.83, 126.34, and 138.22 ppm.
(*A*2): (85.4%) was obtained as a yellowish precipitate. ^{1}H-NMR (400 MHz, CDCl3) δ 2.13 (*m*, 2H), 4.01 (*t*, $J = 4.8$ Hz, 4H), 6.96 (*dd*, $J_1 = 1.2$ Hz, $J_2 = 2.8$ Hz, 2H), 7.26 (*dd*, $J_1 = 1.2$ Hz, $J_2 = 2.8$ Hz, 2H), 7.67 (*t*, $J = 1.2$ Hz, 2H) ppm; ^{13}C-NMR (125 MHz, CDCl3): δ 30.81, 45.55, 118.89, 129.57, and 137.72 ppm.
(*A*2*S*): (51.2%) was obtained as a yellowish precipitate. 1H-NMR (400 MHz, CDCl3) δ 2.18 (*m*, 2H), 2.06 (*m*, 2H), 2.6 (*m*, 4H), 3.58 (*t*, $J = 4.4$ Hz, 4H), 4.05 (*t*, $J = 4.8$ Hz, 4H), 4.67 (*t*, $J = 4$ Hz, 4H), 7.47 (*dd*, $J_1 = 1.6$ Hz, $J_2 = 4.4$ Hz, 2H), 7.82 (*dd*, $J_1 = 2$ Hz, $J_2 = 4$ Hz, 2H), 10.26 (*t*, $J = 2$ Hz, 2H) ppm; ^{13}C-NMR (125 MHz, CDCl3): δ 30.44, 30.67, 32.94, 47.05, 49.06, 121.82, 126.35, and 138.16 ppm.
(*B*1): (69.4%) was obtained as a yellowish precipitate. ^{1}H-NMR (400 MHz, CDCl3) δ 1.83 (*m*, 2H), 1.89 (*m*, 2H), 3.57 (*t*, $J = 3.2$ Hz, 2H), 3.98 (*t*, $J = 1.6$ Hz, 2H), 6.96 (*dd*, $J_1 = 1.2$ Hz, $J_2 = 2.8$ Hz, 1H), 7.26 (*dd*, $J_1 = 1.2$ Hz, $J_2 = 3.2$Hz, 1H), 7.67 (*t*, $J = 3.2$ Hz, 1H) ppm; ^{13}C-NMR (125 MHz, CDCl3): δ 29.32, 29.81, 30.77, 48.77, 118.84, 129.56, and 137.69 ppm.
(*B*1*S*): (59.8%) was obtained as a brownish precipitate. ^{1}H-NMR (400 MHz, CDCl3) δ 1.84 (*m*, 2H), 1.89 (*m*, 2H), 2.01 (*m*, 2H), 2.23 (*m*, 2H), 3.48 (*t*, $J = 2$Hz, 2H), 3.56 (*t*, $J = 2.8$ Hz, 2H), 4.095 (*t*, $J = 4.8$ Hz, 2H), 4.34 (*t*, $J = 4.4$ Hz, 2H), 7.47 (*dd*, $J_1 = 1.2$ Hz, $J_2 = 2.8$ Hz, 1 H), 7.82 (*dd*, $J_1 = 1.2$ Hz, $J_2 = 2.8$ Hz, 1H), 10.25 (*t*, $J = 1.2$ Hz, 1H) ppm; ^{13}C-NMR (125 MHz, CDCl3): δ 29.12, 29.40, 30.34, 30.78, 30.81, 33.06, 49.45, 49.46, 121.85, 126.33, and 138.34 ppm.
(*B*2): (73.1%) was obtained as a yellowish precipitate. ^{1}H-NMR (400 MHz, CDCl3) δ 1.76 (*m*, 4H), 3.98 (*t*, $J = 4.8$ Hz, 4H), 6.96 (*dd*, $J_1 = 1.2$ Hz, $J_2 = 2.8$ Hz, 2H), 7.26 (*dd*, $J_1 = 1.2$ Hz, $J_2 = 2.8$ Hz, 2H), 7.67 (*t*, $J = 1.2$ Hz, 2H) ppm; ^{13}C-NMR (125 MHz, CDCl3): δ

27.72, 48.44, 118.84, 129.56, and 137.71 ppm.
(*B2S*): (53.4%) was obtained as a brownish precipitate. ^{1}H-NMR (400 MHz, CDCl3) δ 1.77 (*m*, 4H), 2.01 (*m*, 4H), 2.23 (*m*, 4H), 3.48 (*t*, $J = 4$ Hz, 4H), 4.34 (*t*, $J = 4.4$ Hz, 4H), 7.47 (*dd*, $J_1 = 1.6$ Hz, $J_2 = 4.4$ Hz, 2H), 7.82 (*dd*, $J_1 = 2$ Hz, $J_2 = 4$ Hz, 2H), 10.25 (*t*, $J = 2$ Hz, 2H) ppm; ^{13}C-NMR (125 MHz, CDCl3): δ 27.60, 29.40, 30.33, 33.06, 49.35, 49.45, 121.85, 126.33, and 138.1 ppm.
(*C1*): (61.7%) was obtained as a yellowish precipitate. ^{1}H-NMR (400 MHz, DMSO) δ 4.61 (*s*, 2H), 5.3 (*s*, 2H), 6.91 (*dd*, $J_1 = 1.2$ Hz, $J_2 = 2.8$ Hz, 1H), 7.17–7.31 (m, 5H), 7.784 (*t*, $J = 3.2$ Hz, 1H) ppm; ^{13}C-NMR (125 MHz, CDCl3): δ 46.01, 49.80, 119.84, 126.81, 127.66, 128.11, 129.12, 129.12, 137.22, and 137.76 ppm.
(*C1S*): (55.3%) was obtained as a yellowish precipitate. ^{1}H-NMR (400 MHz, CDCl3) δ 4.61 (*s*, 4H), 5.28 (*s*, 2H), 5.787 (*s*, 2H), 7.18–7.4 (*m*, 8H), 7.79 (*dd*, $J_1 = 1.2$ Hz, $J_2 = 2.8$ Hz, 1H), 7.83 (*dd*, $J_1 = 1.2$ Hz, $J_2 = 2.8$ Hz, 1H), 9.95 (*t*, $J = 1.2$ Hz, 1H) ppm; ^{13}C-NMR (125 MHz, CDCl3): δ 46.26, 51.83, 51.96, 123.31, 124.17, 126.1, 127.04, 127.16, 127.66, 128.3, 128.46, 128.81, 129.07, 136.56, 136.88, 137.11, 137.94, and 138.9 ppm.
(*C2*): (64.8%) was obtained as a yellowish precipitate. ^{1}H-NMR (400 MHz, CDCl3) δ 5.3 (*s*, 4H), 6.91 (*dd*, $J_1 = 1.2$ Hz, $J_2 = 2.8$ Hz, 2H), 6.96 (*m*, 1H), 7.1–7.35 (*m*, 5H), 7.78 (*t*, $J = 1.2$ Hz, 2H) ppm; ^{13}C-NMR (125 MHz, CDCl3): δ 49.59, 119.84, 126.02, 127.54, 129.12, 129.37, 137.76, and 138.4 ppm.
(*C2S*): (49.6%) was obtained as a yellowish precipitate. ^{1}H-NMR (400 MHz, CDCl3) δ 4.61 (*s*, 4H), 5.28 (*s*, 4H), 5.78 (*s*, 4H), 6.95 (*m*, 1H), 7.1–7.41 (*m*, 11H), 7.79 (*dd*, $J_1 = 1.2$ Hz, $J_2 = 2.8$ Hz, 2H), 7.83 (*dd*, $J_1 = 1.2$ Hz, $J_2 = 2.8$ Hz, 2H), 9.96 (*t*, $J = 1.2$ Hz, 2H) ppm; ^{13}C-NMR (125 MHz, CDCl3): δ 46.26, 51.83, 52.13, 123.31, 124.28, 126.09, 127.16, 128.32, 128.46, 128.81, 129.43, 136.56, 137.03, 137.11, and 137.94 ppm.

3.2. SEM of Nanoparticles

The morphology of nanoparticles is studied by means of the scanning electron microscopy images.

The image gives information about the size and shape of the particles and their surface morphology.

Figure 6 shows a scanning electron microscopy (SEM) image of the imidazolium salts.

The particles appear to be heterogeneous in shape, irregular in size, their size ranges between 40 to 180 nm, and their average size is 70 nm.

They have a rough surface that appears to be composed of a cluster of tiny (18 nm)-sized particles.

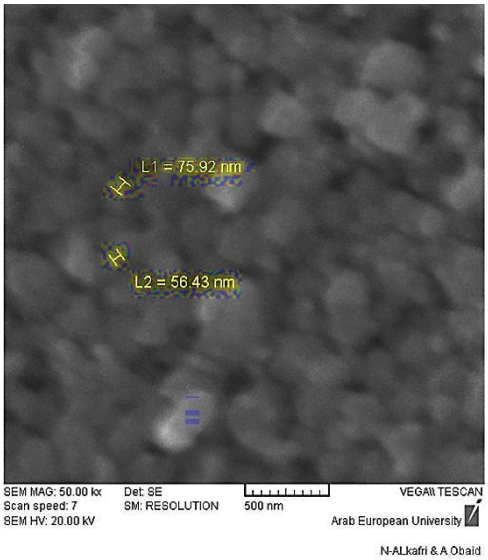

Fig. 6. SEM images of (*A*1*S*).

3.2. Antibacterial Activity Study

The antibacterial efficacy of the prepared compounds was tested against *Escherichia coli*, and *Staphylococcus aureus* bacteria comparing with gentamicin (as a reference). Two different concentrations (50 and 1000 mg/ml) of the compounds and gentamicin have been selected for antibacterial assay. In our research, we chose to study *E. coli* and *S. aureus* bacteria, because of their wide spread in society so they affect in the daily life of humans, as *Escherichia* is a common bacterium found in the intestines of humans and warm-blooded animals. It is often used as an indicator for faecal contamination in water and soil [38].

Pathogenic strains of *E. coli* are often transmitted through contaminated food or water [39], and can be particularly dangerous for young children, elderly individuals, and those with weakened immune systems. This bacterium can cause a range of infections, including intestinal, skin, wound sepsis, septicaemia, neonatal septicaemia, and urinary tract infections [40]. Studies have shown that some non-steroidal pain relievers, such as diclofenac sodium, can play an inhibitory role in the growth of some bacteria, whether negative or positive, in addition to using it as an anti-inflammatory [41–43]. *Escherichia coli* is also commonly used in scientific research, as it is easy to grow and manipulate in the laboratory. It has been used as a model organism for studying various biological processes, and has contributed to many important discoveries in mi-

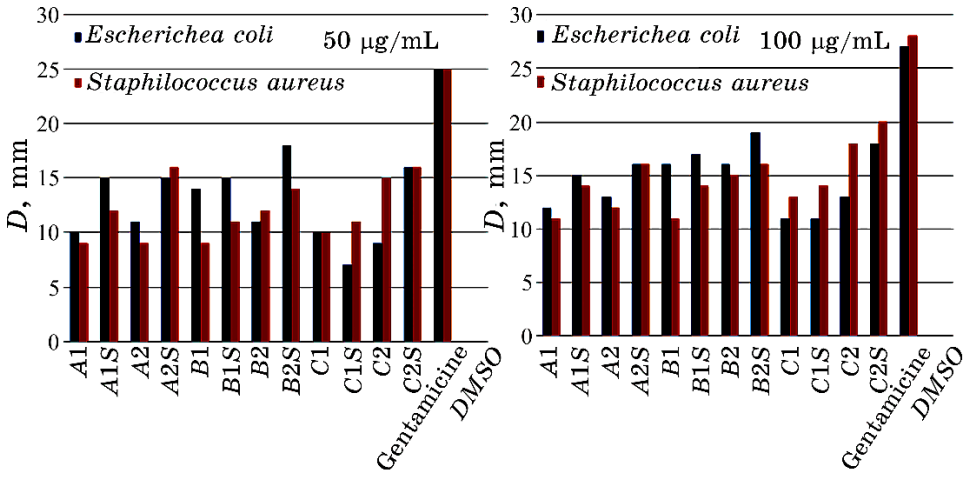

Fig. 7. Biological activity of prepared compounds.

TABLE 2. Biological test results of the *E. coli* and *S. aureus*.

Entry	50 (μg/mL)		100 (μg/mL)	
	E. coli	*S. aureus*	*E. coli*	*S. aureus*
*A*1	10	9	12	11
*A*1*S*	15	12	15	14
*A*2	11	9	13	12
*A*2*S*	15	16	16	16
*B*1	14	9	16	11
*B*1*S*	15	11	17	14
*B*2	11	12	16	15
*B*2*S*	18	14	19	16
*C*1	10	10	11	13
*C*1*S*	7	11	11	14
*C*2	9	15	13	18
*C*2*S*	16	16	18	20
gentamicin	25	25	27	28
DMSO	0	0	0	0

crobiology and genetics [44].

S. aureus is a major bacterial human pathogen that causes a wide variety of clinical manifestations. Infections are common both in community-acquired as well as hospital-acquired settings and treatment remains challenging to manage due to the emergence of multi-drug resistant strains such as MRSA (methicillin-resistant *Staphylococcus aureus*) [45, 46]. *S. aureus* is found in the environment and is also found in normal human flora, located on the skin and mucous membranes (most often the nasal area) of most healthy

individuals. *S. aureus* does not normally cause infection on healthy skin; however, if it is allowed to enter the bloodstream or internal tissues, these bacteria may cause a variety of potentially serious infections [47]. Transmission is typically from direct contact. However, some infections involve other transmission methods [48].

The results are arranged in Table 2 and presented graphically in the bar graph (Fig. 7).

4. CONCLUSIONS

In summary, a new number of mono- and di-substituted derivatives of imidazole and its salts were prepared and characterized using ^{1}H-NMR, ^{13}C-NMR, and IR methods. In addition, the biological activity against *Escherichia coli* and *Staphylococcus aureus* bacteria was studied. It was found that the prepared salts have more biologically activity than imidazole derivatives, which promises with amazing results for the prepared compounds in various pharmacological applications.

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