RESEARCH ARTICLE

Synthesis and Identification of Heterocyclic Derivative from 2-amino-4-hydroxy-6-methyl pyrimidine and Study their Biological Activity

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ABSTRACT

This study includes the synthesis of some hetrocyclic compounds (oxazepine, β-lactam, imedazolidene, thiazolidine, tetrazole) starting from reacting 2-amino-4-hydroxy-6-methyl pyrimidine with 3-amino acetophenone in acid medium to get schiff base derivative (1). Then (1) react with 4-hydroxy acetophenone in acid medium to get schiff base derivative (2). There after (2) react with (phthalic anhydride, maleic anhydride and succenic anhydride) to give oxazepine derivative (3-5). Also (2) react with (chloroacetyl chloride, glycine, alanine, thioglygolic acid, sodumazide) to get (β-lactam (6), imidazolidine (7,8), Thiazolidine (9), tetrazole (10), respectively. Fourier transform infrared spectroscopy (FTIR), ^{1}H-Nuclear Magnetic Resonance (^{1}H-NMR), Carbon-13 nuclear magnetic resonance (^{13}C-NMR) characterize all these derivative. After that, we determine the biological activity for all derivatives toward two kinds of bacteria.

Keywords : β-lactam, Imedazolidene, Oxazepine, Schiff bases, Tetrazole, Thiazolidine.

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INTRODUCTION

Heterocyclic compounds are cyclic compounds that contain one or more hetero-atom. However, among the commonly known hetero atoms are usually oxygen, nitrogen, and sulphur, in addition to other hetero atoms.[1,2] Schiff base bear azomethine or imine (-C=N) unit. However, it forms the main condensation known of amines with carbonyl compounds. Schiff base derivatives showed a variety of pharmacological and biological activities as an antidepressant, antimicrobial, anti-HIV, analgesic, cytotoxicity, antileishmanial, fungicides, anticonvulsant, tuberculostatic, insecticides, anticancer, and anti-inflammatory.[3,4]

Imidazolidines (saturated imidazoles), also called tetrahydroimidazoles are considered as biologically active nitrogen include heterocyclic moiety that has been reported as demonstrating a vast array of important nutrients bioactivities.[5,6]

Oxazepine is hetrocyclic compound seven members ring that contains two heteroatoms (Nitrogen and Oxygen).[7,8] Oxazepine compounds are regarded as having biological and medical significance having pharmaceutical and medical applications. However, the hetero-polymer, which is seen as among the chemical derivatives, has an active role in resisting cancer and proved effective against fungi and bacteria. It has also been claimed that some oxazepine derivatives are a medical drug used against disease.[9,10]

The four-membered β-lactam ring forms an important class of antibiotic families like penicillins, carbapenems, cephalosporins and monobactams.[11]

Thiazolidine derivatives having nitrogen at position 3, sulfur atom at position 1, and a carbonyl group at position 4,[12] Thiazolidin-4-ones and its derivatives have been a great success in the field of chemistry and pharmacological properties such as antifungal, anti-oxidant, and anti-tubercular.[13,14]

Tetrazole analogs are regarded as having a pharmacological activity in the medical chemistry division. Many Active Pharmaceutical Drug Intermediates (API) of tetrazole derivatives are seen as playing their role in regins related to Pharmaceutics and agrochemistry. These compounds, however, usually act as multidimensional biological active drug candidates like Angiotensin (AT1), Angiotensin (AT2) receptor (Hypertension).[15,16]

MATERIALS

(FTIR) Spectra (400–4000 cm^{-1}) in KBr disk were recorded on SHIMADZU FTIR-8400S Fourier transform. Melting points were measured using Stuart, UK. ^{13}C-NMR and ^{1}HNMR were recorded on Fourier transformation Bruker spectrometer operating at (400MHz) with (DMSO-d6) measurements were made at the Department of Chemistry, Kashan University, Isfahan Province, Iran.

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METHODS

Synthesis Schiff Base 1[17]

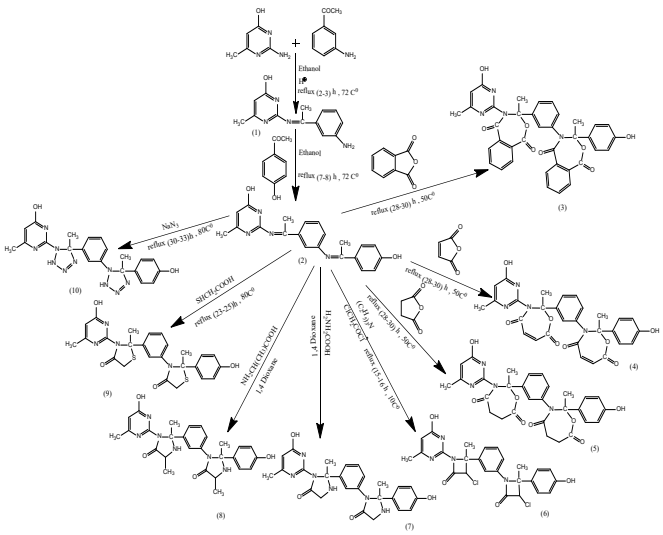
Mix equal moles of (2-amino-4-hydroxy-6-methel pyrimidine) with (3-amino acetophenone) (0.01 mole) in 30 mL ethanol and then put 3 drops of Glacial acitic acid and then refluxed for (3 hours) after the cold solution and leave for (24 hours) then filtered and recrystallized by ethanol.

Synthesis Schiff Base 2[18]

Mix equal moles of the (compound 1) with 4-hydroxy acetophenone (0.01 mole) in 30 mL ethanol and place three drops of Glacial acetic acid and refluxed for (8 hours) then filtered and recrystallized by ethanol.

Synthesis Oxazepine Derivatives (3, 4, 5)[19]

Dissolve (0.001 mol) of compound (2) in (25 mL) benzene and addition (0.001 mol) of (phthalic anhydride, maleic anhydride, succenic anhydride) them refluxed for (30 hours) and after cold product, recrystallized by ethanol.



Scheme 1: Synthesis of some heterocyclic compounds derivatives.

Synthesis β-lactam Derivative (6)[20]

Mix the compound (2) (0.001 mol) with (0,0009 mol) of tri ethyl amine in (30 mL) 1,4-dioxane and after addition to mixture drops chloroacetyl chloride, in 10°C for 15 hours and filer the precipitation.

Synthesis Imedazolidine Derivative (7, 8)[21]

Mixed the compounds (2) (0.001 mol) dissolved in (20 mL) tetrahydrofuran with (0.02 mol) of (Galycin, Alanin) dissolved in (20 mL) THF and then refluxed for (27 hours) after cold and left for (40 hours) and recrystallized by ethanol.

Synthesis Thiazolidine Derivative (9)[22]

The compounds (2) (0.001 mol) were mixed with (0.003 mol) dissolved thioclacolic acid in (30 mL) 1,4 dioxane and then (0.4 g) of anhydrous zinc chloride was added and then the precipitation was increased for (24 hours) and then left for (72 hours) them filtered and recrystallized by ethanol.

Synthesis Tetrazole Derivative (10)[23]

Mix the compound (2) (0.001 mol) dissolve in (20 mL) 1,4-dioxane with sodiumazide (0.001 mol) the dissolve in (20 mL) 1,4-dioxane and refluxed for (33 hours) them filtered and recrystallized by ethanol.

Preparation of Microbiology Culture Median

10 g of nutrient agar is dissolved in (250 mL) of distillation water, then put in an autoclave for 25 minutes at 170°C for sterilization. Pouring the media after becoming at 37°C in Petri dishes, made ready for streaking by bacteria. It was getting (*Staphylococcus aurous*) and (*Escherichia coli*) isolated bacteria from the hospital. It was cultured, and these plates were incubated at 37°C for 24 hours for both bacteria.

RESULTS AND DISCUSSION

Compound 1: ((E)-2-((1-(3-aminophenyl) ethylidene) amino)-6-methylpyrimidin-4-ol)

FT-IR spectrum data for compound (1) show band at 3463 cm^{-1} for (NH_2), 3332 cm^{-1} for (O-H), 3078 cm^{-1} for(Ar-H), 2947 cm^{-1}

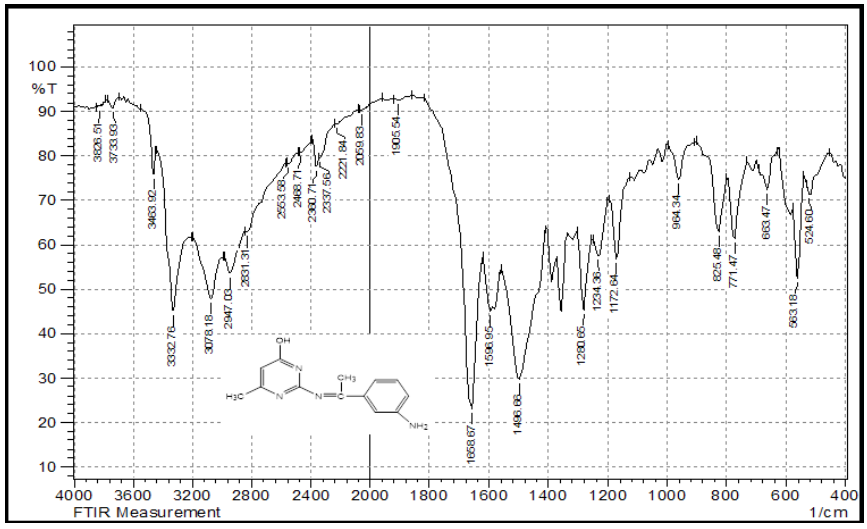


Figure 1: FT-IR spectra of compound (1)

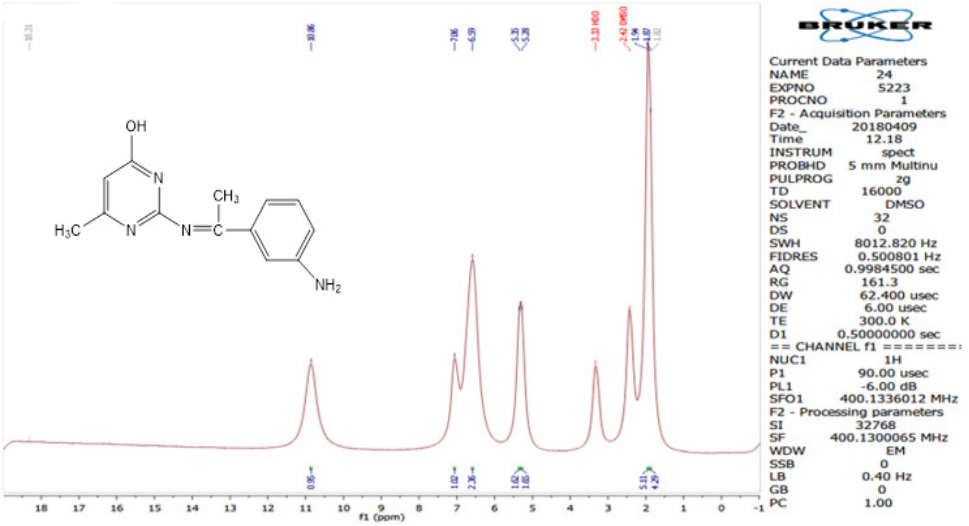


Figure 2: ^{1}H-NMR spectrum of compound (1)

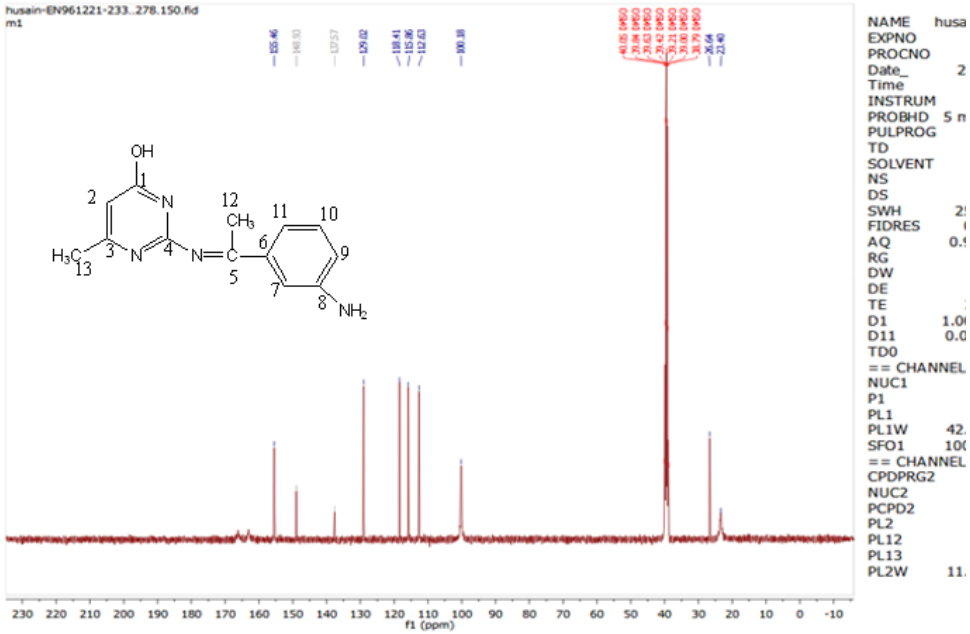


Figure 3: ^{13}C-NMR spectrum of compound (1)

for (C-H) of (CH_3), 1658 cm^{-1} for (C=N) and 1496 cm^{-1} for (C=C) aromatic.^{1}H NMR (DMSO) spectrum data of compound (1) show 1.8 ppm (S, 3H, $CH_{3)}$, 3.33 ppm (S, 3H, CH_3 pyrimidine ring), 5.2 ppm (S, 2H, $NH_{2)}$, 5.3 ppm (S, 1H, OH) 6.5-7 ppm (M, 4H, Ar-H), 10.8 ppm (S, 1H, pyrimidine ring). The ^{13}C- NMR (DMSO) spectrum data of compound (1) show: 23 ppm (C_{12}), 26 ppm (C_{13}), 100 ppm(C_5), 155 ppm (C_4), 137 ppm ($C_{8)}$, 148 ppm (C_1), 112-129 ppm (C_{Arom}). Figures (1, 2 and 3)

Compound 2 : (4-(4-hydroxy-6-methylpyrimidin-2-yl)-3-(3-(3-(4-hydroxyphenyl)-3-methyl-1,5-dioxo-1,5-dihydrobenzo[e][1,3]oxazepin-4(3H)-yl)phenyl)-3-methyl-3,4-dihydrobenzo [e][1,3] oxazepine-1,5-dion)

FT-IR spectrum data for compound (2) show band 3332 cm^{-1} for (O-H), 3078 cm^{-1} for (Ar-H), 2947 cm^{-1} for (C-H) of (CH_3), 1658 cm^{-1} for (C=N) and 1596 cm^{-1} for (C=C) aromatic. ^{1}H NMR (DMSO) spectrum data of compound (2) show 1.9-2.1 ppm (S, 6H, CH_3), 3.3 ppm (S, 3H, CH_3 in pyrimidin 5.34 ppm (S, 1H, OH in phenol), 5.39 ppm (S, 1H, OH in pyrimidin) 6.59-7.82 ppm (M, 7H, Ar-H), 10.34 ppm (S, 1H, CH in pyrimidine ring). The C13-NMR (DMSO) spectrum data of compound (2) show: 23 ppm (C_{21}), 26.2 ppm (C_{20}), 26.6 ppm (C_{19}), 100 ppm ($C_{5,12}$), 164 ppm (C_4), 163 ppm (C_1), 161 ppm (C_{16}), 155 ppm (C_{10}), 112-148 ppm (C_{Arom}).

Compound 3 :(4-(4-hydroxy-6-methylpyrimidin-2-yl)-3-(3-(3-(4-hydroxyphenyl)-3-methyl-1,5-dioxo-1,5-dihydrobenzo[e][1,3]oxazepin-4(3H)-yl)phenyl)-3-methyl-3,4-dihydrobenzo [e] [1,3] oxazepine-1,5-dione)

FT-IR spectrum data for compound (3) show band at 3332 cm^{-1} (O-H), 3078 cm^{-1} for (Ar-H), 2947 cm^{-1} for (C-H) of (CH_3),

1666 cm^{-1} (C=O), (1171) cm^{-1} for (C-O-C) and 1357 cm^{-1} for (C-N) of oxazepine. ^{1}H NMR (DMSO) spectrum data of compound (3) show 1.7-1.8 ppm (S, 6H, $CH_{3)}$, 3.4 ppm (S, 3H, CH_3 in pyrimidine ring), 5.4 ppm (S, 2H, OH) 6.6-8.2 ppm (S, 15H, Ar-H), 10.3 ppm (S, 1H, CH in pyrimidine ring). The ^{13}C-NMR (DMSO) spectrum data of compound (3) show: 168 ppm (C_4), 26.2 ppm (C_{37}), 167 ppm (C_1), 197 ppm ($C_{5,}C_{12,}C_{27,}C_{20}$), 100-155($C_{Arom}$), 163 ($C_{32}$), 161 ($C_{18}$).

Compound 4 : (3-(4-hydroxy-6-methylpyrimidin-2-yl)-2-(3-(2-(4-hydroxyphenyl)-2-methyl-4,7-dioxo-4,7-dihydro-1,3-oxazepin-3(2H)-yl)phenyl)-2-methyl-2,3-dihydro-1,3-oxazepine-4,7-dione)

FT-IR spectrum data for compound (4) show band at 3379 cm^{-1} (O-H), 3178 cm^{-1} for (Ar-H), 2931 cm^{-1} for (C-H) of (CH_3), 1674 cm^{-1} (C=O), (1087) cm^{-1} for (C-O-C) and 1365 cm^{-1} for (C-N) of oxazepine). ^{1}H-NMR (DMSO) spectrum data of compound (4) show 2 ppm (S, 6H, CH_3), 3 ppm (S, 3H, CH_3 pyrimidine ring), 5.5 ppm (S, 2H, OH), 6.8-7.8 ppm (M, 7H, Ar-H), 6.1 ppm (d, 4H, CH=CH), 10.3 ppm (S, 1H, CH pyrimidine ring) The ^{13}C-NMR (DMSO) spectrum data of compound (4) show: 21 (C_{27}), 26.2 ppm (C_{28}), 26.4 ppm (C_{29}), 38.7 ppm (C_9,C_{20}), 101 ppm (C_{20}), 167 ppm (C4), 163 ppm (C1), 196 ppm ($C_{5,}C_{8,}C_{16,}C_{19}$), 101 ppm ($C_{6,}C_{7,}C_{17,}C_{18}$), 161 ppm ($C_{24}$), 159 ppm ($C_{14}$), 112-154 ppm ($C_{Arom}$).

Compound 5:(3-(4-hydroxy-6-methylpyrimidin-2-yl)-2-(3-(2-(4-hydroxyphenyl)-2-methyl-4,7-dioxo-1,3-oxazepan-3-yl)phenyl)-2-methyl-1,3-oxazepane-4,7-dione)

FT-IR spectrum data for compound (5) show band at 3332 cm^{-1} (O-H), 3070 cm^{-1} for (Ar-H), 2923 cm^{-1} for (C-H) of (CH_3), 1712 cm^{-1} (C=O), 1666 cm^{-1} is due C=C aromatic, (1087) cm^{-1} for (C-O-C) and 1365 cm^{-1} for (C-N) of oxazepine. ^{1}H-NMR (DMSO) spectrum data of compound (5) show: 0.8-1.2 ppm (S, 6H, CH_3), 2 ppm (S, 3H, CH_3 in pyrimidine ring), 5.47-5.48 ppm (S, 2H, OH), 6.7-8.1 ppm (M, 7H, Ar-H), 2.45-2.49 ppm (t, 6H, CH_2-CH_2), 10.1 ppm (S, 1H, CH in pyrimidine ring). The ^{13}C-NMR (DMSO) spectrum data of compound (5) show: 26.6 ppm (C_{29}), 22 ppm, 26.2 ppm ($C_{27,}C_{28}$), 26.7 ppm ($C_{7,}C_{18}$), 28.6 ppm, 28.7 ppm (C_8,C_{19}), 170 ppm (C_1), 173 ppm (C_4), 30 ppm ($C_{5,}C_{16}$), 154 ppm (C_{24}), 154 (C_{14}), 195 ppm ($C_{6,}C_{17}$), 197 ppm, 198 ppm ($C_{9,}C_{20}$), 110-148 ppm (C_{Arom}).

Compound 6:(3-chloro-1-(3-(3-chloro-1-(4-hydroxy-6-methylpyrimidin-2-yl)-2-methyl-4-oxoazetidin-2-yl) phenyl)-4-(4-hydroxyphenyl)-4-methylazetidin-2-one)

FT-IR spectrum data for compound (6) show band at 3332 cm^{-1} (O-H), 3078 cm^{-1} for (Ar-H), 2947 cm^{-1} for (C-H) of (CH_3), 1658 cm^{-1} (C=N), 1596 cm^{-1} is due (C=C) aromatic, 1272 cm^{-1} for (C-N) in beta lactame ring, (779) cm^{-1} for (C-Cl) in beta lactame ring. ^{1}H NMR (DMSO) spectrum data of compound (6) show 1.1-2 ppm (S, 6H, CH_3 beta lactame ring) 3.1 ppm (S, 3H, CH_3 in pyrimidine ring), 4.35 ppm (S, 2H, CH-Cl), 4.39 ppm (S, 1H, OH phenol), 5.5 ppm (S, 1H, OH in pyrimidine ring) 6.4-8.3 ppm (M, 7H, Ar-H), 10.4 ppm (S, 1H, CH in pyrimidine ring).The 13C-NMR (DMSO) spectrum data of compound (6) show: 8 ppm (C_{25}), 22 ppm (C_{24}), 45 ppm, 46 ppm ($C_{7,16}$), 196 ppm,197 ppm (C_{5},C_{14}), 164 ppm (C_1), 169 ppm (C_4), 163 ppm (C_{20}), 162 ppm (C_{12}), 43 ppm (C_{15},C_6), 100-155 ppm (C_{Arom}).

Compound 7: (3-(4-hydroxy-6-methylpyrimidin-2-yl)-2-(3-(2-(4-hydroxyphenyl)-2-methyl-5-oxoimidazolidin-1-yl)phenyl)-2-methylimidazolidin-4-one)

FT-IR spectrum data for compound (8) show band at 3332 cm^{-1} (O-H), 3078 cm^{-1} for (Ar-H), 2923 cm^{-1} for (C-H) of (CH_3), 1658 cm^{-1} (C=O), 1596 cm^{-1} is due (C=N) in pyrimidine ring, 1512 cm^{-1} for (C=C) aromatic, 1272 cm^{-1} for (C-N). ^{1}H NMR (DMSO) spectrum data of compound (7) show 1.2-2 ppm (S, 6H, CH_3 in imedazolidine ring), 2.4 ppm (S, 3H, CH_3 pyrimidine ring), 3.2 ppm (S, 4H, CH_2 in imedazolidine ring$_{)}$, 5.4 ppm (S, 2H, OH), 6.8-8.3 ppm (M, 7H, Ar-H), 3.6 ppm (S, 1H, NH imedazolidine ring), 10.5 ppm (S, 1H, CH in pyrimidine ring). The ^{13}C-NMR (DMSO) spectrum data of compound (7) show 22.4 ppm (C_{24}, C_{25}), 26.7 ppm (C_{23}), 57.2 ppm (C_6, C_{15}), 60.1 ppm ($C_{7,}$ 16), 196 ppm,197 ppm (C_5, C_{14}), 159 ppm (C_1), 163 ppm (C_4), 155 ppm (C_{20}), 137 (C_{12}), 100.2-129 ppm (C_{Arom}).

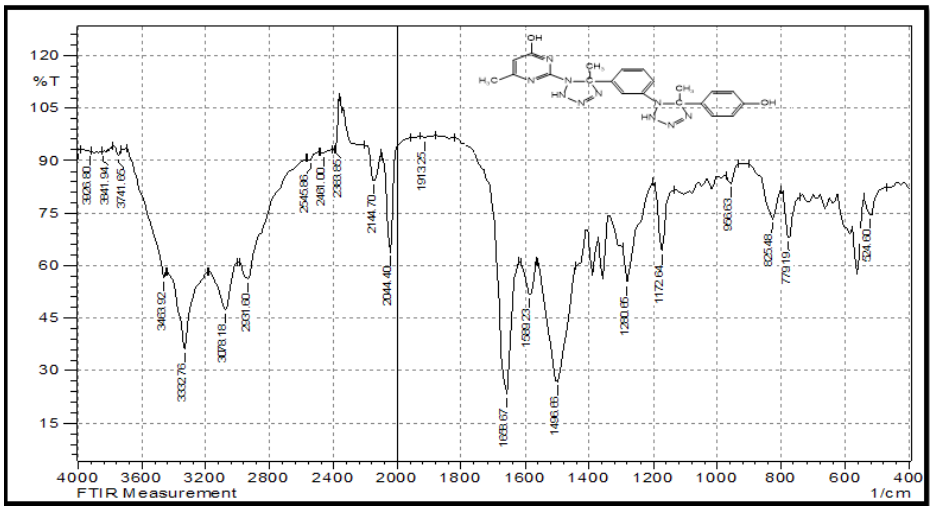


Figure 4: FT-IR spectra of compound (10)

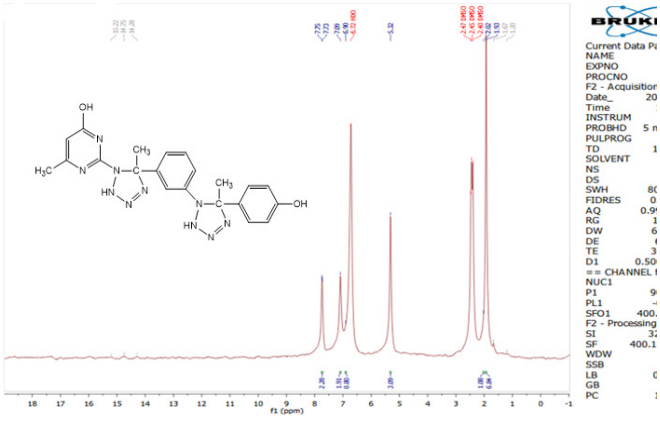


Figure 5: ^{1}H-NMR spectrum of compound (10)

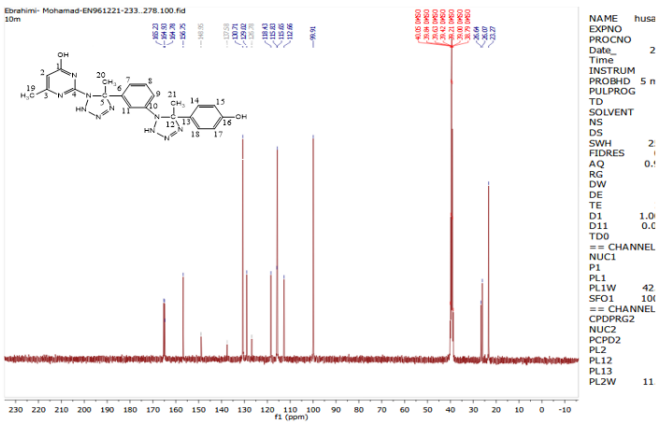


Figure 6: ^{13}C-NMR spectrum of compound (10)

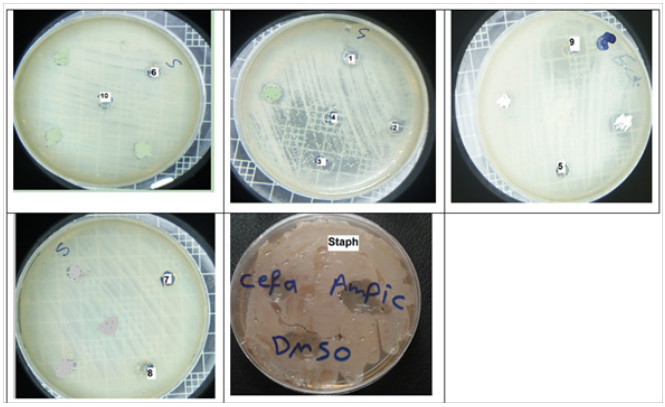


Figure 7: Biological activity of compound prepared against *S. aureus*

Table 1: Showing biological activity for compounds (1-10).

Compounds NO.	*Bacterial species*	
	Staph.aureus	*E. coli*
1	+	_
2	+	_
3	++	+
4	++	_
5	+	+
6	++	_
7	_	+
8	_	+
9	+++	+++
10	+	+++

No inhibition = in active, += (5–10) mm =slightly active, ++= (11–20) mm moderately active = -+++ = More than 20, good active

Compound 8 : (3-(4-hydroxy-6-methylpyrimidin-2-yl)-2-(3-(2-(4-hydroxyphenyl)-2,4-dimethyl-5-oxoimidazolidin-1-yl)phenyl)-2,5-dimethylimidazolidin-4-one)

FT-IR spectrum data for compound (9) show band at 3332 cm^{-1} (O-H), 3078 cm^{-1} for (Ar-H), 2923 cm^{-1} for (C-H) of (CH_3), 1658 cm^{-1} (C=O), 1596 cm^{-1} is due (C=N) in pyrimidine ring, 1512 cm^{-1} for (C=C) aromatic, 1280 cm^{-1} for (C-N). ^{1}H NMR (DMSO) spectrum data of compound (8) show 2.63-3.44 ppm (S, 12H, CH_3 imedazolidine ring) 3.47 ppm (S, 3H, CH_3 pyrimidine ring), 5.45 ppm (S, 1H, OH) 6.86-7.32 ppm (S, 8H, Ar-H), 3.81 ppm (S, 1H, NH imedazolidine ring) 10.51 ppm (S, 1H, pyrimidine ring). The ^{13}C-NMR (DMSO) spectrum data of compound (8) show 16.23 ppm (C_{25}, C_{27}), 26.7 ppm (C_{23}), 28,37 ppm (C_{24}, C_{26}), 57 ppm (C_7, C_{16}), 49 ppm (C_6, C_{15}), 57 ppm (C_7, C_{14}), 159 ppm (C_1), 162 ppm (C_4), 155 ppm (C_{20}), 138 (C_{12}), 115 ppm (C_{10}), 196 ppm, 197 ppm (C_5,C_{16}) 100-129 ppm (C_{Arom}).

Compound 9: (3-(4-hydroxy-6-methylpyrimidin-2-yl)-2-(3-(2-(4-hydroxyphenyl)-2-methyl-4-oxothiazolidin-3-yl) phenyl)-2-methylthiazolidin-4-one)

FT-IR spectrum data for compound (9) show band at 3201 cm^{-1} for (O-H), 1689 cm^{-1} is due (C=O), 1612 cm^{-1} for C=N in pyrimidine ring, 1512 cm^{-1} for (C=C) aromatic. ^{1}H NMR (DMSO) spectrum data of compound (9) show 1.8-2 ppm (S, 6H, CH_3 in thiazolidine ring) 3.1 ppm (S, 3H, CH_3 in pyrimidine ring), 3.6 ppm (S,CH_2 in thiazolidine ring), 5.54 ppm (S, 2H, OH),6.7-7.8 ppm (M, 7H, Ar-H), 10.4 ppm (S, 1H, pyrimidine ring). The 13C-NMR (DMSO) spectrum data of compound (8) show:21 ppm (C_{24}, C_{25}), 26 ppm (C_{23}), 62 ppm (C_7, C_{16}), 40.5 ppm (C_6, C_{15}), 196 ppm,198 ppm (C_5,C_{14}), 170 ppm (C_4), 163 ppm (C_1), 161 ppm (C_{20}), 154 ppm (C_{12}), 100-148 ppm (C_{Arom})

Compound 10: (2-(5-(3-(5-(4-hydroxyphenyl)-5-methyl-2,5-dihydro-1H-tetrazol-1-yl)phenyl)-5-methyl-2,5-dihydro-1H-tetrazol-1-yl)-6-methylpyrimidin-4-ol)

FT-IR spectrum data for compound (10) show band at 3463 cm^{-1} for (N-H) in tetrazole ring, 3332 cm^{-1} (O-H), 3078 cm^{-1} for (Ar-H), 2931 cm^{-1} for (C-H) of (CH_3), 1658 cm^{-1} (C=N), 1589 cm^{-1} is due C=C aromatic, 1496 is due (N=N), 1280 cm^{-1} for (C-N). ^{1}H-NMR (DMSO) spectrum data of compound (10) show 1.2-1.93 ppm (S, 6H, CH_3 in tetrazole ring), 2 ppm (S, 3H, CH_3 in pyrimidine ring), 5.32 ppm (S, 2H, OH), 6.7-7.7 ppm (M, 7H, Ar-H), 14 ppm, 15 ppm (S, 2H,NH in tetrazol), 10 ppm (S, 1H, CH in pyrimidine ring). The ^{13}C- NMR (DMSO) spectrum data of compound (7) show: 23.2 ppm, 26 ppm (C_{20}, C_{21}), 26.6 ppm (C_{19}), 164.9 ppm (C_1), 165 ppm (C_4), 164.7 ppm (C_{16}), 164 ppm (C_{10}), 99 (C_5, C_{12}), 112-156 ppm(C_{Arom}). Figures (4, 5 and 6); Biologicla activity

Table 2: Physical properties for compound (1-10)

No.	*Name of coump.*	*M.F*	*M.W*	*M.P (°C)*	*R.F*	*Colour*	*%*
1	(E)-2-((1-(3-aminophenyl)ethylidene)amino)-6-methylpyrimidin-4-ol	$C_{13}H_{14}N_4O$	242.12	153	0.58	White	80
2	2-(((E)-1-(3-(((E)-1-(4-hydroxyphenyl)ethylidene)amino) phenyl)ethylidene)amino)-6-methylpyrimidin-4-ol	$C_{21}H_{20}N_4O_2$	360.42	296	0.58	Brown gray	77
3	4-(4-hydroxy-6-methylpyrimidin-2-yl)-3-(3-(3-(4-hydroxyphenyl)-3-methyl-1,5-dioxo-1,5-dihydrobenzo[e][1,3]oxazepin-4(3H)-yl)phenyl)-3-methyl-3,4-dihydrobenzo[e][1,3]oxazepine-1,5-dione	$C_{37}H_{28}N_4O_8$	656.65	162	0.42	White	77
4	3-(4-hydroxy-6-methylpyrimidin-2-yl)-2-(3-(2-(4-hydroxyphenyl)-2-methyl-4,7-dioxo-4,7-dihydro-1,3-oxazepin-3(2H)-yl)phenyl)-2-methyl-2,3-dihydro-1,3-oxazepine-4,7-dione	$C_{29}H_{24}N_4O_8$	556.53	185	0.52	White	90
5	3-(4-hydroxy-6-methylpyrimidin-2-yl)-2-(3-(2-(4-hydroxyphenyl)-2-methyl-4,7-dioxo-1,3-oxazepan-3-yl) phenyl)-2-methyl-1,3-oxazepane-4,7-dione	$C_{29}H_{28}N_4O_8$	560.56	125.5	0.25	Nutty	65
6	3-chloro-1-(3-(3-chloro-1-(4-hydroxy-6-methylpyrimidin-2-yl)-2-methyl-4-oxoazetidin-2-yl)phenyl)-4-(4-hydroxyphenyl)-4-methylazetidin-2-one	$C_{25}H_{22}C_{l2}N_4O_4$	513.38	Serum	0.52	Brown	71
7	3-(4-hydroxy-6-methylpyrimidin-2-yl)-2-(3-(2-(4-hydroxyphenyl)-2-methyl-5-oxoimidazolidin-1-yl)phenyl)-2-methylimidazolidin-4-one	$C_{25}H_{26}N_6O_4$	474.52	Serum	0.57	Brown red	66
8	3-(4-hydroxy-6-methylpyrimidin-2-yl)-2-(3-(2-(4-hydroxyphenyl)-2,4-dimethyl-5-oxoimidazolidin-1-yl) phenyl)-2,5-dimethylimidazolidin-4-one	$C_{27}H_{30}N_6O_4$	502.58	Serum	0.58	Brown red	72
9	3-(4-hydroxy-6-methylpyrimidin-2-yl)-2-(3-(2-(4-hydroxyphenyl)-2-methyl-4-oxothiazolidin-3-yl)phenyl)-2-methylthiazolidin-4-one	$C_{25}H_{24}N_4O_4S_2$	508.61	Serum	0.55	Brown red	71
10	2-(5-(3-(5-(4-hydroxyphenyl)-5-methyl-2,5-dihydro-1H-tetrazol-1-yl)phenyl)-5-methyl-	$C_{21}H_{22}N_{10}O_2$	446.48	225.5	0.63	Brown gray	77

have been shown in Table 1 and physical properties have been shown in Table 2.

CONCLUSION

From the above studies, it can be concluded that the synthesized compounds exhibit significant antibacterial activity against bacteria *E. coli* and *S. aureus*. The compound that appeared good activity are (3,4,6,9) against (*S. aureus*), and compounds that appeared good activity are (9,10) against (*E. coli*). The results of the antibacterial activity are shown in the Figure 7. The derivatives that have been prepared and diagnosed in different ways have a different biological effects, and this depends mainly on the composition of the compound in general and the groups compensated in particular

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