Received: 24 April 2022 | Revised: 31 May 2022 | Accepted: 05 June 2022
DOI: 10.22034/ecc.2022.343900.1473
Eurasian Chemical Communications
SAMI

FULL PAPER

# Synthesis and characterization of new derivatives using Schiff's bases for alcoholic extract of (Cordia myxa) medical plant

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In this study, Cordia myxa (bumper) plant was initially extracted in the presence of alcohol, and then Schiff's bases were prepared from the reaction of the active substance of the bumper plant with different aromatic and aliphatic aldehydes during nucleophilic substitution reaction, after that the rom reaction of Schiff's bases with (Chloro acetyl chloride, $NaN_3$, Phthalic, and maleic anhydrides) to produce four, five, and seven-member rings. The prepared compounds were characterized by FT-IR,$^1$H-NMR, and the biological activity of synthesized compounds was studied against positive and negative bacteria (*Staphylococcus aureus, Pseudomonas aeroginosa, E. coli, Klebsiella*) as well as fungi (*candida Albicans)*, and then they were compared with anti-allergic drugs.

**KEYWORDS**

Cordia myxa; Schiff base; β-Lactam; Oxazole and Oxazepine; biological activity.

## Introduction

Nature's gift to humans is medicinal plants, which aid in the pursuit of a disease-free, healthy existence. Humans have been using plants as medicines for thousands of years. All of the global civilizations exist now as a consequence of collected experience from previous generations, and have a thorough understanding of herbal medicine. Two-thirds of the newly discovered compounds in higher plants were harvested on an annual basis. Plants were used by 75% of the population worldwide. Therapy and prevention are both significanct and chemical synthesis dominates the pharmaceutical industry in the United States, as well. Plant-derived compounds account for 25% of pharmaceuticals in the industry [1]. Plants provide a rich source of secondary metabolites which are employed in medications, agrochemicals, flavorings, scents, colors, biopesticides, and food. Oil, glycosides, flavonoids, sterols, saponins, terpenoids, alkaloids, phenolic acids, coumarins, tannins, resins, gums, and mucilage were discovered in the early phytochemical screening of Cordia myxa fruit extract. Analgesic, anti-inflammatory, immunomodulatory, antibacterial, antiparasitic, insecticidal, cardiovascular, respiratory, and insecticidal properties in pharmacological tests are used to examine the effects on the gastrointestinal tract as well as protection. The chemical ingredients will be highlighted in this review and Cordia myxa's pharmacological effects [2-4].

β-Lactam commonly referred to as azetidine-2-one, β-lactderivativeves with diverse pharmacological activities like anticancer activity, human tryptase, cholesterol absorption inhibitory activity,

thrombin, and chymase inhibition [5]. Tetrazoles have the prominent function with wide-ranging applications in photography and information recording systems, pharmaceutical, and material sciences [6]. Oxazepines are a class of heterocyclic compounds of the seven-membered ring with two heteroatoms (O and N). The oxygen atom is located at position 1 and a nitrogen atom in positions -2,-3, or -4 [7].

## Experimental

### Materials and instruments

All ingredients and solvents were obtained from Fluka and Sigma-Aldrich. Gallen Kamp capillary melting point apparatus was utilized to measure melting points. Furthermore, Shimadzu model FT-IR-8400S was used to take FT-IR measurements. $^1$H-NMR spectra were further collected in DMSO-$d_6$ solution by a Bruker spectrophotometer ultra-shield at 300 MHz by using TMS as an internal standard.

### Methods

*Synthesis of Schiff base compounds (1-5) [8]*

(2 gm, 0.01 mol) compound (N-acetyl hydrazide) and (0.01mol) different aliphatic and aromatic aldehydes (acetaldehyde, formaldehyde, propionaldehyde, p-nitrobenzaldehyde, and 4-dimethylaminobenzaldehyde) in 25 mL absolute ethanol drops of glacial AcOH had been reflex for 6-8 hours. The mixture was cooled at room temperature and filtered, and then recrystallized from chloroform. Physical properties of compounds (1-5) are listed in Table 1.

*Synthesis of B-lactam compound (6) [9]*

(0.5 g, 0.0058 mol) Schiff's base 3 in 20 mL dioxin as put into the mixture a few drops $Et_3N$, and then add drop by drop (0.004 mol) chloroacetyl chloride. The mixture was combined well at (0-5) ℃ stirring at 20 ℃ for 6-8 hours. After that, the reaction mixture was kept at room temperature for two days, and then poured into crushed-ice water. The solid precipitate was filtered off, washed with water, and purified from methanol/$H_2O$ (1:1). The physical properties of compound 6 are presented in Table 1.

*Synthesis of tetrazole compound (7) [10]*

(1.5 g, 0.007 mol) Schiff's base 4 in 20 mL DMF, and then (0.025 g, 0.01 mol) $NaN_3$ was added and it was refluxed for 22 hours. The reaction completion was checked by using TLC, evaporated the remaining solvent the forming precipitate rinsed with cold water, filtrated, and recrystallized with ethanol. The physical properties of compound 7 are provided in Table 1.

*Synthesis of Oxazepine compound (8) [11]*

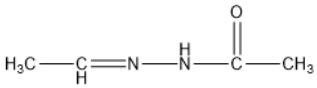
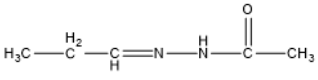
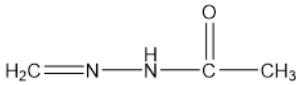
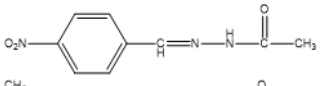
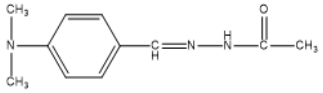
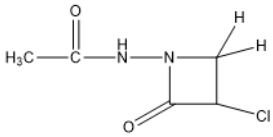
A mixture of equimolar quantities (0.01 mol) of Schiff's bases 5 and (0.78 g, 0.01 mol) Phthalic anhydride in 20 mL dry benzene were refluxed for 14 hours. The reaction was checked by using TLC. The solvent had been evaporated and resocialized of the product by ethanol. Physical properties of compound 8 are indicated in Table 1.

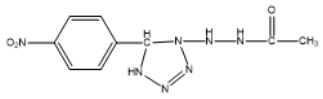
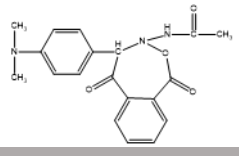
## Results and discussion

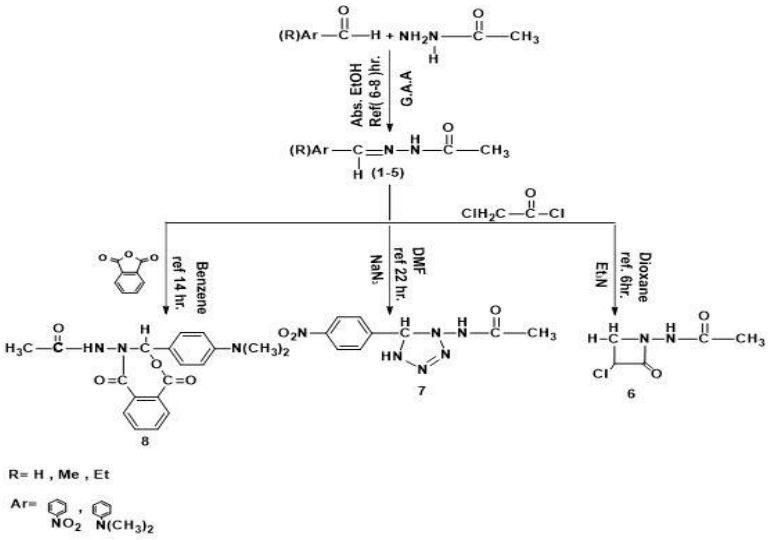
Table 1 exhibited the structural formula, the percentage of yield, melting point, and color. The best yield is for the compound 1, while the lower yield is for the compound 4, the higher melting point was 88-90 ℃ for compound 4, and the lower melting point was 55-57 ℃ for compound 8. The compounds (1- 5) were prepared by reacting N-acetyl hydrazide with different aliphatic and aromatic aldehydes (acetaldehyde, formaldehyde, propionaldehyde, p-nitrobenzaldehyde, and 4-dimethylamino benzaldehyde), in the presence of ethanol as a solvent. The synthesized compounds (1-5) were diagnosed

by FTIR spectrum, as illustrated in Table 1. These spectra revealed absorption (NH), respectively at (3321.24, 339472, 3398.57, 3383.14, 3325.28) $cm^{-1}$, ν(C=O), respectively at (1728.22, 1728.22, 1732.08, 1705.07, 1654.92) $cm^{-1}$, other absorption compounds are exhibited in Table 1. The compound 6 was prepared by reacting Schiff's base 3 with $Et_3N$ and chloroacetyl chloride. These spectra revealed absorption υ (NH) at (3356.14) $cm^{-1}$, ν(C=O) at (1705.07) $cm^{-1}$, and ν(C-H) aliphatic at (2920-2850) $cm^{-1}$, other absorption compound are proposed in Table 1. Compound 7 was prepared from the reaction of Schiff's base 4 with $NaN_3$ in the case of DMF as a solvent, indicated an absorption band (3275.13) $cm^{-1}$ belonging to υ (NH) and appearance the (C=O) at (1720-1654) $cm^{-1}$, also υ (CH aromatic) at (3091) cm-1, υ (CH aliphatic) at (2924-2850), υ (C=N) at (1597.06), and other absorption compound are observed in Table 1. The compound 8 was prepared from the reaction of Schiff's base 5 with phthalic anhydride in the presence of benzene as a solvent, and demonstrated absorption υ (NH) at (3390) $cm^{-1}$, υ (CH aromatic) at (3022) $cm^{-1}$, υ (CH aliphatic) at (2920-2854), υ (C=O) at (1728.22) and other absorption compound are indicated in Table 1. The H-NMR spectrum of compound 3 in solvent ethanol (Table 2) illustrated chemical shifts, δ (ppm), doublet in 1.5 (2H, CH2-C=N), singlet in 2.50 (3H, O=C-CH3), singlet in 5(1H, CH2=NNH). The H-NMR spectrum of compound 5 in solvent ethanol (Table 2) exhibited chemical shifts, δ (ppm), singlet in 2.50 (3H, O=C-CH3), singlet in 3 (1H, H-C=N-H), singlet in 4.5 (6H, $N(CH_3)_2$, multiplet in 6.8-7.6 (4H, arom), singlet in 9.5 (1H, H-C=N-H). The H-NMR spectrum of compound 7 in solvent ethanol (Table 2) indicated chemical shifts, δ (ppm), singlet in 1.9 (1H, CH), singlet in 3.5 (1H, N-H), tetrazoline ring singlet in 2.7 (3H, CH3-CO), doublet in 2(1H, NHC=O), multiplet in 7.5-8.5 (4H, Ar-H), and doublet in 9.2 (1H, NH-NH-C=O). The H-NMR spectrum of compound 8 in solvent ethanol (Table 2) depicted chemical shifts, δ (ppm), singlet in 1.5 (3H, CH3C=O), singlet in 3(1H, NH-C=O), singlet in 6(6H, N-$(CH_3)_2$, multiplet in 6.92-8.22 (8H, Ar-H) and singlet in 9 (1H, H-NH). Compound 3 demonstrated the highest biological activity.

**TABLE 1** The physical properties and FT-IR spectral data cm-1 of synthesized compounds (1-8)

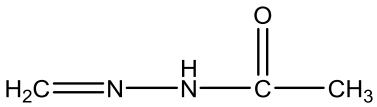
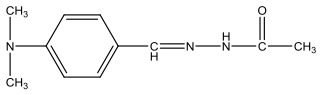
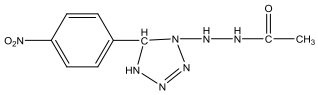
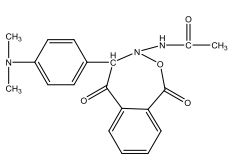
| Physical properties | | | | | Major FT-IR absorption $cm^{-1}$ | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Compound No.** | **Structure of compounds** | **m.p. °C** | **color** | **Yield %** | ***ν* (N-H)** | **υ (C-H) Arom.** | **υ(C-H) Aliph** | **υ (C=O)** | **Other bands** |
| 1 |  | sticky | Light brown | 69 | 3321.24 | ... | 2924-2858 | 1728.22 | |
| 2 |  | sticky | Dark brown | 73 | 3394.72 | ... | 2920-2850 | 1728.22 | |
| 3 |  | sticky | Light brown | 86 | 3398.57 | ... | 2920-2854 | 1732.08 | |
| 4 |  | 88-90 | Dark gray | 37 | 3383.14 | 3109.25 | 2924-2850. | 1705.07 | |
| 5 |  | 78-70 | Light brown | 78 | 3325.28 | 3100 | 2920-2845 | 1654.92 | |
| 6 |  | Dos.in 249 | Light brown | 73 | 3356.14 | ... | 2920-2850 | 1705.07 | υ(C-Cl) (775.38) |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 7 |  | Dos .in381 | Brown | 52 | 3275.13 | 3091 | 2924-2850 | 1720 | υ (NO2): 1396 1539 N=N(2048) |
| 8 |  | 55-57 | Brown | 61 | 3390 | 3022 | 2920-2854 | 1728.22 | υ(N-O) 1531 |




**SCHEME 1** All synthesis compounds [1-8]

**TABLE 2** $^1$H-NMR spectral data (δ ppm) for some compounds

| Compound No. | Compound structure | $^1$H-NMR data of (δ-H) in ppm |
|---|---|---|
| 3 |  | 1.5 (d,2H, C<u>H</u>$_2$=N), 2.50 (S, 3H, O=C-C<u>H</u>$_3$); 5(S,1H,CH$_2$=NN<u>H</u>) |
| 5 |  | 2.50 (S, 3H, O=C-C<u>H</u>$_3$); 3 (S,1H, H-C=N-N-<u>H</u>), 4.5(S,6H, N(C<u>H</u>$_3$)$_2$ 6.8-7.6(M,4H, arom) 9.5 (S,1H, <u>H</u>-C=N-NH) |
| 7 |  | 1.9 (s, 1H, C<u>H</u>); 3.5(S,1H, N-<u>H</u>); tetrazoline ring 2.7 (S, 3H, C<u>H</u>$_3$-CO); 2 (d, 1H, NH<u>C</u>=O), 7.5-8.5. (M, 4H, Ar-H),9.2(d,1H,NH-NH-C=O |
| 8 |  | 1.5 (s, 3H, C<u>H</u>$_3$C=O); 3. (S, 1H, N<u>H</u>-C=O); 6 (S, 6H, N-(C<u>H</u>$_3$)$_2$; 6.92-8.22 (M, 8H, Ar-H) and 9 (S, 1H, CH-C=O) |

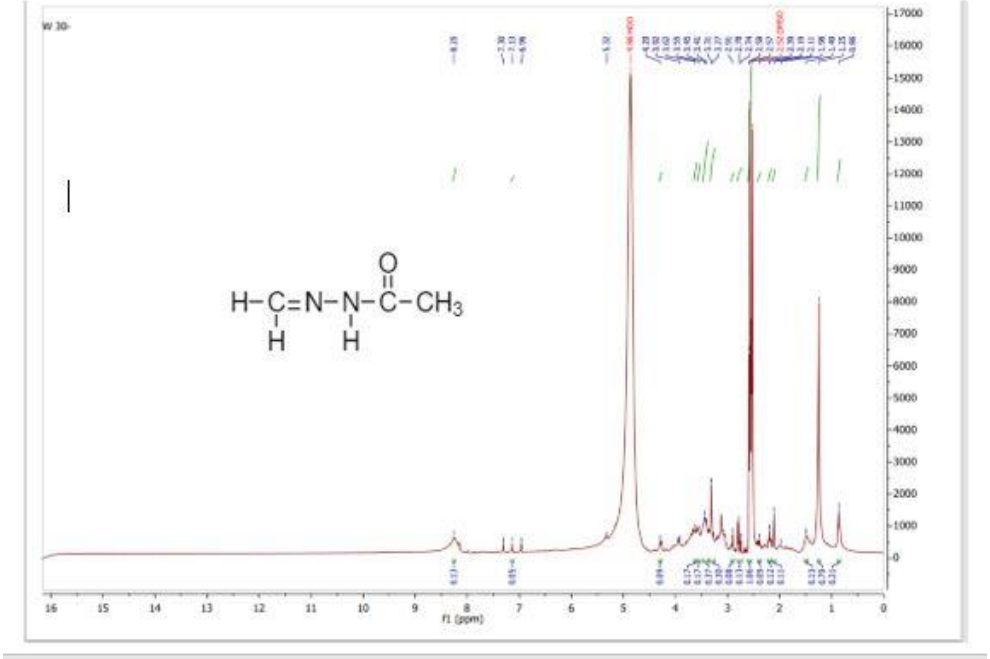



**FIGURE 1** H-NMR Spectra of compound 3

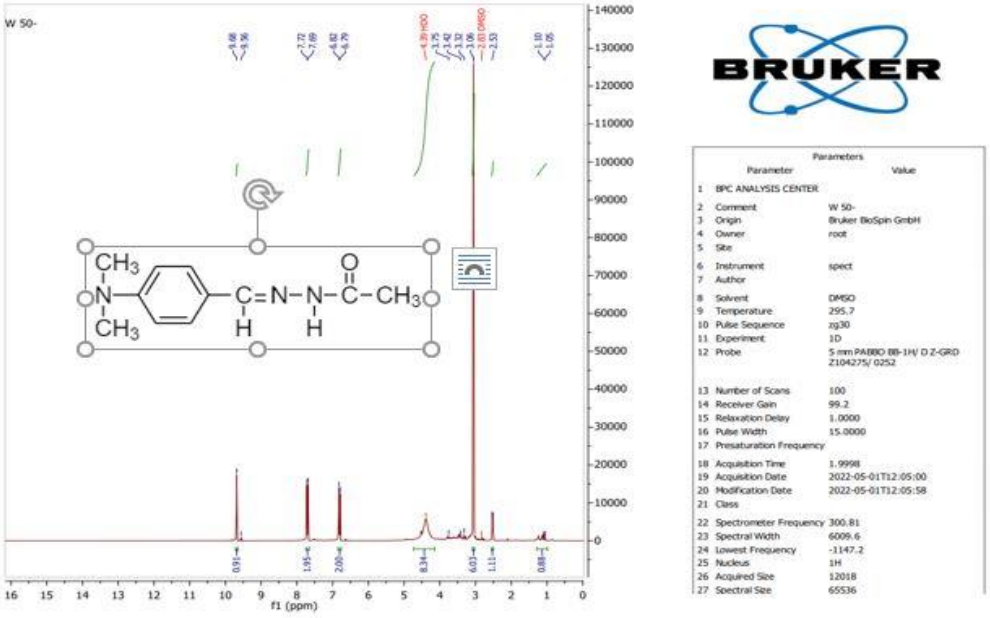



**FIGURE 2** H-NMR Spectra of compound 5

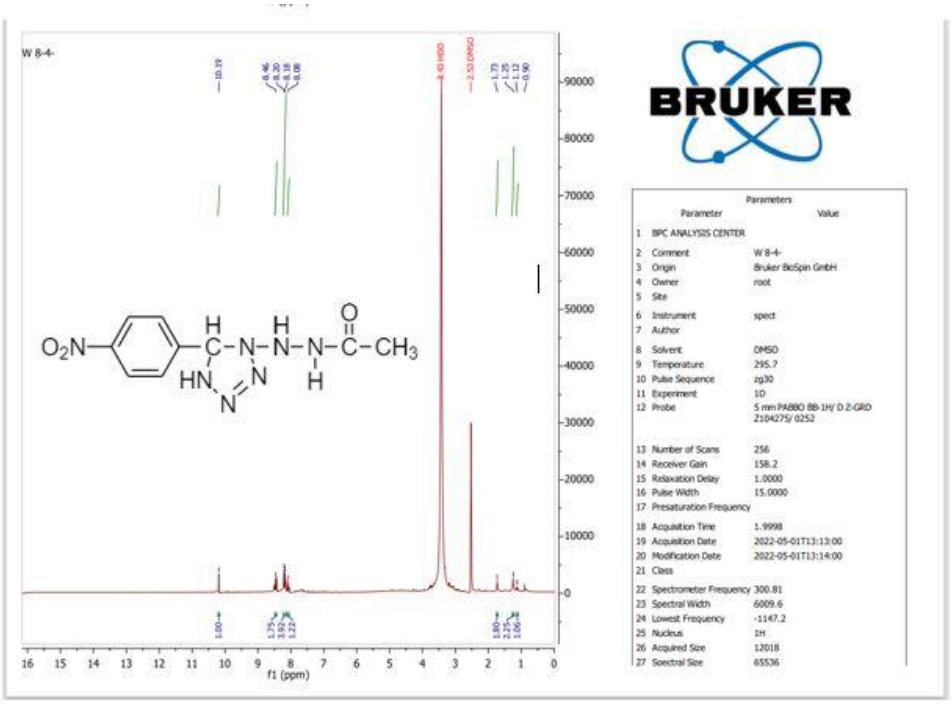



**FIGURE 3** H-NMR Spectra of compound 7

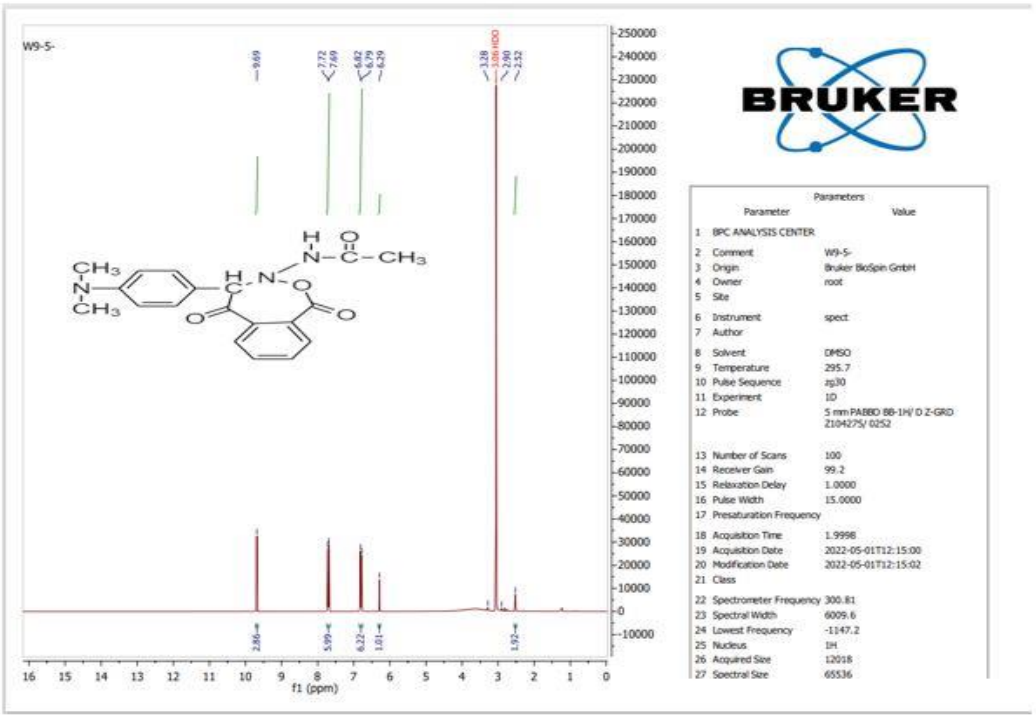



**FIGURE 4** H-NMR Spectra of compound 8

*Biological activates*

Some produced compounds (2, 4, and 5) were examined for biological activity against a variety of bacterial strains. Agar well diffusion method was used to isolate bacteria (Staphylococcus aureus, Pseudomonas aeroginosa, E. coli, and Klebsiella). Anti-bacterial results are presented in Table 3.

**TABLE 3** Biological activity for some synthesized compounds

| Compound No. | | *Staphylococcus aureus* | *Pseudomonas aeroginosa* | *E.coli* | *Klebsiella* |
|---|---|---|---|---|---|
| 1(2) | 50mg/ml | NIL | NIL | NIL | 10 |
| | 100mg/ml | 12 | 10 | 10 | 13 |
| | 200mg/ml | NIL | NIL | NIL | 13 |
| Methanol control | | NIL | NIL | NIL | 10 |
| Antibiotic disc diffusion(ciprofloxacin) | | 25 | 30 | 50 | 10 |
| 2(4) | 50mg/ml | 20 | 10 | 12 | 10 |
| | 100mg/ml | 12 | 10 | 12 | 10 |
| | 200mg/ml | 20 | 10 | 25 | 20 |
| Methanol control | | NIL | NIL | NIL | 10 |
| Antibiotic disc diffusion(ciprofloxacin) | | 20 | 20 | 20 | 10 |
| 3(5) | 50mg/ml | 10 | 20 | 15 | 20 |
| | 100mg/ml | 10 | 10 | 20 | 12 |
| | 200mg/ml | 15 | 15 | 20 | 15 |
| Methanol control | | 10 | NIL | NIL | 5 |
| Antibiotic disc diffusion(ciprofloxacin) | | 25 | 30 | 20 | 5 |

## Conclusion

In this study, Schiff bases have been synthesized, derivatives with new heterocyclic compound as (oxazepine, tetrazole, β-Lactam) with characterization

1. Spectral data (FT-IR, 1H-NMR) to verify the suggested structures.

2. The prepared compounds proved to be resistant to some types of bacteria and fungi these compound have medical application.

## Acknowledgments

The authors thank the staff of the Department of Chemistry, College of Science, University of Baghdad for achieving this work well. Likewise, they are to grateful Biologist Qabas Nather Latef from the College of Pharmacy/ Al-Mustansiriya University for helping to complete the biological activity tests and obtaining the Candida isolates from Karkh General Hospital.

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**How to cite this article:** Weam Neamah Nayyef Mezaal*, Sanaa A. ALsahib. Synthesis and characterization of new derivatives using Schiff's bases for alcoholic extract of (Cordia myxa) medical plant. *Eurasian Chemical Communications*, 2022, 4(11), 1054-1061. **Link:** http://www.echemcom.com/article_152250.html