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Synthesis and Characterization of Some New Pyrazoline and Isoxazoline Derivatives as Antibacterial Agents

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Abstract:

In this paper some chalcones (C1-C8) are prepared based on the reaction of one mole of substituted acetophenone with one mole of substituted benzaldehydes in the presence of (40%) sodium hydroxide as a base. Pyrazolines (P1–P8) are prepared from the reaction of chalcones (C1-C8) with hydrazine hydrate.

Isoxazoline (I1-I8) is prepared from the reaction of chalcones (C1-C8) with hydroxyl amine hydrochloride in the presence of (10%) sodium hydroxide as a base. These compounds are characterized by using various physical and spectral methods. The compounds are screened for their in vitro antibacterial activity using gram-positive bacteria and gram-negative bacteria. Several derivatives of pyrazolines and isoxazolines are produced well to moderate activities against number of bacteria.

Key words: Chalcones, Pyrazolines, Isoxazolines, Antibacterial.

Introduction:

Chalcones are α, β-unsaturated ketone containing the reactive ketoethylenic group –CO-CH=CH-. These are coloured compounds because of the presence of the chromophore -CO-CH=CH-, which depends on the presence of other auxochromes. Different methods are available for the preparation of Chalcones [1-3].Chalcones are used to synthesize several derivatives like cyanopyridines, pyrazolines, isoxazoli- nes and pyrimidines have different heterocyclic ring systems [4-8].

Pyrazolines can be effectively utilized as antibacterial, antifungal, antiviral, anticancer, anti-parasitic, antitubercular, antidepressant and insecticidal agents and considerable attention has been given to this class [9-15]. In addition, pyrazolines have played a crucial part in the development of theory in heterocyclic chemistry and also used extensively in organic synthesis [16-17].

Isoxazoline represents one of the active classes of compounds possessing a wide spectrum of biological activities. Isoxazolines have been reported to possess anti-diabetic [18], diuretic [19], analgesic [20], anthelmintic [21], hypolipaemic [22], anti- microbial [23], anti-proliferative and apoptotic activities in a micro molar concentration range [24].

In view of these observations and continuation of the research work on bioactive heterocycles [25-28], it is intended to design and synthesize some new isoxazoline and pyrazoline derivatives and evaluate them for antimicrobial activities.

Materials and Methods:

Melting points are uncorrected and measured in open capillary tubes using a Gallenkamp electric melting point apparatus. IR spectra are recorded on FT-IR 100 Fisher company thermo scientific spectroph- otometers, using samples in KBr disks.

^{1}H-NMR spectra are taken on FT.NMR-Bruker, Shield, Model 2003 Ultra spectrometer (300 MHz) using DMSO-$d_6$as solvent and TMS as the internal standard at Al-Albiat universi-ty in Jordan.

Synthesis of Substituted Pyrazoline and Isoxazoline Derivatives:

Step-1. Procedure for the Synthesis of Substituted Chalcone Derivatives:

A solution of sodium hydroxide (40%) in water and rectified spirit is placed in a flask provided with a mechanical stirrer. The flask is immersed in a bath of crushed ice. Substituted acetophenones (A1) (0.006 M) are poured with constant stirring; and substituted benzaldehydes (B1) (0.006 M) are added to the solution. The temperature of the mixture is kept at about 25ºC and is stirred vigorously until the mixture becomes thick enough to retard the stirring (4-6 hr). The stirrer is removed and the reaction mixture is kept at 8ºC overnight. The products (C1-C8) are filtered with suction on a Buchner funnel, washed with cold water until the washings were neutral to litmus and then with ice cold ethanol. The crude product was recrystallized from ethanol.

Step-2. Procedure for the Synthesis of Substituted Pyrazoline Derivatives:

A mixture of substituted chalcones (C1-C8) and hydrazine hydrate in ethanol is taken in a round bottom flask. The reaction mixture is refluxed for 4 hrs on a water bath followed with the addition of ice cold water at room temperature. The precipitated crude products are filtered, washed with distilled water and dried. The product is filtered and recrysta- llized from ethanol to get the final products (P1-P8).

Step-3. Procedure for the Synthesis of Substituted Isoxazoline Derivatives:

A mixture of substituted chalcones (C1-C8) and hydroxylamine hydrochloride in ethanol is taken in a round bottom flask. The reaction mixture is refluxed for 6 hrs on a water bath followed with the addition of ice cold water at room temperature. The mixture is kept overnight at 8ºC. The precipitates are filtered, washed with distilled water and dried. The product is recrystallized with ethanol to get the final products (I1–I8).

Biological Evaluation:

In-vitro Antimicrobial Screening:

The in-vitro antibacterial screenings of synthesized compounds are performed against the following standard bacterial strains: *Pseudo-monas aeruginosa* (MTCC 424), *Escherichia coli* (MTCC 1573), *Bacillus subtilis* (MTCC 441) and *Staphylococcus aureus* (MTCC 1430).

Cylinder Plate Method [29]**:**

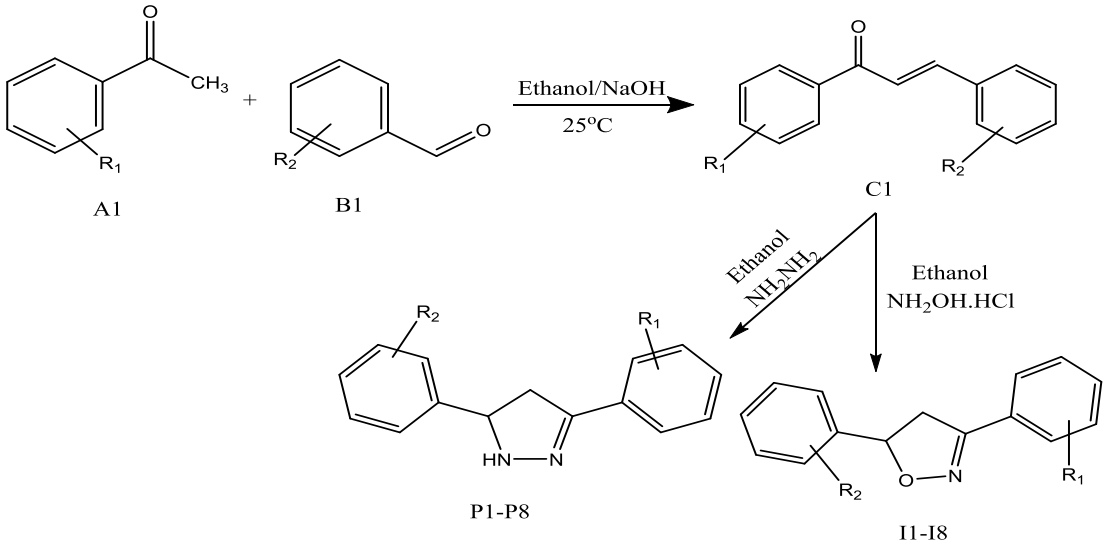
A definite volume of the microbial suspension (inoculums) is poured into the sterilized nutrient agar media (cooled at 40ºC) and mixed thoroughly. About 20 ml of this suspension is poured aseptically in the petri plates and kept till the solidification. The surface of agar plates is pierced using a sterile cork borer. The prepared wells are filled with equal volume of a solution of

synthesized compounds and standard drugs, separately. After a period of pre-incubation diffusion, the plates are incubated face up for a definite time under specified conditions. The zones of inhibition are measured as a parameter of antimicrobial properties of synthesized derivatives.

Results and Discussion:

New pyrazoline (P1-P8) and isoxazoline (I1-I8) derivatives were synthesized based on the cyclization of substituted chalcone derivatives in the presence of hydrazine hydrate or hydroxylamine hydrochloride success-sively (Scheme 1).

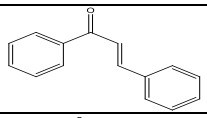
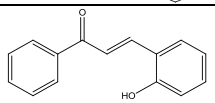
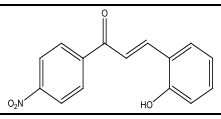
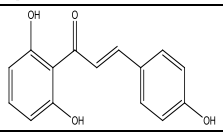
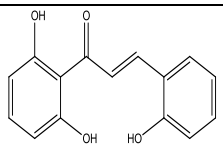
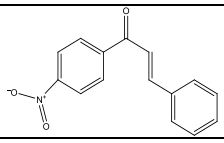
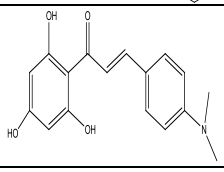
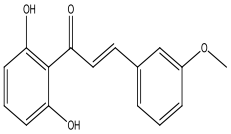
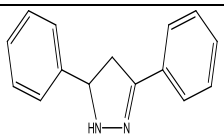
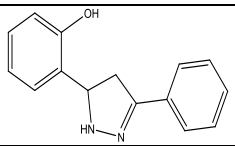
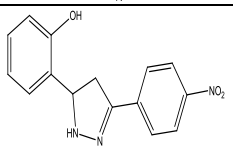
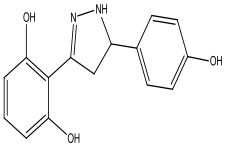
Physiochemical properties of synthesized compounds were determined in terms of melting point, Color and percentage yield with the elemental analysis Table (1).

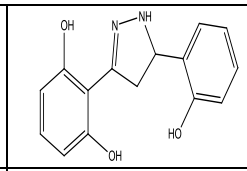
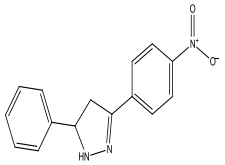
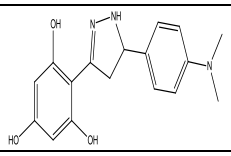
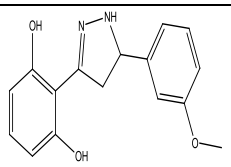
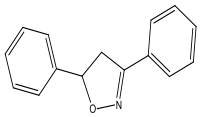
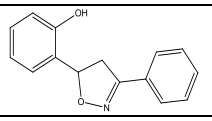
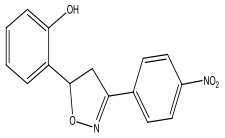
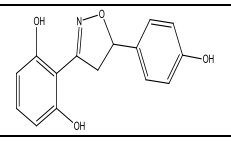
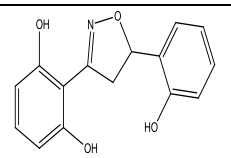
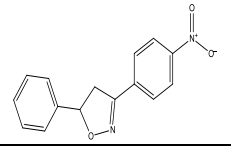
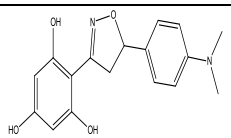
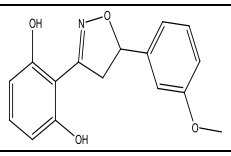


Products	R1	R2	Products	R1	R2
I1	-H	-H	P1	-H	-H
I2	-H	2-OH	P2	-H	2-OH
I3	4-NO_2	2-OH	P3	4-NO_2	2-OH
I4	2-OH, 6-OH	4-OH	P4	2-OH, 6-OH	4-OH
I5	2-OH, 6-OH	2-OH	P5	2-OH, 6-OH	2-OH
I6	4-NO_2	-H	P6	4-NO_2	-H
I7	2-OH, 4-OH, 6-OH	4-$N(CH_3)_2$	P7	2-OH, 4-OH, 6-OH	4-$N(CH_3)_2$
I8	2-OH, 6-OH	3-OCH_3	P8	2-OH, 6-OH	3-OCH_3

Scheme(1): The Synthesis of Substituted Pyrazoline and Isoxazoline Derivatives

Table 1: Physical Characterization Data and Elemental Analysis of the Synthesized Pyrazoline & Isoxazoline Derivatives

Comp. code	Structure	Name	Formula	m.p.(c°)	Yield (%)	Color	Elemental analysis Calc. % (Found)		
							C	H	N
C1		(E)-Chalcone	$C_{15}H_{12}O$	48	59%	Light yellow	86.51 (86.55)	5.81 (5.86)	-
C2		(E)-3-(2-hydroxyphenyl)-1-phenylprop-2-en-1-one	$C_{15}H_{12}O_2$	156 -158	60%	Light green	80.34 (80.30)	5.39 (5.36)	-
C3		(E)-3-(2-hydroxyphenyl)-1-(4-nitrophenyl)prop-2-en-1-one	$C_{15}H_{11}NO_4$	65 - 66	74%	Brown	66.91 (66.97)	4.12 (4.20)	5.20 (5.22)
C4		(E)-1-(2,6-dihydroxyphenyl)-3-(4-hydroxyphenyl)prop-2-en-1-one	$C_{15}H_{12}O_4$	> 240	80%	Light yellow	70.31 (70.33)	4.72 (4.76)	-
C5		(E)-1-(2,6-dihydroxyphenyl)-3-(2-hydroxyphenyl)prop-2-en-1-one	$C_{15}H_{12}O_4$	110-112	85%	Yellow	70.31 (70.29)	4.72 (4.71)	-
C6		(E)-1-(4-nitrophenyl)-3-phenylprop-2-en-1-one	$C_{15}H_{11}NO_3$	220-222	77%	Greenish brown	71.14 (71.11)	4.38 (4.39)	5.53 (5.50)
C7		(E)-3-(4-(dimethylamino)phenyl)-1-(2,4,6-trihydroxyphenyl)prop-2-en-1-one	$C_{17}H_{17}NO_4$	95	80%	Black	68.21 (68.19)	5.72 (5.69)	4.68 (4.69)
C8		(E)-1-(2,6-dihydroxyphenyl)-3-(3-methoxyphenyl)prop-2-en-1-one	$C_{16}H_{14}O_4$	140-142	83%	Yellow	70.10 (70.11)	5.22 (5.25)	-
P1		3,5-diphenyl-4,5-dihydro-1H-pyrazole	$C_{15}H_{14}N_2$	211	85%	White	81.05 (81.09)	6.35 (6.31)	12.6 (12.4)
P2		2-(3-phenyl-4,5-dihydro-1H-pyrazol-5-yl)phenol	$C_{15}H_{14}N_2O$	194	64%	Brown	75.61 (75.59)	5.92 (5.96)	11.76 (11.72)
P3		2-(3-(4-nitrophenyl)-4,5-dihydro-1H-pyrazol-5-yl)phenol	$C_{15}H_{13}N_3O_3$	260	40%	Brown	63.60 (63.55)	4.63 (4.68)	14.83 (14.80)
P4		2-(5-(4-hydroxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl)benzene-1,3-diol	$C_{15}H_{14}N_2O_3$	280	82%	Black	66.66 (66.69)	5.22 (5.20)	10.36 (10.38)

P5		2-(5-(2-hydroxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl)benzene-1,3-diol	$C_{15}H_{14}N_2O_3$	155	92%	Black	66.66 (66.64)	5.22 (5.20)	10.36 (10.40)
P6		3-(4-nitrophenyl)-5-phenyl-4,5-dihydro-1H-pyrazole	$C_{15}H_{13}N_3O_2$	190	75%	Brown	67.40 (67.42)	4.90 (4.92)	15.72 (15.69)
P7		2-(5-(4-(dimethylamino)phenyl)-4,5-dihydro-1H-pyrazol-3-yl)benzene-1,3,5-triol	$C_{17}H_{19}N_3O_3$	275	50%	Light brown	65.16 (65.18)	6.11 (6.13)	13.41 (13.43)
P8		2-(5-(3-methoxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl)benzene-1,3-diol	$C_{16}H_{16}N_2O_3$	135	78%	Light brown	67.59 (67.60)	5.67 (5.65)	9.85 (9.87)
I1		3,5-diphenylisoxazole	$C_{15}H_{13}NO$	115	55%	White	81.43 (81.40)	5.01 (5.02)	6.33 (6.34)
I2		2-(3-phenyl-4,5-dihydroisoxazol-5-yl)phenol	$C_{15}H_{13}NO_2$	242	65%	Green	75.30 (75.33)	5.48 (5.49)	5.85 (5.81)
I3		2-(3-(4-nitrophenyl)-4,5-dihydroisoxazol-5-yl)phenol	$C_{15}H_{12}N_2O_4$	165	82%	Brown	63.38 (63.39)	4.25 (4.21)	9.85 (9.84)
I4		2-(5-(4-hydroxyphenyl)-4,5-dihydroisoxazol-3-yl)benzene-1,3-diol	$C_{15}H_{13}NO_4$	>290	81%	Black	66.41 (66.39)	4.83 (4.85)	5.16 (5.14)
I5		2-(5-(2-hydroxyphenyl)-4,5-dihydroisoxazol-3-yl)benzene-1,3-diol	$C_{15}H_{13}NO_4$	280	87%	Brown	66.41 (66.42)	4.83 (4.81)	5.16 (5.17)
I6		3-(4-nitrophenyl)-5-phenyl-4,5-dihydroisoxazole	$C_{15}H_{12}N_2O_3$	175	55%	Red	67.16 (67.14)	4.51 (4.50)	10.44 (10.45)
I7		2-(5-(4-(dimethylamino)phenyl)-4,5-dihydroisoxazol-3-yl)benzene-1,3,5-triol	$C_{17}H_{18}N_2O_4$	245	56%	Black	64.96 (64.99)	5.77 (5.78)	8.91 (8.93)
I8		2-(5-(3-methoxyphenyl)-4,5-dihydroisoxazol-3-yl)benzene-1,3-diol	$C_{16}H_{15}NO_4$	210	68%	Brown	67.36 (67.39)	5.30 (5.35)	4.91 (4.94)

The synthesized compounds are also characterized by using FT-IR and ^{1}H-NMR. The IR spectrum of the synthesized compounds reveales presence of C=O (1630-1689 cm^{-1} C=O str.), C=C(aromatic) stretching at 1645-1672 cm^{-1}, 850-640 cm^{-1}(aromatic C-H oop) [30], 1223-1244 cm^{-1}(C-O str.),3412-3363 cm^{-1}(O-H str.) for chalcones, and 3445-3416 cm^{-1}(N-H str.), 1645-1670 cm^{-1}(C=N str.), 1025-1106 cm^{-1}(C-N str.), 1040-1099 cm^{-1}(N-N str.), etc. for pyrazoline derivatives and the isoxazoline derivatives reveales presence of C-O stretching at 1070-1263 cm^{-1}, 1024-1071 cm^{-1}(N-O str.), etc. In ^{1}H-NMR spectra δ value of various synthesized compounds are found in the range of 3.06-3.8 for methyl proton, 5.3-5.4 for hydroxyl proton and 8.3-6.5 for benzyl proton Table (2).

Table 2: Spectral Analysis of the Synthesized Pyrazoline & Isoxazoline Derivatives

Comp. code	IR spectra (cm^{-1})	^{1}H-NMR spectra (δ) in ppm
C1	1686 (C=O str.), 1580,1487,1462 (aromatic C=C str.), 805 (aromatic C-H def.)	8-7.7 (s,2H, (-CH=CH-), 7.6 -7.5 (r, 5H, aromatic ring), 7.4 -7.2 (r, 5H, aromatic ring)
C2	3366 (O-H str.), 1652 (C=O str.), 1568, 1460,1420 (aromatic C=C str.),1227 (C-O str.), 840,640 (aromatic C-H def.)	8.3 (s,1H, -CO-CH-ring), 7.8- 7.6 (r, 5H, aromatic ring) ,7.5 - 6.7 (r, 4H, aromatic ring), 7.4 (m, 1H,-CO-CH=C-), 5.3 (r,1H, OH)
C3	3381 (O-H str.), 1689 (C=O str.), 1541,1475,1420 (aromatic C=C str.),1223 (C-O str.), 1495,1325(N=O str.), 837,650 (aromatic C-H def.)	8.4-8.2 (s, 4H, aromatic ring) , 8.1 (s,1H, -CO-CH-ring), 7.6 -6.7 (r, 4H, aromatic ring), 7.4 (m, 1H,-CO-CH=C-), 5.3(r,1H, OH)
C4	3412 (O-H str.), 1655 (C=O str.), 1597,1480,1450 (aromatic C=C str.),1243 (C-O str.), 843,684 (aromatic C-H def.)	8 (s,1H, -C=CH-ring), 7.5 -6.6 (r, 4H, aromatic ring), 7.5 (m, 1H,-CO-CH=C-), 7.3 -6.5 (s, 3H, aromatic ring), 5.4(s,3H, OH)
C5	3412 (O-H str.), 1630 (C=O str.), 1546,1465,1440 (aromatic C=C str.),1244 (C-O str.), 850,670 (aromatic C-H def.)	8.3 (s,1H, -C=CH-ring), 7.4 (m, 1H,-CO-CH=C-), 7.6 -6.7 (r, 4H, aromatic ring), 7.3 -6.5 (s, 3H, aromatic ring), 5.3(s,3H, OH)
C6	1689 (C=O str.), 1599,1485,1465 (aromatic C=C str.),1235 (C-O str.), 1490,1330 (N=O str.) ,856,665 (aromatic C-H def.)	8.4-8.1 (r, 4H, aromatic ring), 8 (s,1H, -C=CH-ring), 7.6 (s, 1H,-CO-CH=C-),7.5-7.3 (r, 5H, aromatic ring),
C7	3409 (O-H str.), 1659 (C=O str.), 1570,1452,1440 (aromatic C=C str.),1235 (C-O str.),1330,1100(C-N str.) 865,675 (aromatic C-H def.)	8.1(s,1H,-C=CH-ring),7.7-6.7 (r,4H,aromatic ring), 7.6(m,1H,-CO-CH=C-), 5.9(m,2H,aromatic ring), 5.4(s,3H,OH), 3.1(r,6H,-N(CH_3)$_2$)
C8	3363 (O-H str.), 1633 (C=O str.), 1531,1465,1450 (aromatic C=C), 1225 (C-O str.), 831, 660 (C-H def.)	8.1 (s,1H, -C=CH-ring),7.6 (m,1H,-CO-CH=C-),7.5 (r,4H, aromatic ring),7.4-6.5 (m,3H, aromatic ring),6.9-5.3(s,2H,-OH), 3.8 (s,3H, -OCH_3)
P1	3441(N-H str.), 1670(C=N str.), 1576, 1450, 1440 (aromatic C=C), 1025(C-N), 1069(N-N), 708(C-H def.)	7.7 -7.3 (r,10H, aromatic ring), 7 (r,1H, H-N), 4 (m,1H,C-H), 3.9-3.7 (m,2H,-CH_2-)
P2	3436(N-H str.), 3334(O-H str.), 1647(C=N str.), 1589, 1499, 1445 (aromatic C=C), 1098(C-N), 1279(C-O str.), 1056(N-N), 813,756(C-H def.)	7.5-7.7 (r,5H, aromatic ring), 7 (r,1H, H-N), 3.9 (m,1H,C-H), 3.7-3.94 (m,2H,-CH_2-), 5.4 (s,1H,OH), 6.9-7.12 (r,4H, aromatic ring)
P3	3440(N-H str.), 3378(O-H str.), 1655(C=N str.), 1571, 1457, 1445 (aromatic C=C), 1106(C-N), 1265(C-O str.), 1095(N-N), 1404,1313(N=O str.), 841,783(C-H def.)	8.3-8.1 (r,4H, aromatic ring), 7.1- 6.9 (r,4H, aromatic ring),7 (r,1H, N-H), 5.35 (s,1H,OH), 4 (m,1H,C-H), 3.9-3.7 (m,2H,-CH_2-)
P4	3445(N-H str.), 3354(O-H str.), 1645(C=N str.), 1513, 1475, 1440 (aromatic C=C), 1101(C-N), 1262(C-O str.), 1056(N-N), 830,702(C-H def.)	7.1- 6.6 (r,7H, aromatic ring),7 (s,1H,N-H), 5.4 (s,3H,OH), 4 (m,1H,C-H), 3.9-3.7 (m,2H,-CH_2-),
P5	3439(N-H str.), 3369(O-H str.), 1647(C=N str.), 1519, 1451, 1440 (aromatic C=C), 1100(C-N), 1248(C-O str.), 1050(N-N), 842,648(C-H def.)	7.2-6.6 (r,7H, aromatic ring),7 (s,1H,N-H), 5.4 (s,3H,OH), 3.9 -3.8 (m,2H,-CH_2-) 3.7 (m,1H,C-H),
P6	3442(N-H str.),1650(C=N str.), 1515, 1495, 1440 (aromatic C=C), 1106(C-N),1099(N-N), 1390,1312 (N=O str.), 839,784(C-H def.)	8.3-8.1 (s,4H, aromatic ring),7.4-7.3 (r,5H, aromatic ring),7 (r,1H,N-H), 4 (m,1H,C-H), 3.9-3.7 (m,2H,-CH_2-),
P7	3416(N-H str.), 3370(O-H str.), 1665(C=N str.), 1519, 1451, 1440 (aromatic C=C), 1100(C-N), 1235(C-O str.), 1040(N-N),2900(aliphatic C-H) 812,694(C-H def.)	7.1-6.7(r,6H, aromatic ring),7(r,1H,N-H),5.4(r,3H,OH), 3.9-3.8(m,2H,-CH_2-), 3.7(m,1H,C-H),3.1 (s,6H,-N(CH_3)$_2$),
P8	3444(N-H str.), 3370(O-H str.), 1670(C=N str.), 1520,1451,1440(aromatic C=C), 1098(C-N), 1248 (C-O str.), 1098(N-N),2936(aliphatic C-H) 801,646(C-H def.)	7.3-6.6 (r,7H, aromatic ring),7 (r,1H,N-H), 5.4 (r,2H,OH), 4(m,1H,C-H), 3.9-3.8 (r,2H,-CH_2-), 3.7 (r,3H,-CH_3)
I1	1688(C=N str.), 1579, 1455, 1440 (aromatic C=C), 1066(N-O), 1174(C-O), 804,705(C-H def.)	7.9-7.5 (r,10H, aromatic ring), 5.9 (m,1H,C-H), 3.9-3.6 (m,2H,-CH_2-)
I2	3352(O-H str.),1651(C=N str.), 1595, 1491, 1455 (aromatic C=C), 1067 (N-O), 1175 (C-O), 813,754 (C-H def.)	7.8-6.9 (r,9H, aromatic ring), 5.9 (m,1H,C-H), 5.4 (s,1H,OH), 3.8-3.6 (m,2H,-CH_2-),
I3	3387(O-H str.),1647(C=N str.), 1559, 1452, 1440 (aromatic C=C), 1067 (N-O), 1070 (C-O), 1397,1314(N=O str.), 840,757 (C-H def.)	8.2-8.1 (s,4H, aromatic ring),7.2-6.9 (r,4H, aromatic ring), 5.9 (m,1H,C-H), 5.4 (s,1H,OH), 3.9-3.6 (m,2H,-CH_2-)
I4	3431(O-H str.),1663(C=N str.), 1537, 1479, 1440 (aromatic C=C), 1060 (N-O), 1256 (C-O), 715,675 (C-H def.)	7.2-6.5 (r,7H, aromatic ring), 5.9 (m,1H,-CH_2-), 5.4 (s,3H,OH)
I5	3431(O-H str.),1672(C=N str.), 1537, 1483, 1445 (aromatic C=C), 1055 (N-O), 1247 (C-O), 748,674 (C-H def.)	7.2-6.6 (r,7H, aromatic ring), 5.9 (m,1H,C-H), 5.3 (s,3H,OH), 3.9-3.6 (m,2H,-CH_2-)
I6	3431(O-H str.),1652(C=N str.), 1560, 1486, 1455 (aromatic C=C), 1050 (N-O),1350,1317(N=O str.), 1259 (C-O), 858,751 (C-H def.)	8.1-8(m,4H, aromatic ring),7.4-7.3(r,5H, aromatic ring),5.9(m,1H,C-H), 3.8-3.6 (m,2H,-CH_2-)
I7	3424(O-H str.),1662(C=N str.), 1536,1474,1440 (aromatic C=C), 1042 (N-O), 2926 (aliphatic C-H str.), 1321(C-N str.), 1255 (C-O), 852,673 (C-H def.)	7.2-6.7 (r,4H, aromatic ring), 7.1 (s,2H, aromatic ring), 5.4 (m,1H,C-H), 5.3 (s,3H,OH), 3.9-3.6 (m,2H,-CH_2-), 3.1 (s,6H,-N(CH_3)$_2$)
I8	3422(O-H str.),1663(C=N str.), 1551, 1472, 1445 (aromatic C=C), 1071 (N-O), 1263 (C-O), 2949 (aliphatic C-H str.), 850,673 (C-H def.)	7.3-6.6 (r,7H, aromatic ring), 5.9(m,1H,CH), 5.4 (s,2H,OH), 3.9-3.6 (m,2H,-CH_2-), 3.8 (s,3H,-OCH_3),

Antibacterial activities are also performed as in-vitro antimicrobial screening against bacterial strain (Table 3).According to the preliminary antibacterial screening by paper disc method, some compounds are found to have comparable antibacterial activity against *S. aureus* and *B. subtilis* as Gram positive bacteria with *E. coli* and *P.aeruginosa* as Gram negative bacteria compared to Norfloxacin as a standard drug. The antimicrobial

screening reveales that the compound (P7) and compound (I7) exhibited potent antibacterial activity as compared to other derivatives. Compound P7 is found to exhibit potent in-vitro antibacterial activity against *Escherichia coli* and *Pseudomonas aeruuginosa* while compound I7 is found to exhibit potent in-vitro antibacterial activity against *Staphylococcus aureus* and *Bacillsubtilis* Table (3).

Table 3: Antibacterial Activity of the Synthesized Pyrazoline & Isoxazoline Derivatives

	Gram Negative Bacteria		**Gram Positive Bacteria**	
	Escherichia coli	*Pseudomonas aeruuginosa*	*Staphylococcus aureus*	*Bacillsubtilis*
Compounds	Zone of inhibition (mm)			
P1	12	12	13	12
P2	17	10	10	16
P3	17	13	09	15
P4	14	15	12	14
P5	11	14	08	11
P6	17	16	10	13
P7	18	19	17	16
P8	13	12	16	15
I1	12	11	13	15
I2	09	12	07	11
I3	15	14	12	16
I4	13	15	17	09
I5	10	08	07	11
I6	10	07	10	08
I7	16	18	19	20
I8	15	17	18	16
Norfloxacin	21	19	21	23

Conclusion:

The present research work involves synthesis of novel substituted pyrazoline and isoxazoline derivatives to explore their antibacterial activity. Compounds P7 exhibit the highest antibacterial activity for Gram negative bacteria and compound I7 exhibits potent antibacterial activity for Gram positive bacteria respectively. Hence, it is concluded that there is an ample scope for further study in developing these as good lead compounds for the treatment of bacterial strain as well as fungal strain.

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تحضير وتشخيص بعض مشتقات البرايزولين والايزوكسازولين الجديدة كعوامل مضادة للبكتريا

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الخلاصة:

حضر في هذا البحث عدد من الجالكونات (C1-C8) بتفاعل مول واحد من الاسيتوفينون المعوض مع مول واحد من البنزالديهايد المعوض بوجود (40%) هايدروكسيد الصوديوم كقاعدة. حضرت مشتقات البرايزولين (P1–P8) من تفاعل الجـــــالكونات المحضرة (C1-C8) مع الهايدرازين.

حضرت مشتقات الايزوكسازولين (I1-I8) من تفاعل الجالكونات المحضرة (C1-C8) مع هايدروكسيل امين هايدروكلورايد بوجود (10%) هايدروكسيد الصوديوم كقاعدة. وقد درست وشخصت هذه المركبات المحضرة بواسطة قياس بعض الخواص الفيزيائية والطرق الطيفية، كما تم دراسة الفعالية المضادة للبكتريا للمركبات المحضرة في المختبر باستخدام أنواع بكتيرية موجبة وأخرى سالبة لصبغة كرام، أظهرت العديد من مشتقات البرايزولين والايزوكسازولين المحضرة نشاط معتدل جداً ضد عدد من البكتريا.

الكلمات المفتاحية: الجالكونات، البرايزولين، الايزوكسازولين، مضاد للبكتريا.