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New Pyrazoline Derivatives Containing Imine Moiety: Synthesis, Characterization and Antimicrobial Study

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ABSTRACT

A new series of pyrazoline derivatives (3-10) have been synthesized and characterized on the basis of FT-IR, ^{1}H-NMR, and Mass techniques. 1-(4-Aminophenyl)-3-(pyridin-4-yl)prop-2-en-1-one (1) as a starting material was prepared by the reaction of 4-aminoacetophenone and 4-pyridinecarboxaldehyde in ethanol, using sodium hydroxide as a catalyst. Pyrazoline derivatives 2 was obtained via the cyclization reaction of compound 1 by the action of hydrazine hydrate 80% in ethanol. The target derivatives (3-8) were obtained by the reaction of pyrazoline derivative (2) with the corresponding aldehyde in ethanol. The novel pyrazoline derivatives 9 and 10 were synthesized by the reaction of pyrazoline derivative 2 with the corresponding anhydride (maleic or phthalic anhydride) in presence of anhydrous sodium acetate in glacial acetic acid. The synthesized derivatives were screened against several bacterial strains: *Staphylococcus aureus*, *Staphylococcus espidermididis*, *Escherichia coli*, *Klebsiella* and *Candida albicans*. The synthesized compounds showed promising bio-activity compared with amoxicillin.

KEYWORDS: Chalcone; Pyrazoline; Schiff's-Base and antimicrobial.

الخلاصة

تم تحضير و تشخيص سلسلة جديدة من مشتقات البايرازولين (3-10) باستخدام عدة طرق تحليلية. تم تحضير 1-(4-Aminophenyl)-3-(pyridin-4-yl)prop-2-en-1-one (1) كمادة اساس بواسطة تفاعل 4-امينو اسيتوفينون و 4- بيريدين كاربوكسي الديهايد في الايثانول، باستخدام هيدروكسيد الصوديوم كعامل محفز. مشتق البايرازولين 2 تم الحصول عليه من تفاعل الغلق الحلقي للمركب 1 بواسطة تفاعله مع الهيدرازين المائي 80% في الايثانول. المشتقات الهدف (3-8) تم الحصول عليها من تفاعل مشتق البايرازولين 2 مع عدد من الالديهايدات المقابلة في الايثانول. مشتق البايرازولين 9 و 10 تم تحضيرهما بواسطة تفاعل مشتق البايرازولين 2 مع الانهدريدات المقابلة (فثالك او ماليك انهيدرايد) في حامض الخليك الثلجي و كمية قليلة من خلات الصوديوم اللامائية . جميع المشتقات المحضرة تم فحصها ضد عدة اصناف من البكتريا و نوع واحد من الفطريات : *Staphylococcus aureus*, *Staphylococcus espidermididis*, *Escherichia coli*, *Klebsiella* and *Candida albicans*. ثم مقارنة نتائج التثبيط للمشتقات المحضرة مع الاموكسيسيلين.

INTRODUCTION

Pyrazoline is a member of heterocyclic, the name of pyrazole was given by Ludwig Knorr in 1883, referring to the simple aromatic ring organic compound of the heterocyclic series characterized by a 5-membered ring structure composed of three carbon atoms and two nitrogen atoms in adjacent positions[1]. In the 19th century, Fischer and Knoevenagel used a very simple reflux reaction of α,β-unsaturated aldehydes and ketones with phenylhydrazine in acetic acid to synthesize and characterize 2-pyrazoline, which became one of the most popular methods [2]. The development of heterocyclic chemistry is very rapid, especially in the development of synthetic methods and the biological activity of synthetic materials[3]. Pyrazoline has been widely incorporated into the structure of many important medical and biochemical reagents that have been effectively utilized as anti-bacterial [4], anti-inflammatory [5], anti-viral [6], anti-fungal [7], anti-cancer [8], analgesic and insecticidal agents [9]. In the last few years, a significant and important portion of research in the field of heterocyclic chemistry has been dedicated to pyrazolines and their derivatives, especially those linked by various functional groups such as imine group (Schiff's-Base). Therefore, great importance appeared in

studying the biological effects of these kinds of derivatives due to their activity against several pathogenic bacteria and fungi [10], this encouraged us to synthesize a new series of pyrazoline derivatives. The synthesized compounds (3-10) were screened against some bacterial species (gram positive and gram negative) and fungal against (Candida albicans) and the screened results showed moderate to high efficacy.

MATERIALS AND METHODS

General Synthesis

All the starting materials and chemicals were from Sigma-Aldrich, Fluka and BDH. In this study, uncorrected melting points were measured using an electrothermal open capillary tube in a Stuart SMP-30 melting points apparatus. The Shimadzu model FTIR-8400S was used for recording FTIR measurements. Mass spectra were recorded on a Shimadzu GCMS-QP2010 Ultra apparatus. ^{1}H-NMR spectra measurements were acquired with a Varian spectrophotometer model ultra-shield at 500 MHz in DMSO-d_6 or $CDCl_3$ solution standard.

Synthesis of 1-(4-aminophenyl)-3-(pyridine-4-yl)prop-2-en-1-one (1)

This compound was synthesized according to the procedure described in the published work[11]. Alkaline solution of sodium hydroxide (1ml, 40%) was added to a solution of 4-aminoacetophenone (1mmol) in ethanol (10 ml) and the reaction mixture was stirred for 30minutes.After that,4-pyridinecarboxaldehyde (1 mmol) was added, and the reaction mixture was left to stirring overnight. The reaction mixture crude was left to stand at room temperature. The collected product was filtered, dried and purified from ethanol as a recrystallizing solvent.

Yellow powder, yield 87%, m.p194-196C°; FT-IR ($\bar{\upsilon}$ cm^{-1}): 3441, 3304 (*NH_2*), 3043 (*aromatic C-H*), 1647 (*C=O*), 1618 (*CH=CH*), 1589 (*C=N pyridine*), 1562 (*aromatic C=C*). ^{1}H-NMR (500MHz, DMSO-d6) δ (ppm) , 6.25 (s, 2H, *NH_2*), 6.63 (d, 2H, *Ar-H*, j=9.99 Hz), 7.54 (d, 1H, *CH=CH*, j=14.98 Hz), 7.79 (d, 2H, *Ar-H pyridine*, j=10 Hz), 7.94 (d, 2H, *Ar-H*, j=5 Hz), 8.08 (d, 1H, *CH=CH*, j=14.98 Hz), 8.63 (d, 2H, *Ar-H pyridine*, j=5 Hz). Mass (NCI) m/z): 224 M^+ for $C_{14}H_{12}N_2O$, R_f = 0.31 (1:4, Hexane: Ethyl acetate).

Synthesis of 4-(5-(pyridine-4-yl)-4,5-dihydro-1H-pyrazol-3-yl)aniline (2)

The synthetic procedure of these compounds were slightly modified from that described previously [12]. The reaction mixture of chalcone compounds (1) (1mmol) in ethanol absolute (10 ml) and excess of (1ml) hydrazine hydrate was refluxed for 6 hrs. The reaction 80% was monitored by TLC using Hexane: Ethylactate (1:4) as an eluent. The mixture was precipitated by adding to a crushed ice, and the collected product was filtered, washed with water, dried and recrystallized from ethanol.

Light yellow powder, yield 61%, m.p 221-223 C°; FT- IR ($\bar{\upsilon}$ cm^{-1}): 3358, 3410 (*NH_2, group*), 3211 (*NH-pyrazoline*), 3037 (*C-H aromatic*), 2970, 2885 (*C-H aliphatic*), 1622(*C=N pyrazoline*), 1593 (*C=N pyridine*), 1519 (*C=C aromatic*). ^{1}H-NMR (500 MHz, DMSO-d6) δ (ppm): 2.71,2.75 (dd, 1H, j= 14.97, 9.98 Hz, *Ha-pyrazoline*), 3.38-3.41 (dd, 1H, j= 9.98, 14.97 Hz, *Hb-pyrazoline*), 4.73 (t, 1H, j=9.98 Hz, *Hx-pyrazoline*), 6.53-6.55 (d, 3H, *NH_2* , *NH-pyrazoline*), 7.30-8.51 (m, 8H,*8Ar-H*). Mass (NCI) m/z: 238 M^+ for $C_{14}H_{14}N_4$, R_f =0.27 (1:4, Hexane: Ethyl acetate).

Synthesis of Schiff's-Bases (3-8)

These compounds were synthesized according to the modified method described in the reported references [13] .To a solution of aromatic aldehydes (1mmol) was dissolved in ethanol absolute (20 ml) containing few drops of glacial acetic acid and then the pyrazoline derivative (2) (1mmol) was added. The mixture was refluxed for (10-12 hrs) and the reaction process was monitored by TLC using Hexane: Ethylactate (1:4) as an eluent. The precipitate was filtered, washed with ethanol and dried.

1-(4-nitrophenyl)-N-(4-(5-(pyridine-4-yl)-4,5-dihydro-1H-pyrazol-3-yl)phenyl)methanimine (3)

Orange powder, yield 65 %, m.p180-182C°; FT-IR ($\bar{\upsilon}$ cm^{-1}) : 3365 (*NH-pyrazoline*) , 3032 (*C-H aromatic*) , 2928 (*HC=N*) , 1653 (*C=N*), 1621 (*C=N pyrazoline),* 1593 (*C=N pyridine*),1519 (*C=C aromatic*), 1558,1342 (*NO_2*). ^{1}H-NMR (500MHz, DMSO-d6) δ (ppm): 3.78 (m, 1H, *Ha-pyrazoline*), 4.72 (m, 1H, *Hb –pyrazoline*), 6.02 (t, 1H, *Hx-pyrazoline*), 6.53 (s, 1H, *NH-pyrazoline*), 7.16-8.62 (m, 12H, *Ar-H*), 8.89 (s, 1H, *CH=N*). Mass (NCI) m/z: 371 M^+ for $C_{21}H_{17}N_5O_2$, R_f = 0.7 (1:4, Hexane: Ethyl acetate).

4-(5-(pyridine-4-yl)-4,5-dihydro-1H-pyrazol-3-yl)phenyl)-1-(thiophen-2-yl)methanimine (4)

Yellow powder, yield 62 %, m.p150-153C°; FT-IR ($\bar{\upsilon}$ cm^{-1}) : 3398 (*NH-pyrazoline*) , 3032 (*C-Haromatic*), 2928 (*HC=N*), 1653(*C=N*) , 1622 (*C=N pyrazoline*),1593 (*C=N pyridine*) ,1519 (*C=C aromatic*). ^{1}H-NMR (500MHz, DMSO-d6) δ (ppm): 3.24 (m,1H, *Ha-pyrazoline*), 3.59 (m, 1H, *Hb-pyrazoline*), 4.38 (m, 1H, *Hx-pyrazoline*), 6.11 (s, 1H, *NH-pyrazoline*) , 6.92-8.50 (m, 11H, *Ar-H*), 8.85 (s, 1H, *HC=N*). Mass (NCI) m/z: 332 M^+ for $C_{19}H_{16}N_4S$, R_f = 0.52 (1:4, Hexane: Ethyl acetate).

1-(pyridine-4-yl)-N-(4-(5-(pyridine-4-yl)-4,5-dihydro-1H-pyrazol-3-yl)phenyl)methanimine (5)

Yellow powder, yield 75 %, m.p208-210C°; FT-IR ($\bar{\upsilon}$ cm^{-1}): 3367 (*NH-pyrazoline*), 3034 (*C-H aromatic*), 2926 (*HC=N*), 1647(*C=N*) , 1622 (*C=N pyrazoline*) ,1593 (*C=N pyridine*), 1519 (*C=C aromatic*). ^{1}H-NMR (500MHz, DMSO-d6) δ (ppm): 3.12 (m, 1H, *Ha- pyrazoline*), 3.31 (m, 1H, *Hb-pyrazoline*), 5.11 (m, 1H, *Hx-pyrazoline*), 6.10 (s, 1H, *NH-pyrazoline*), 6.92-8.50 (m, 11H, *Ar-H*), 9.1 (s, 1H, *HC=N*). Mass (NCI) m/z: 327 M^+ for $C_{20}H_{17}N_5$, R_f = 0.62 (1:4, Hexane: Ethyl acetate).

1-(furan-2-yl)-N-(4-(5-(pyridine-4-yl)-4,5-dihydro-1H-pyrazol-3-yl)phenyl)methanimine (6)

Yellow powder, yield 61 %, m.p202-204C°; FT-IR ($\bar{\upsilon}$ cm^{-1}) : 3470 (*NH-pyrazoline*), 3032 (*C-H aromatic*), 2926 (*HC=N*), 1647(*C=N*) , 1625 (*C=N pyrazoline*), 1593 (*C=N pyridine*) ,1519 (*C=C aromatic*). ^{1}H-NMR (500MHz, DMSO-d6) δ (ppm) : 3.01 (m,1H, *Ha-pyrazoline*), 3.88 (m, 1H, *Hb-pyrazoline*), 5.11 (m, 1H, *Hx-pyrazoline*),6.12 (s, 1H, *NH-pyrazoline*) , 6.88-8.78 (m, 11H, *Ar-H*), 8.81 (s, 1H, *HC=N*). Mass (NCI) m/z : 316 M^+ for $C_{19}H_{16}N_4O$, R_f= 0.65(1:4, Hexane: Ethyl acetate).

1-phenyl-N-(4-(5-(pyridine-4-yl)-4,5-dihydro-1H-pyrazol-3-yl)phenyl)methanimine (7)

Yellow powder, yield 58 %, m.p212-214C°; FT-IR ($\bar{\upsilon}$ cm^{-1}) : 3379 (*NH-pyrazoline*), 3063 (*C-H aromatic*), 2914 (*HC=N*), 1653 (*C=N*) , 1621 (*C=N pyrazoline*),1591 (*C=N pyridine*), 1519 (*C=C aromatic*). ^{1}H-NMR (500MHz, DMSO-d6) δ (ppm): 3.22 (m,1H, Ha- pyrazoline), 4.8 (m, 1H, *Hb-pyrazoline*), 5.43 (m, 1H, *Hx-pyrazoline*), 6.10 (s, 1H, *NH-pyrazoline*) , 6.65-8.51(m, 13H, *Ar-H*), 8.59 (s, 1H, *HC=N*). Mass (NCI) m/z : 326 M^+ for $C_{21}H_{18}N_4$,R_f= 0.51(1:4, Hexane: Ethyl acetate).

2-(((4-(5-(pyridine-4-yl)-4,5-dihydro-1H-pyrazol-3-yl)phenyl)imino)methyl)phenol (8)

Green powder, yield 58 %, m.p195-198C°; FT-IR ($\bar{\upsilon}$ cm^{-1}): 3431 (*O-H*), 3350 (*NH-pyrazoline*), 3078, 3028 (*C-H aromatic*), 2945 (*HC=N*), 1620 (*C=N*) , 1595 (*C=N pyridine*) , 1570 (*C=N pyrazoline*),1523 (*C=C aromatic*). ^{1}H-NMR (500MHz, DMSO-d6) δ (ppm): 2.9-3 (m,1H, *Ha-pyrazoline*), 4.8 (m, 1H, *Hb-pyrazoline*), 5.9 (m, 1H, *Hx-pyrazoline*),5.1 (s, 1H, *NH-pyrazoline*) , 6.2-8.5 (m, 11H, *Ar-H*), 8.9 (s, 1H,*OH*) , 9.1 (s, 1H, *HC=N*). R_f= 0.51(1:4, Hexane: Ethyl acetate).

Synthesis 3-(N-substituted-4-aminophenyl)-5-substitutedaryl-pyrazoline derivatives (9 and 10)

These compounds were synthesized according to the modified procedure described earlier [14]. To a solution of pyrazoline derivative (2) (1mmol) and corresponding anhydrides (1mmol) (maleic or phthalic anhydride) in glacial acetic acid (3 ml), anhydrous sodium acetate (1.2 mmol) was added and the solution was refluxed for One houre. The precipitated product was filtered, washed by ethanol then water.

2-(4-(5-(pyridine-4-yl)-4,5-dihydro-1H-pyrazol-3-yl)phenyl)isoindoline-1,3-dione (9)

Brown powder, yield 66 %, m.p 210-212 C°; FT-IR ($\bar{\upsilon}$ cm^{-1}): 3338 (*NH-pyrazoline*), 3109,3053 (*aromatic C-H*), 2914,2870 (*aliphatic C-H*), 1739,1716 (*C=O*), 1662 (*C=N Pyrazoline*), 1591 (*C=N pyridine*), 1519 (*aromatic C=C*). ^{1}H-NMR (500 MHz, DMSO-d6) δ (ppm): 3.39,3.43 (dd, 1H, j= 5 , 5 Hz, *Ha-pyrazoline*), 3.77, 3.81 (dd, 1H, j= 9.98, 14.98 Hz, *Hb-pyrazoline*), 5.67 (t, 1H, j= 9.98 Hz, *Hx-pyrazoline*), 6.34 (s, 1H, *NH-pyrazoline*), 6.40-8.03 (m, 12H, *Ar-H*). Mass (NCI) m/z : 368 M^+ for $C_{22}H_{16}N_4O_2$, R_f =0.48 (1:4, Hexane: Ethyl acetate).

1-(4-(5-(pyridine-4-yl)-4,5-dihydro-1H-pyrazol-3-yl)phenyl)-1H-pyrrole-2,5-dione (10)

Brown powder, yield 61 %, m.p 139-141 C°; FT-IR ($\bar{\upsilon}$ cm^{-1}) : 3329 (*NH-pyrazoline*), 3055 (*aromatic C-H*), 2914, 2870 (*aliphatic C-H*), 1714 (*C=O*), 1635 (*C=N Pyrazoline*), 1591 (*C=N pyridine*), 1521 (*aromatic C=C*). Mass (NCI) m/z : 318 M^+ for $C_{18}H_{14}N_4O_2$, R_f = 0.13 (1:4, Hexane: Ethyl acetate).

Antimicrobial Study

This study describes the activity of the synthesized derivatives (3-10) against *Klebsiella , Escherichia coli. (gram –ve), Streptococcus espidermididis , Staphylococcus aureus (gram+ve)* as well as *C.albicans*. The in vitro assay was achieved by well diffusion method[15] using concentration of 2mg/ml in DMSO. The inhibition zones in mm illustrated in Table 1. The compounds (1-10) exhibit potent antimicrobial activities. Figure 1 shows the inhibition zone of some selected derivatives.

Table 1. In Vitro antimicrobial inhibition zone (mm) of the synthesized compounds.

Pyrazoline derivatives	Gram positive		Gram negative		Fungi
	S. aureus	*S. espidermi*	*E. coli*	*Klebsiella sp.*	*C. albicans*
3	-	14	12	12	9
4	-	15	13	-	9
5	-	9	13	14	9
6	-	-	14	14	9
7	-	12	14	16	9
8	11	12	11	-	11
9	12	10	14	11	13
10	-	11	13	11	14
Amoxicillin	17	18	20	20	25

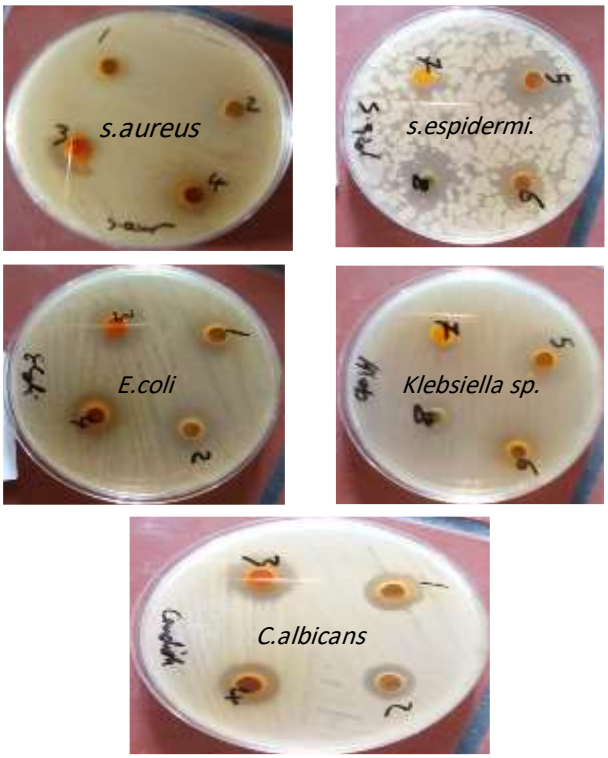
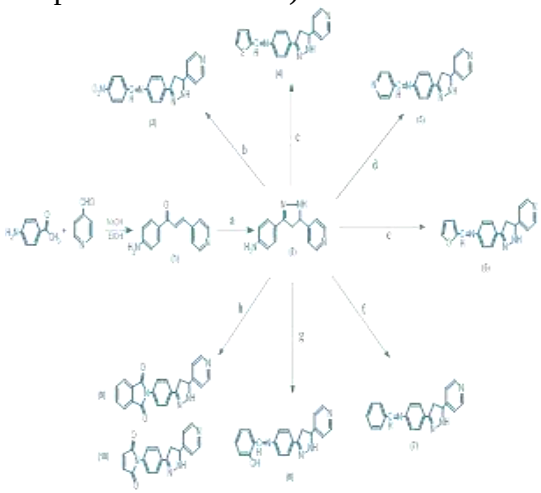


Figure 7. Antimicrobial activity of some pyrazoline derivatives against *S.aureus*, *S.espidermi*. , *E.coli*, *Klebsiella sp*. and *C. albicans.*

RESULTS AND DISCUSSION

Chalcone derivative 1 was prepared by the reaction of 4-aminoacetophenone with 4-pyridinecarboxaldehyde in ethanol, in a presence of sodium hydroxide 40% solution according to Claisen-Schmidt condensation, while the pyrazoline compound (2) was obtained by the reaction of chalcone compound (1) with hydrazine hydrate 80% in ethanol. Schiff's bases (3-8) were synthesized from the reaction of compound 2 with different aromatic aldehydes in acidic ethanolic solution, while the pyrazoline derivatives (9 and 10) were prepared by the reaction pyrazoline derivative (2) with the corresponding anhydride (maleic or phthalic anhydride) in glacial acetic acid in a presence of anhydrous sodium acetate (Scheme 1). The structures of obtained compounds were confirmed by spectral analysis (see experimental section).



Scheme 1. (a) Hydrazine hydrate, EtOH (b) 4-nitrobenzaldehyde,EtOH(c) 2-thiophenecarboxyldehyde, EtOH (d) 4-pyridinecarboxaldehyde, EtOH (e) furan-2-carboxaldehyde, EtOH (f) benzaldehyde, EtOH (g) 2-hydroxybenzaldehyde, EtOH (h) phathalic anhydride of maleic anhydride, glacial acetic acide, AcONa.

The compound (1) showed the FT-IR spectra showed the absorption bands at 3441, 3304 cm^{-1} related *NH_2-group* and absorption at 3043 cm^{-1} which is due to *C-H aromaticity*. The absorption bands at 1647 cm^{-1} and 1618 cm^{-1} related to stretching frequency of (*C=O*) and (*CH=CH*) respectively. While the bands appeared at 1589 cm^{-1} and 1562 cm^{-1} related to stretching frequency of (*C=N pyridine*) and (*aromatic C=C*) respectively. The ^{1}H-NMR spectra of compound (1) showed a singlet signal at 6.25 ppm due to *NH_2-group* protons and the doublet appeared at 6.63 and 7.94 ppm related to two aromatic protons. The doublet signal at 7.54 and 8.08 due

to two hydrogens of the *COCH=CH group*. The doublet signal at 7.79 and 8.63 are due to two protons of the Pyridine ring as shown in Figure 2. The Mass peak at 224 further confirms the molecular ion M^+ as shown in Figure 3. The FT-IR spectra of the compound (2) is showed absorption at 3410 ,3358 cm^{-1} due to absorption band of *NH_2-group*, and at 3211 cm^{-1} which is due to *NH-pyrazoline* stretching frequency, while absorption at 3037 cm^{-1} due to *aromatic C-H* bending frequency, and at 2970, 2885 cm^{-1} which is due to the stretching frequency of *aliphatic C-H*, while 1622 and 1593 cm^{-1} which are due to the stretching frequency of *C=N pyrazoline* and *C=N pyridine* groups respectively.

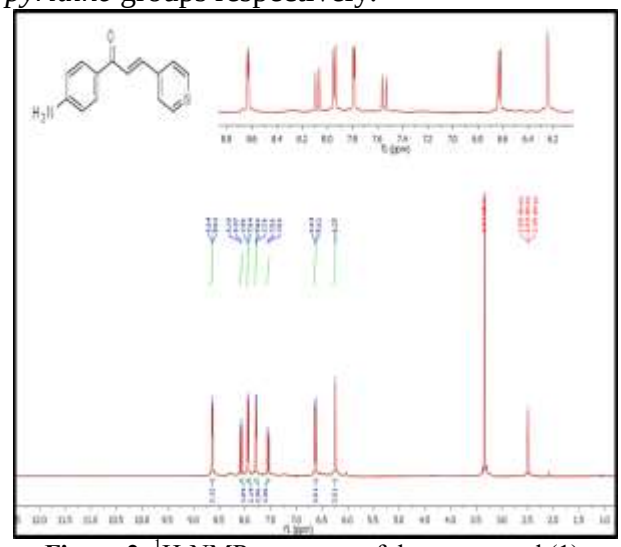


Figure 2. ^{1}H-NMR spectrum of the compound (1).

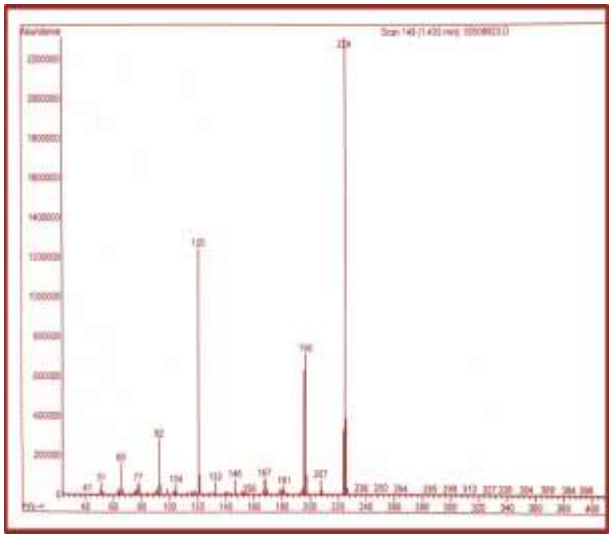


Figure 3. Mass spectrum of the compound (1).

While the band appeared at 1519 cm^{-1} related to stretching frequency of (*aromatic C=C*). The ^{1}H-NMR of the compound (2) showed two doublet doublet signals at (2.71-2.75) and (3.38-3.41) ppm due to Ha and Hb protons of the pyrazoline ring. A triplet signal appeared at 4.73 ppm related to Hx of pyrazoline moiety and a doublet signals at 6.53-6.55 ppm related to *NH_2-group* as well as hydrogen of *NH-pyrazoline*, while multiplet signals 7.30-8.51 ppm due to other aromatic hydrogens as shown in Figure 4. The molecular ion 238 M^+ of (2) confirmed by the Mass spectrum as shown in Figure 5. The FT-IR spectra of Schiff's-Base compound (3) showed absorption at 3365cm^{-1} due to the stretching frequency of *NH-pyrazoline*, and showed the absorption bands at 3032 cm^{-1} due to the stretching vibrations of (*C-H aromatic*), while absorption bands of *CH=N*, *C=N pyrazoline*, *C=N pyridine* and *aromatic C=C* groups appear at 2928, 1653, 1621, 1593 and 1519 cm^{-1} respectively, while absorption bands of *NO2-group* appear at 1558,1342 cm^{-1}. The ^{1}H-NMR of (3) showed two doublet doublet signals at 3.78 and 4.72 ppm due to Ha and Hb protons of pyrazoline ring and triplet signals at 6.02 ppm due to H_X proton of pyrazoline ring, while multiplet signal at 7.16-8.62 ppm related to the aromatic protons as well as singlet signal at 8.89 ppm is related to *CH=N* protons appeared as shown in Figure 6. The molecular ion 371 M^+ of (3) confirmed by the mass spectrum as shown in Figure 7.

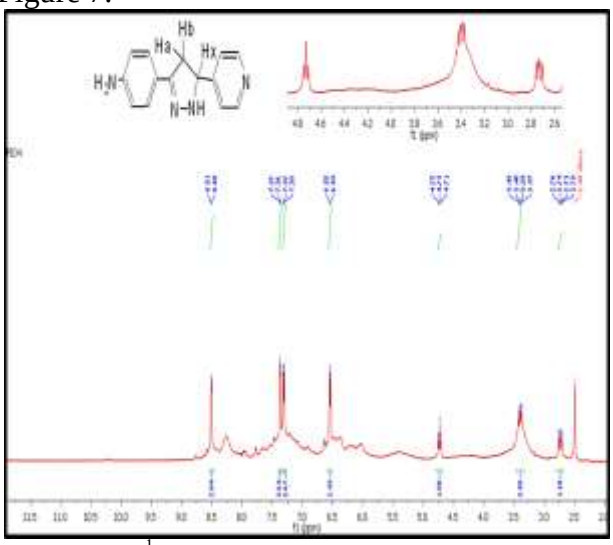


Figure 4. ^{1}H-NMR spectrum of the compound (2).

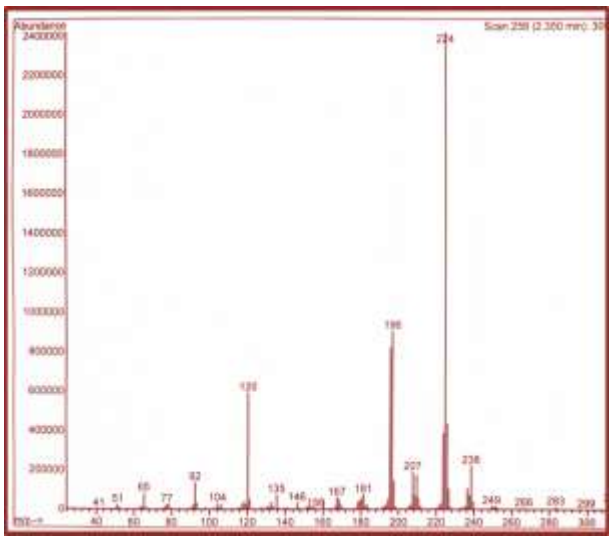


Figure 5. Mass spectrum of the compound (2)

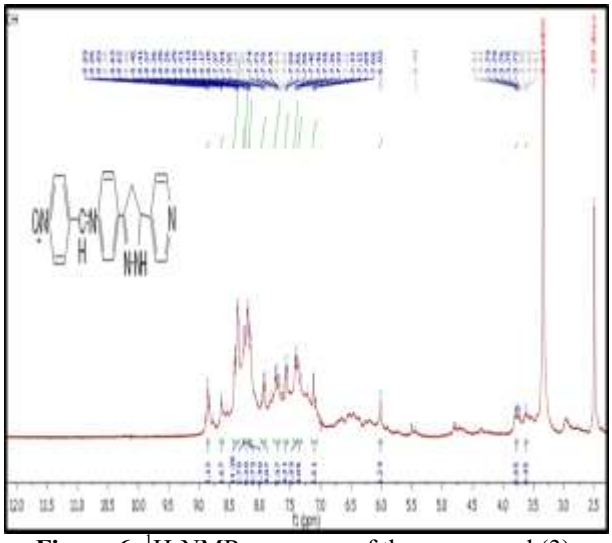


Figure 6. ^{1}H-NMR spectrum of the compound (3).

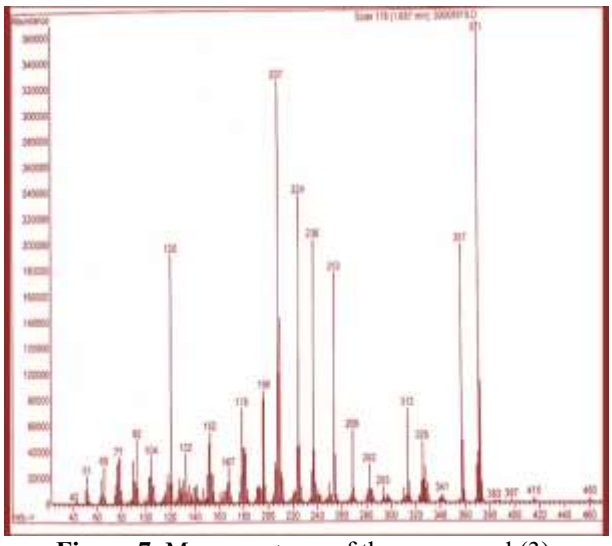


Figure 7. Mass spectrum of the compound (3).

The in vitro assay of the pyrazoline derivatives (3-10) against several pathogenic bacteria and yeast including *Staphylococcus aureus*, *Staphylococcus espidermididis* (gram positive bacteria), *Escherichia coli* and *Klebsiella sp.* (gram negative bacteria) as well as *Candida albicans* (yeast) were achieved using 2 mg/ ml concentration. The antimicrobial inhibition was summarized in Table 1, while Figure 1 shows the inhibition zone for some of the prepared compounds.

CONCLUSIONS

The present research summarized the synthesis of new pyrazoline derivatives containing imine moiety. The new derivatives were screened against several bacterial species, and exhibited a potent antimicrobial agent. Compounds 9 and 10 showed promising activity against *Escherichia coli* and *C. albicans* than other derivatives.

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