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Combination and Identification of Cycles Compounds of Drug with Bio Assessment

Nadia Sadiq Majeed[1] , Rasha Neama Hussein[2]

[1]*Advisor ,Department of Chemistry, College of Education for Girls, University of Kufa, Iraq*

[2]*Ph.D- Student., Part of Thesis ,Department of Chemistry, College of Education for Girls, University of Kufa, Iraq*

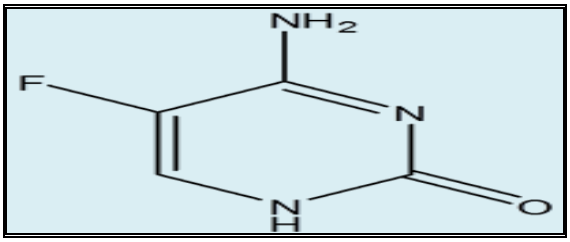
Abstract:

Sundry derivative were prepared in recent study in step of preparing a number of heterogeneous organic compounds with seven-cyclic closure (oxazepines compounds) , which bear the numbers (A5-A8). As well as from Schiff's base compounds, a number of Heterogeneous organic compounds with tetracyclic closure (beta-lactam compounds) using 1,4-dioxane as a solvent bearing the numbers (A9-A12) were prepared. All of these derivatives evaluated via many spectral methods to improve their structures as a heterocyclic compounds, then bio assessment were carried out on same derivatives to improve their activity towards microbs.

Keywords: *Oxazepines, β-lactam,Microwave, Biological activity..*

Introduction:

Aldamine and ketamine compounds[1-3] are organic composites containingan kitamine or aldamine group and identified by the common formula (R1R2C=NR3) where R1,R2and R3are alkyl, aryl, cyclo alkyl or heterocyclic groups [4-7]. Oxazepines [8-12] are a class of seven-membered heterocyclic ring compounds containing an oxygen atom at position 1 and a nitrogen atom in one of the three locations (2,3or 4) in the heptane ring [13-17]. A growing problem is the potential for misuse of prescription drugs to affect all age groups, including adolescents [18-20]. The drugs most commonly abused include opioid analgesics, anxiolytics, sedatives and stimulants. Therefore, some researchers in recent years have prepared medicinal compounds that give the same effect [21] , Some people fear becoming addicted to medications prescribed for their conditions, such as painkillers given after surgery. But you can reduce your risk by carefully following your doctor's instructions about how to take your medication [22-26]. Teens and young adults are the most likely to misuse prescription drugs. One of the risks associated with the misuse of prescription drugs [27-29].Past or present addiction to other substances , and mono bactams, were prepared in this research using green chemistry methods [30-31], by using microwave radiation to reduce the reaction time, reduce energy used, environmental pollution [32-35], and not use chemical solvents during preparation and increase the proportion of the product [36-38]



(figure 1): synthetic formula of flucytosine

Method Part

By carrying all measurements in spectral techniques:

1-Formation of Adamine and ketamine (A1-A4):-

The equimolar (1:1)ratio of Flusytosine and a series of heterocyclic aromatic aldehydes and ketones namely, all mixture was mixed thoroughly in the grinder. The reaction mixture was then irradiated in microwave oven and taking ethanol as a solvent. The reaction was completed in a short time (12-20 min) with higher yield.

2- The general method for preparing Oxazepine compounds(A5-A8):-

(0.1 mole) of Schiff bases (A1-A4) mixed with (0.1 mole)Maleic anhydride In a small dry ceramic mortar, crush the mixture well until it is homogeneous in color and shape The crystals were then transferred to the microwave, after the irradiation was completed The mixture was taken out and left to cool at laboratory temperature. The resulting substance was washed with Benzene.

3- The general method for preparing β-lactam compounds(A9-A12):-

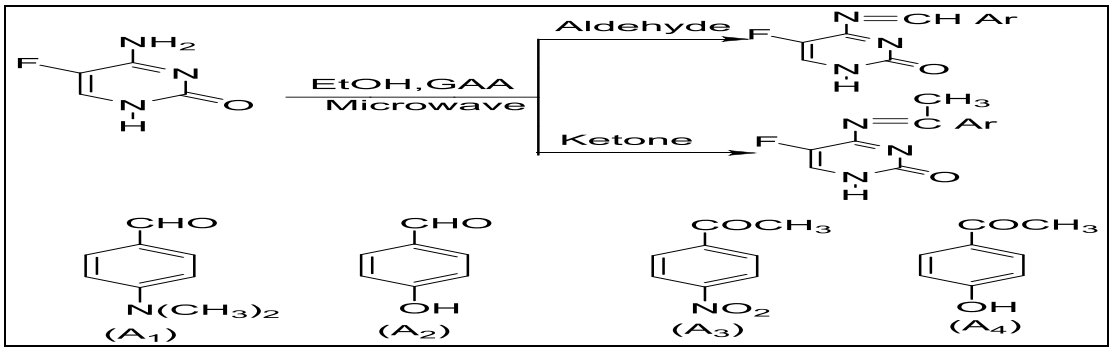
(0.001)mol of the previously prepared Schiff bases(A1-A4) was mixed with (0.001)mol of Triethylamine in (25ml) of 1,4-Dioxane, then added to this mixture cooled at (10^0C) (0.002)mol of Chloroacetyl Chloride in the form of drops with Continuous stirring for a period of (6-10 hours). All these reaction was followed by TLC(ethanol :benzene)(2:3)., then it was filtered, the filtrate was extracted, dried and recrystallized with absolute ethanol.

Biological Commotion Analyze[22-24]**:**

Antibacterial commotion of the synthesized composites **[A1-A12]** have been approved against four types of bacteria like, ***(staphylococcus aureus, Enterococcus* faecalis)** in addition to **(*E. coli, Klebsiella pneumoniae*)** . All bio-data in table below.

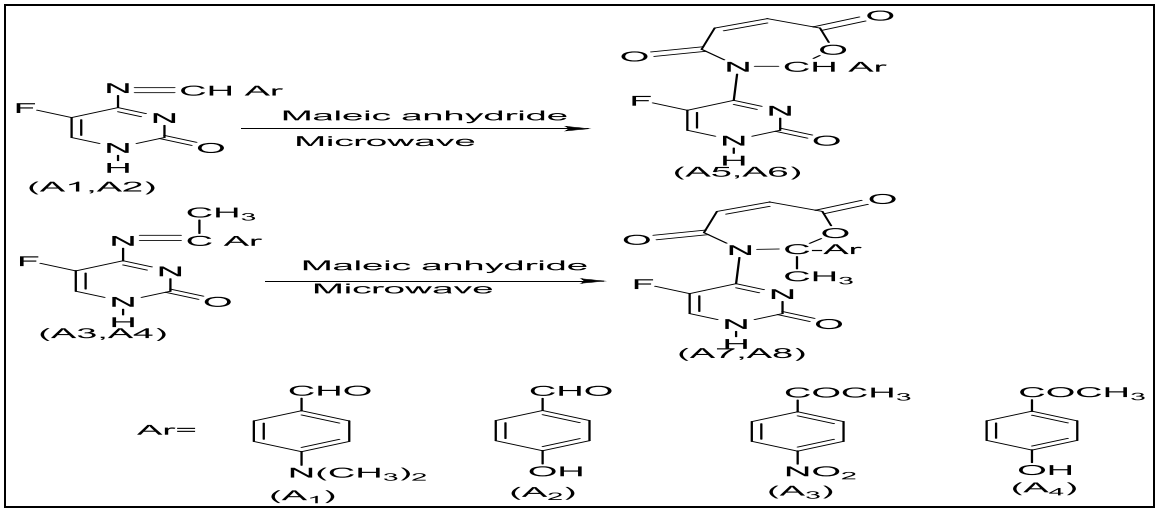
Results And Discussion :

All derivatives prepared according to (Scheme 1).



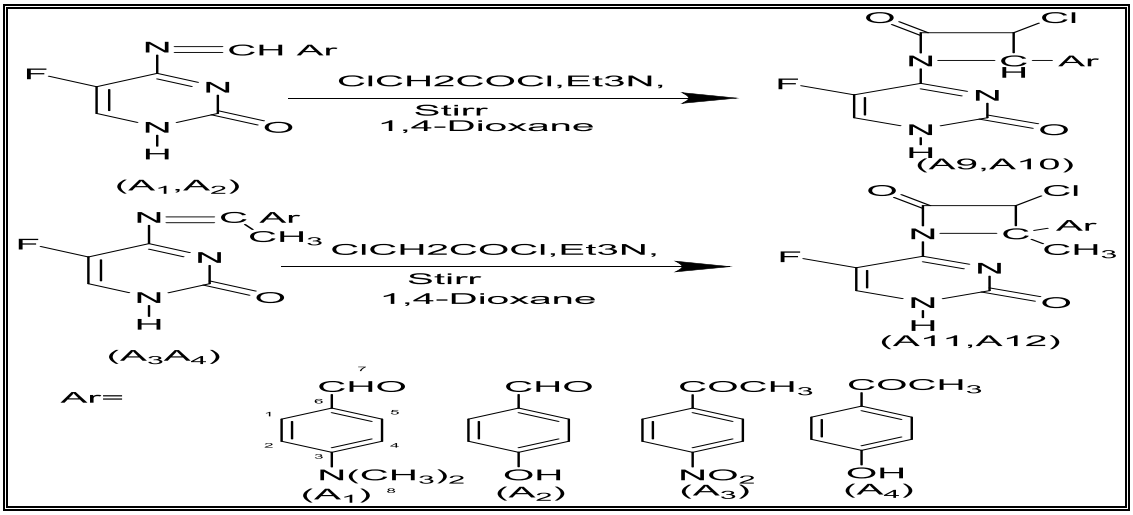
Scheme (1):Synthesis of the compounds (A1-A4)

In preparing a number of heterogeneous organic compounds with seven-cyclic closure (oxazepines compounds) , which bear the numbers (A5-A8) Scheme (2)

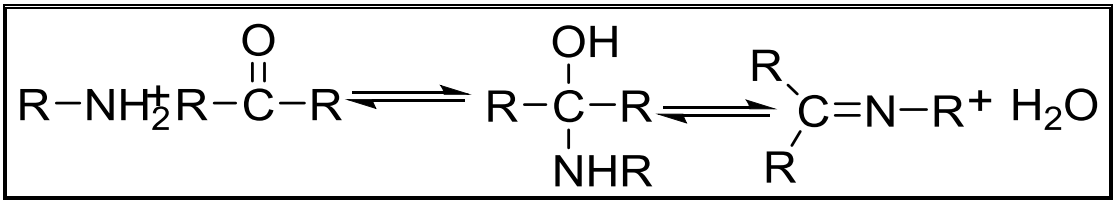


Scheme (2):Synthesis of the compounds (A5-A8)

And tetracyclic closure (beta-lactam compounds) using 1,4-dioxane as a solvent bearing the numbers (A9-A12) were prepared Scheme 3**.**



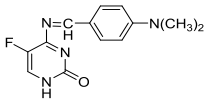
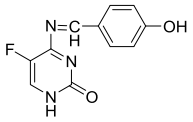
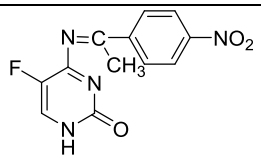
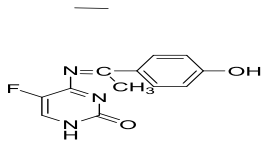
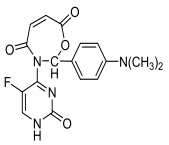
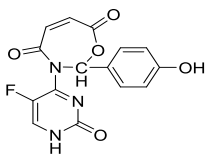
Scheme (3):Synthesis of the compounds (A9-A12)

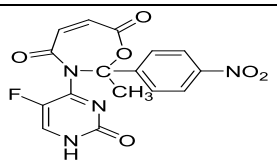
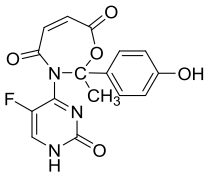
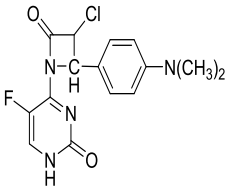
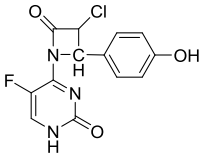
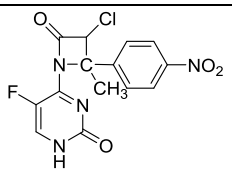
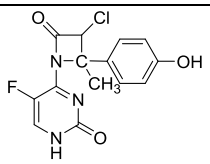


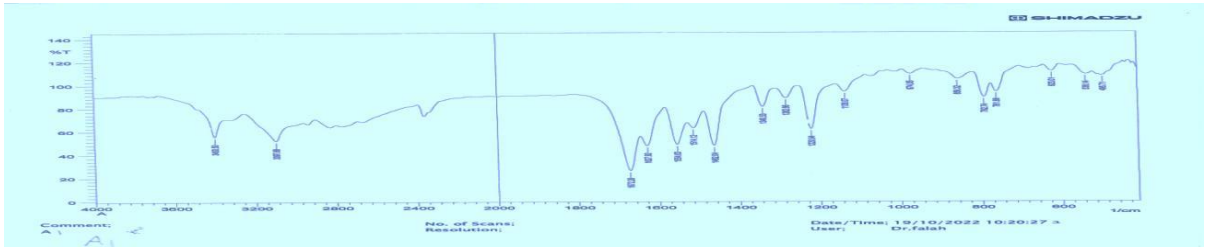
Scheme (4): the Imine formation

The FTIR spectra for compounds (A1- A4) in the Figures and Table of data:

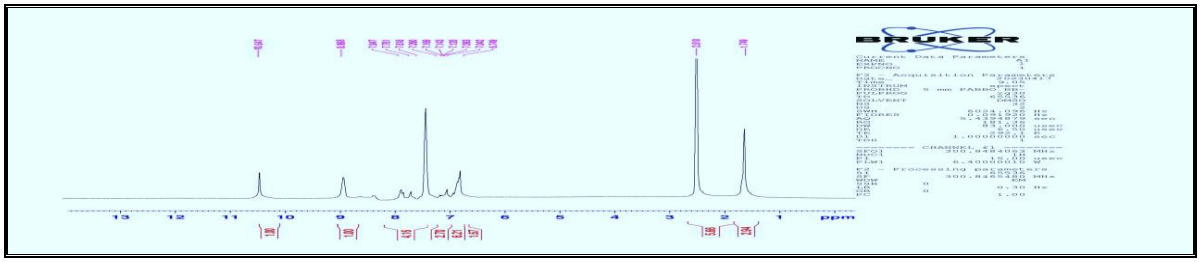
Comp. No .	Compound Structures	1H-NMR Spectral data $^{\delta}$ppm	13C-NMR statistics $^{\delta}$ppm

A1		1.74 (S,6H,2CH_3) 6.74-7.94(m,4H,Ar-H) 8.98(C-H aldehyde) 10.54(S,1H,NH-C-H)	CH3 2(27.45) ,116.39(C-F), 120.61-129. 97, (m,C=C,Ar-H),156.86(C-N) ,157.97 (C=N) cyclo,161.61 (C=N)Imine 169.19and172.46 (C=O)Amide
A 2		7.01-7.64(m,4H,Ar-H) 8.50(S, C-H aldehyde) 10.08(S,1H,NH-C-H) 10.36(S,1H,NH C=O) 11.45(S,1H,OH)	116.97 (C-F),120.61-128.12 (m,C=C,Ar-H),154.42 (C-N) 156.86 (C-OH).158.97(C=N) Cyclo 160.976(Imine) 169.19 (C=O)Amide
A3		1.64 (S,3H, CH_3) 7.20-7.99(m,4H,Ar-H) 10.53(S,1H,NH C=O)	27.45 (CH3) 112.26 (C-F),116.48-126.42 (m,C=C,Ar-H),157.91 (C-N) 159.98 (C=N),161.52(Imine) 169.41 (C=O)Amide
A4		1.63 (S,3H, CH_3) 7.03-7.92(m,4H,Ar-H) 10.50(S,1H,NH C=O) 11.56(S,1H,OH)	27.46 (CH3) 112.26 (C-F),116.48-126.42 (m,C=C,Ar-H),153.52 (C-N) 155.99 (C-OH),157.15 (C=N) 161.90(Imine),169.90 (C=O)Amide
A5		1.59 (S,6H,2CH_3) 6.76-6,78(H-C=C-H) 7.49-7.61(m,8H,Ar-H) 9.57(C-H aldehyde) 10.49(S,1H,NH-C-H)	24.24 (2 CH3) 112.50 (C-F),112.27-130.06 (m,C=C,Ar-H),159.90(C=C) 161.26 (C-N),162.28 (C=N) 169.90 (C=O)Amide (175.35)Lactam,(178.82)Lactone
A6		6.91-6,93(C=C) 7.05-7.62(m,8H,Ar-H) 9.59(C-H aldehyde) 10.59(S,1H,NH C=O) 11.40(S,1H,OH)	111.55 (C-F),112.27-130.06 (m,C=C,Ar-H),132.00(C=C) 154.26 (C-N),158.41(C-OH) 160.87(C=N),169.69 (C=O)Amide,(171.11)Lactam (176.11)Lactone
A7		1.87 (S,3H, CH_3) 6.97-6,99(C=C) 7.68-8.10(m,8H,Ar-H)	25.75 (2 CH3) ,117.06 (C-F), 121.42 – 130.04 (m,C=C,Ar-H), 158.75(C=C) 161.70 (C-N), 162.96 (C=N)

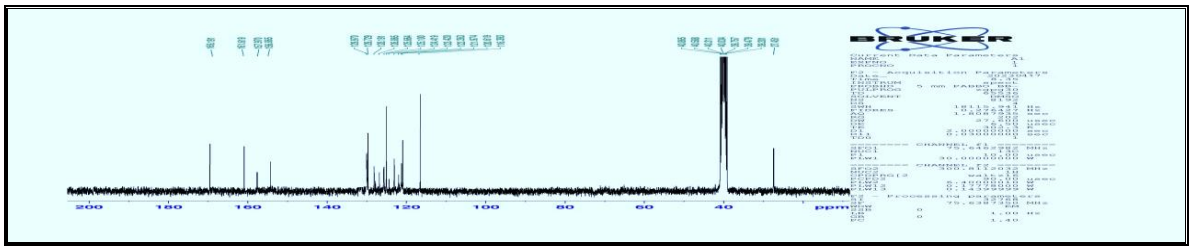
		10.65(S,1H,NH C=O)	169.25 (C=O)Amide (176.75)Lactam,(178.78)Lactone
A8		1.81 (S,3H, CH_3) 6.71-6,74(C=C) 7.49-7.76(m,8H,Ar-H) 10.95(S,1H,NH C=O) 11.73(S,1H,OH)	22.25 (CH3),116.63 (C-F) 121.04 – 130.25,(m,C=C,Ar-H) 155.93(C=C),159.96 (C- N) 161.48(C-OH),162.46 (C=N) 169.46 (C=O)Amide (175.42)Lactam,(178.46)Lactone
A9		1.48 (S,6H,2CH_3) 4.29(CH-Cl) 7.49-7.61(m,8H,Ar-H) 9.57(C-H aldehyde) 10.49(S,1H,NH-C-H)	31.50 (2 CH3) 47.03 (CH-Cl),116.63 (C-F) 121.04–130.25,(m,C=C,Ar-H) 157.13(C=C),159.17(C-N), 160.16(C=N),169.61(C=O) Amide,(198.41)Lactam
A10		4.33(CH-Cl) 7.02-7.95(m,8H,Ar-H) 9.35(C-H aldehyde) 10.61(S,1H,NH C=O) 11.63(S,1H,OH)	111.55 (C-F) 46.87(CH-Cl),112.27-130.06 (m,C=C,Ar-H),153.26(C=C) 158.26 (C-N),159.29(C-OH) 161.29 (C=N),169.29 (C=O) Amide,(198.45)Lactam
A11		1.63(S,3H, CH_3) 4.33(CH-Cl) 7.03-7.90(m,8H,Ar-H) 10.67(S,1H,NH C=O)	29.40 (CH3) 48.86(CH-Cl),116.63 (C-F) 121.04–130.06,(m,C=C,Ar-H) 159.06 (C-N),161.41 (C=N) 169.06 (C=O)Amide (196.97)Lactam
A12		1.47 (S,3H, CH_3) 4.37(CH-Cl) 6.55-7.64-(m,8H,Ar-H) 10.51(S,1H,NH C=O) 11.38(S,1H,OH)	28.11 (CH3),47.25(CH-Cl) 112.56 (C-F),115.82-130.03 (m,C=C,Ar-H),156.68 (C-N) 159.69(C-OH),162.68(C=N) 169.03 (C=O)Amide (175.42)Lactam



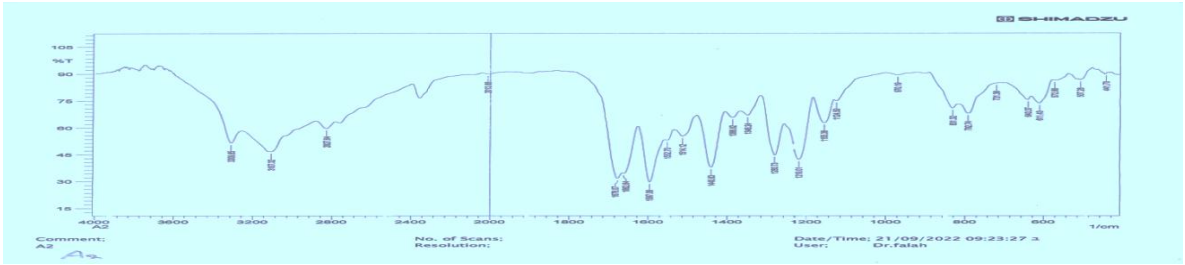
Digit-2: FT-IR. (1)



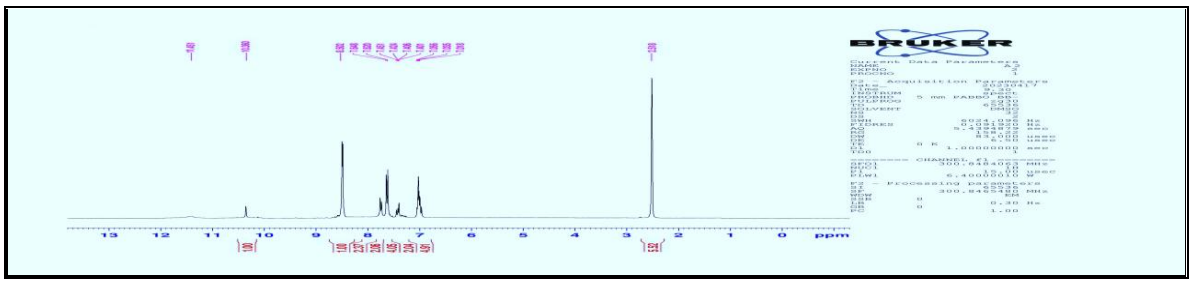
Digit -3: ^{1}HNMR (1)



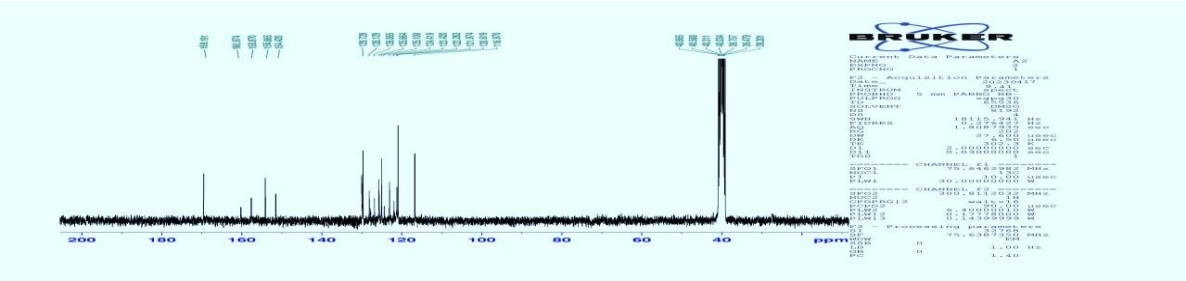
Digit -4: ^{13}C NMR (1)



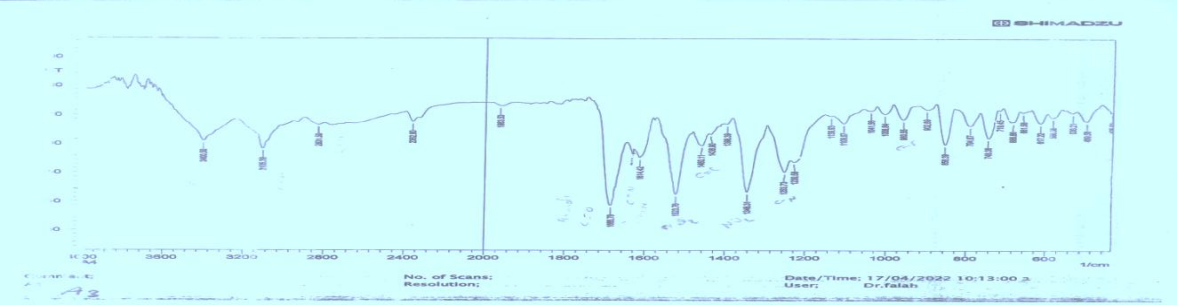
Digit -5: FT-IR (2).



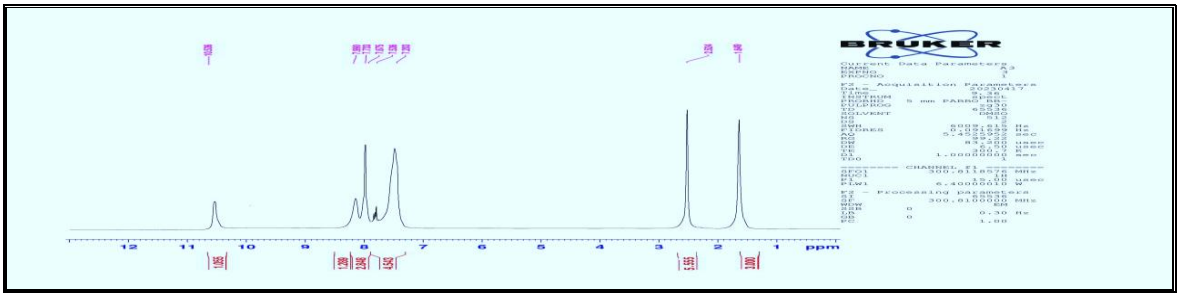
Digit -6: ^{1}HNMR (2)



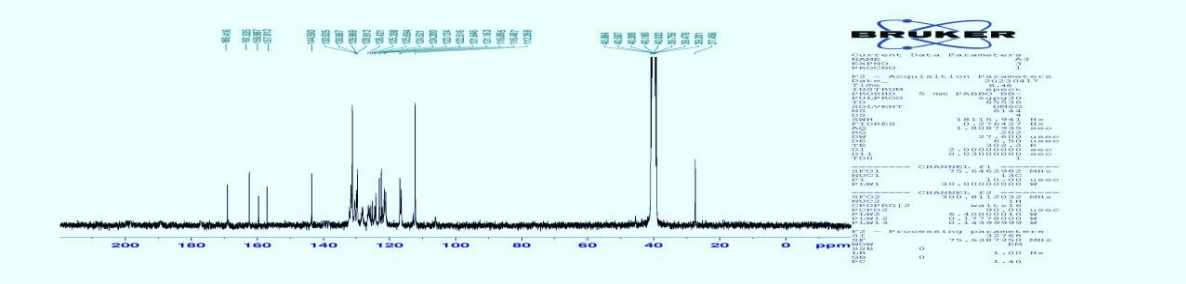
Digit -7: ^{13}C NMR (2)



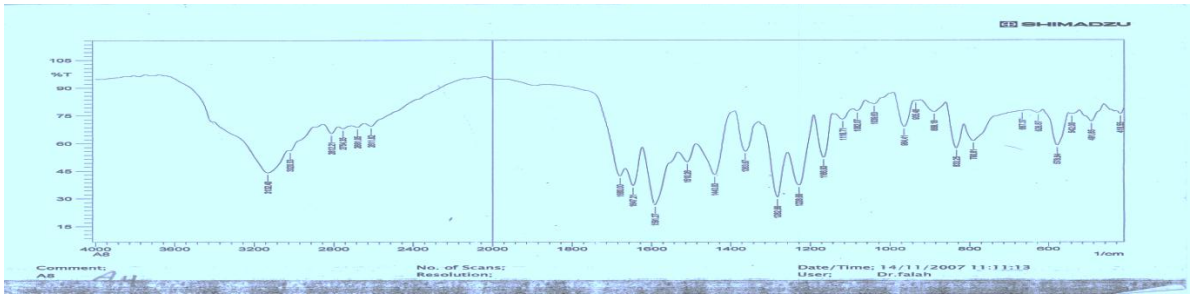
Digit -8: FT-IR. (3)



Digit -9: ^{1}HNMR (3)



Digit -10: ^{13}C NMR (3)



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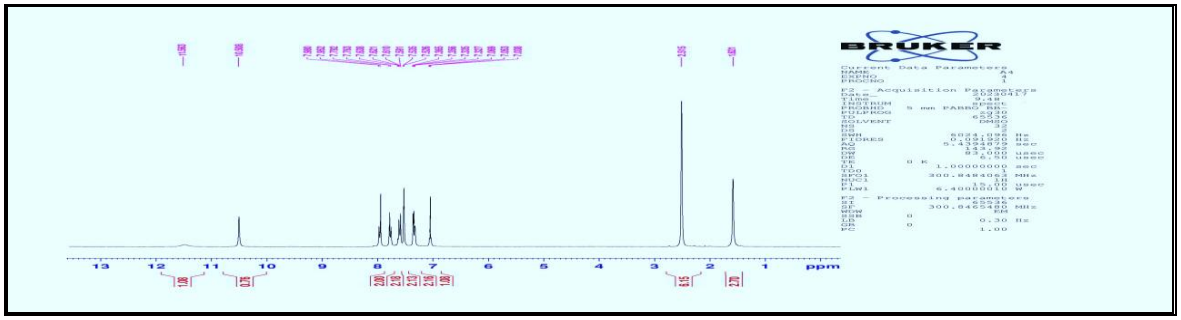

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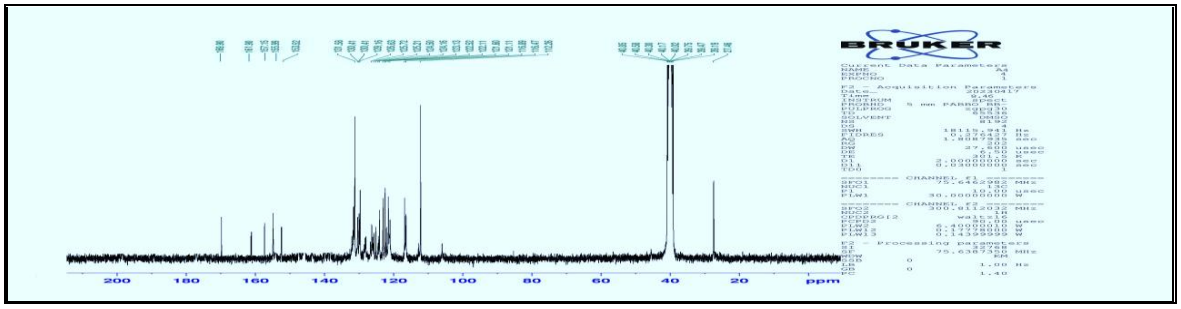
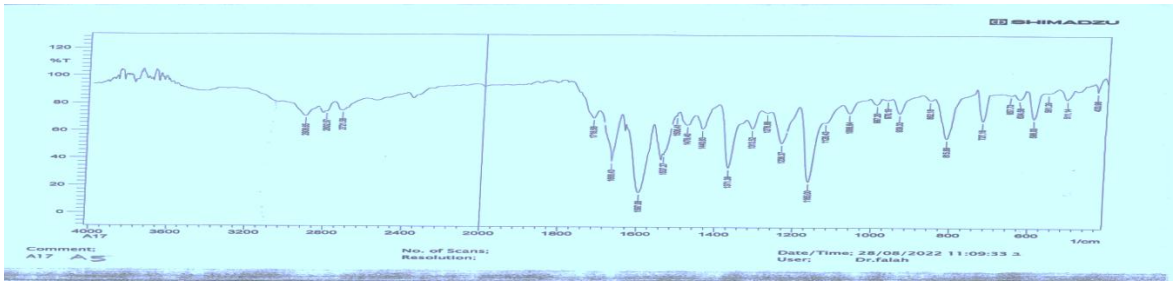


Digit -13: ^{13}C NMR (4)



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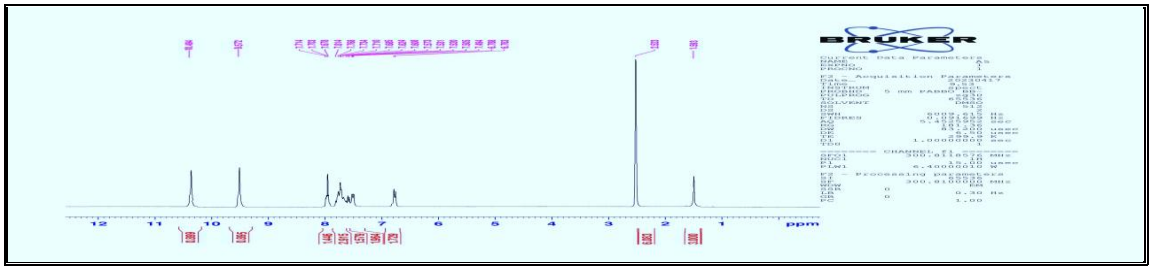

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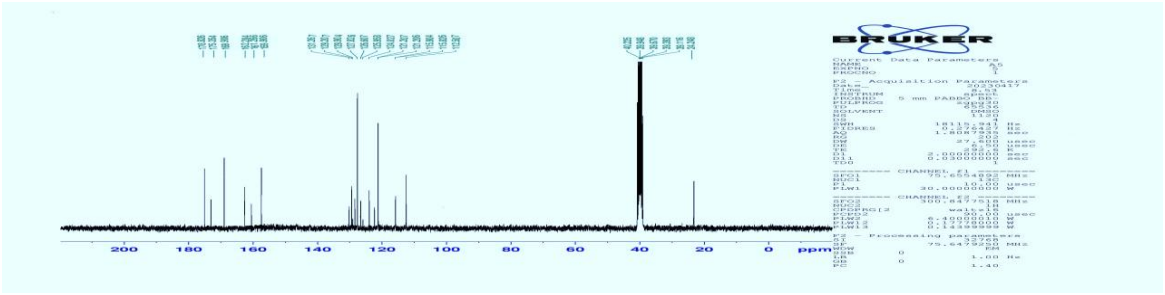
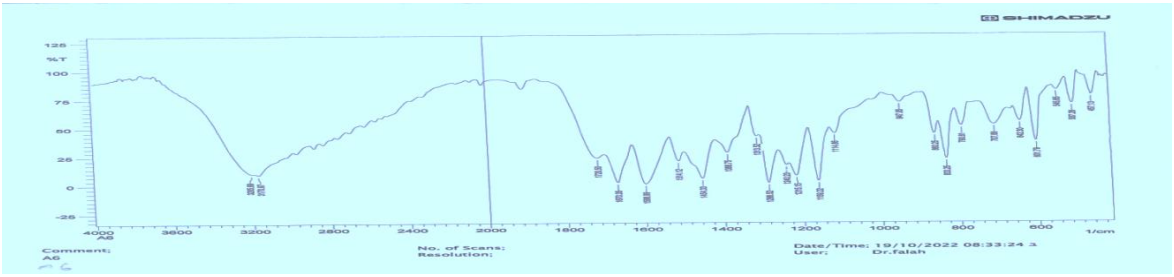


Digit -16: ^{13}C NMR (5)



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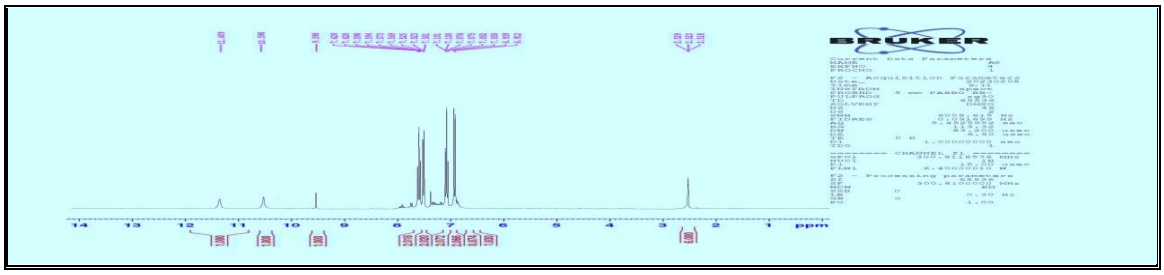

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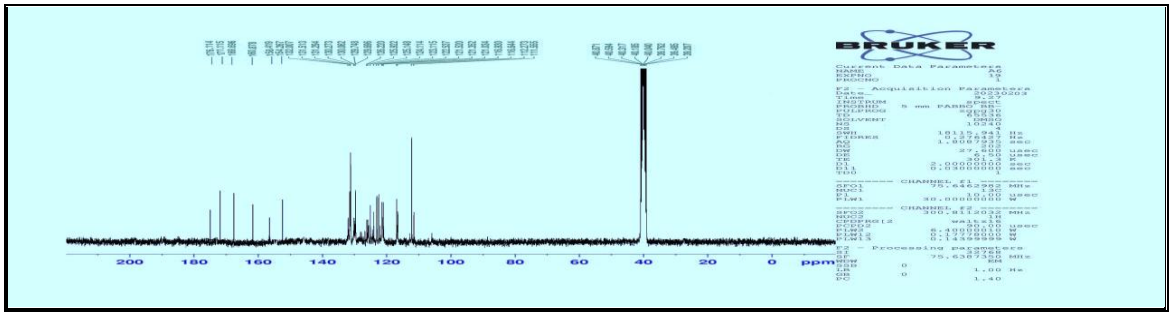

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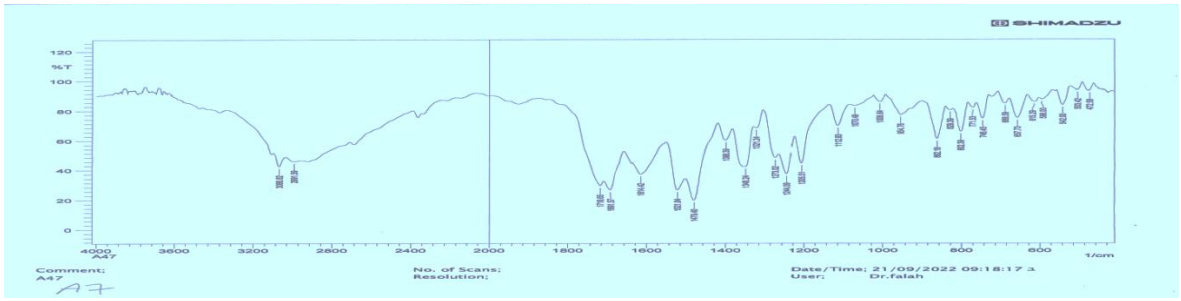
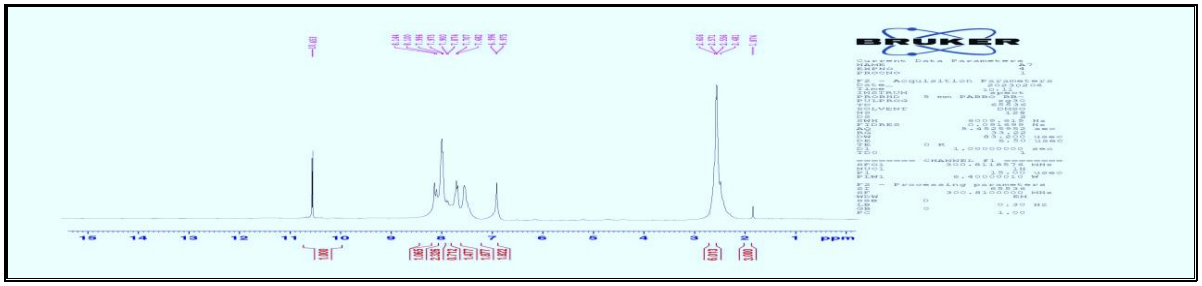
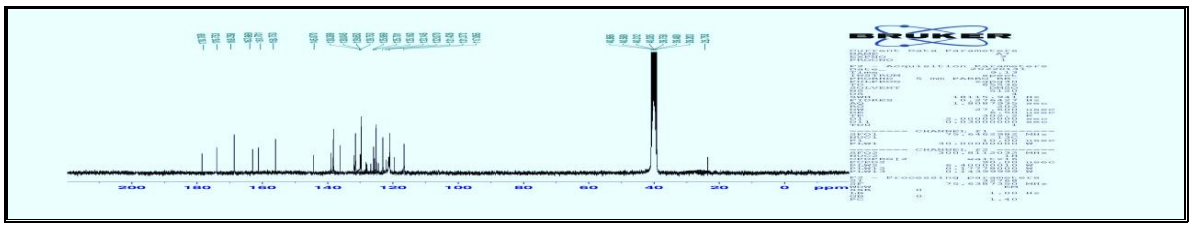


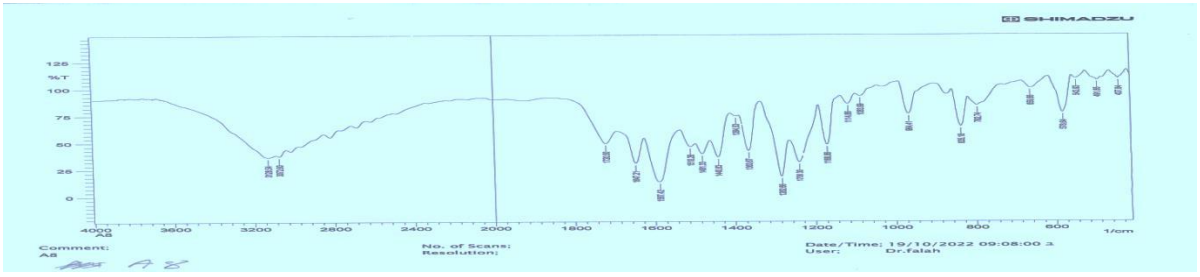
Digit: FT-IR. (7)



Digit: ^{1}HNMR (7)



Digit: ^{13}C NMR (7)



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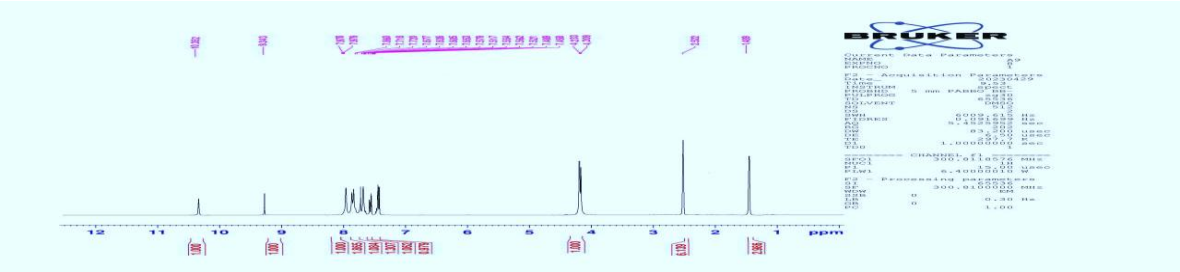

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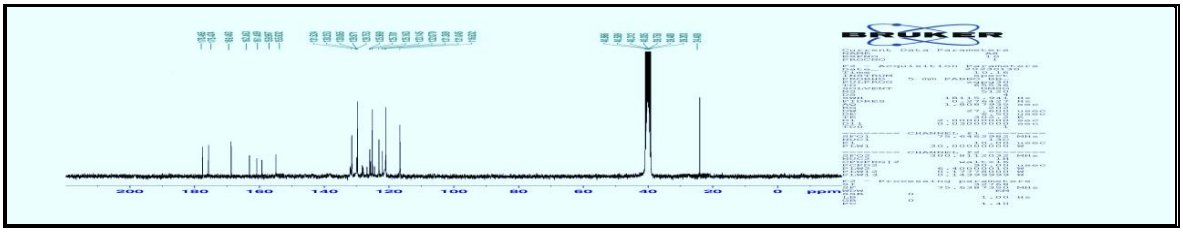

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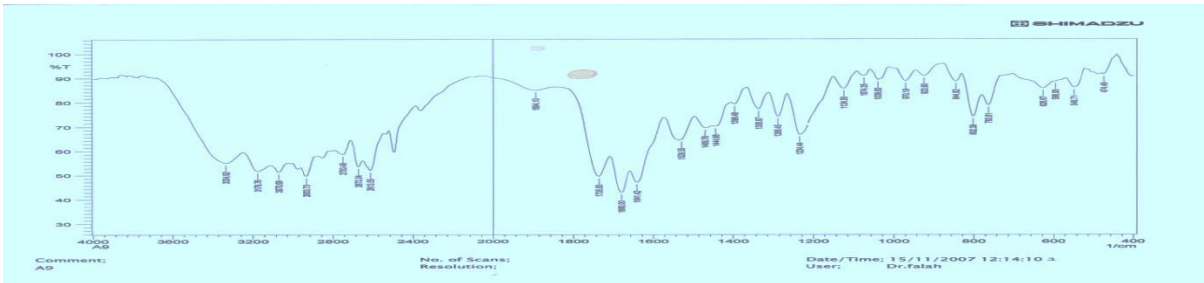

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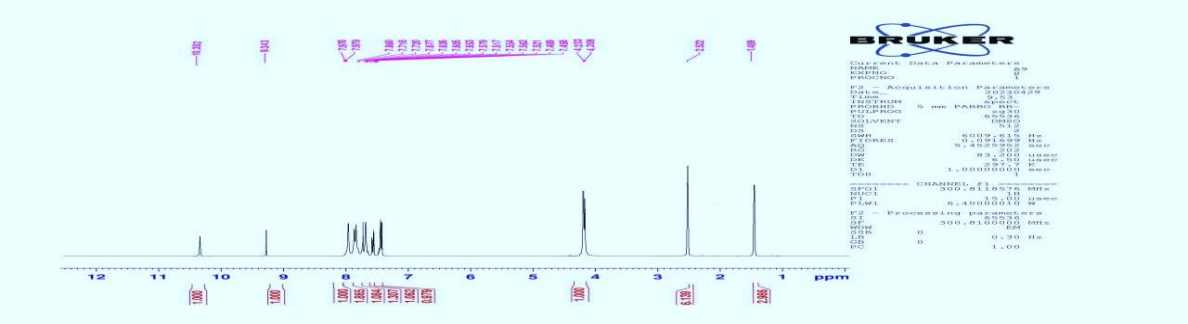
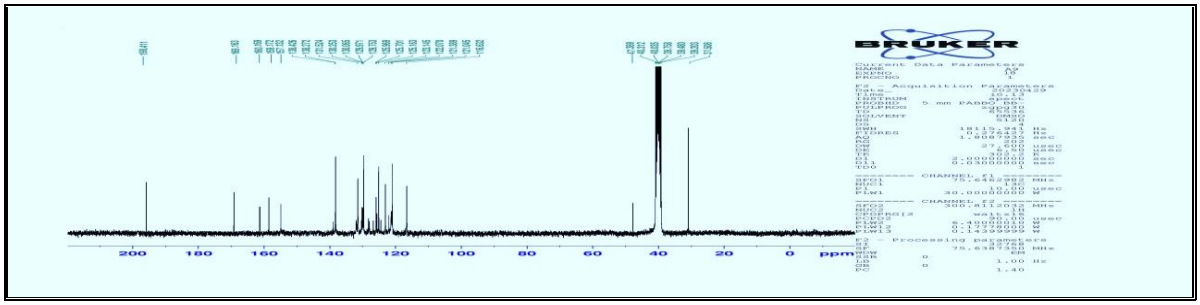
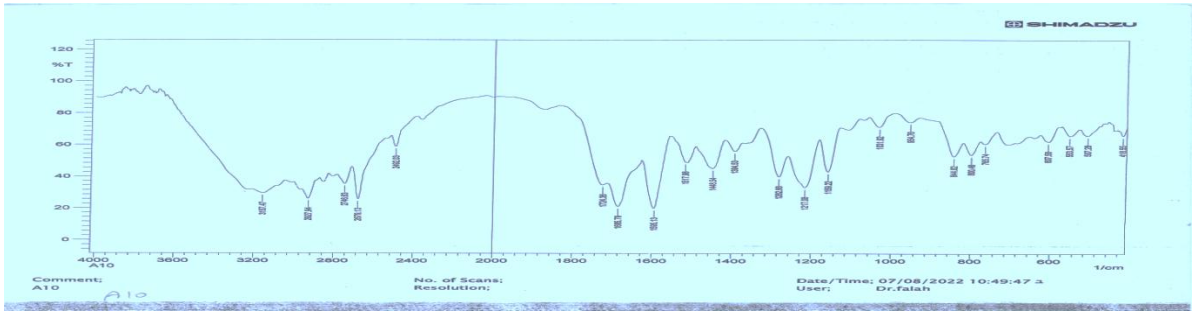


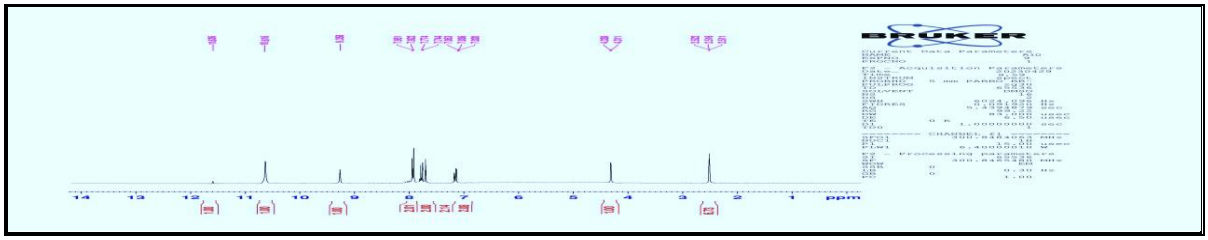
Digit: ^{1}HNMR (9)



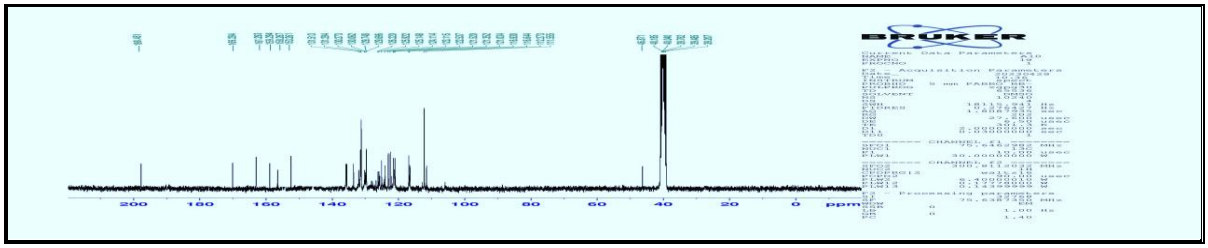
Digit: ^{13}C NMR (9)



Digit: FT-IR. (10)



Digit: $^{1}HNMR$ (10)



Digit: ^{13}C NMR (10)

Table (1):physical properties of synthesized derivatives

No.	M.F	M.WT gm.\mol	M.P	Rf	color	yield

A1	$C_{13}H_{13}N_4OF$	260	75-77	0.50	wight	87%
A2	$C_{11}H_8N_3O_2F$	233	120-122	0.52	yellow	88%
A3	$C_{12}H_9N_4O_3F$	276	88-90	0.75	wight	91%
A4	$C_{12}H_{10}N_3O_2F$	247	106-108	0.60	yellow	90%
A5	$C_{17}H_{15}N_4O_4F$	358	105-107	0.62	yellow	85%
A6	$C_{15}H_8N_3O_5F$	329	108-110	0.50	yellow	89%
A7	$C_{16}H_{11}N_4O_6F$	374	97-99	0.72	yellow	90%
A8	$C_{16}H_{12}N_3O_5F$	335	122-124	0.65	yellow	94%
A9	$C_{15}H_{14}N_3O_2FCl$	322.5	127-129	0.52	orang	71%
A10	$C_{13}H_9N_3O_3FCl$	279.5	133-135	0.54	red	79%
A11	$C_{14}H_{10}N_4O_4FCl$	352.5	143-145	0.70	orange	82%
A12	$C_{14}H_{11}N_3O_3FCl$	323.5	117-119	0.60	red	81%

Table (2): Biological activity of the prepared compounds

No.compound	Staph		E.C		E.F		Kleps	
	C1 10^{-2}	C2 10^{-3}	C1 10^{-2}	C2 10^{-3}	C1 10^{-2}	C2 10^{-3}	C1 10^{-2}	C2 10^{-3}
A1	19	0	19	0	20	0	19	0
A2	19	0	19	0	20	0	18	0
A3	20	0	20	0	18	0	19	0
A4	18	0	21	0	19	9	20	0
A5	25	20	30	24	26	22	24	21
A6	22	19	29	22	25	20	23	22
A7	21	14	20	18	21	15	21	18
A8	22	15	19	14	17	11	17	11
A9	28	21	30	24	23	17	24	20
A10	26	19	28	22	24	16	26	21
A11	25	19	32	23	24	18	25	20
A12	23	20	28	22	22	18	24	18

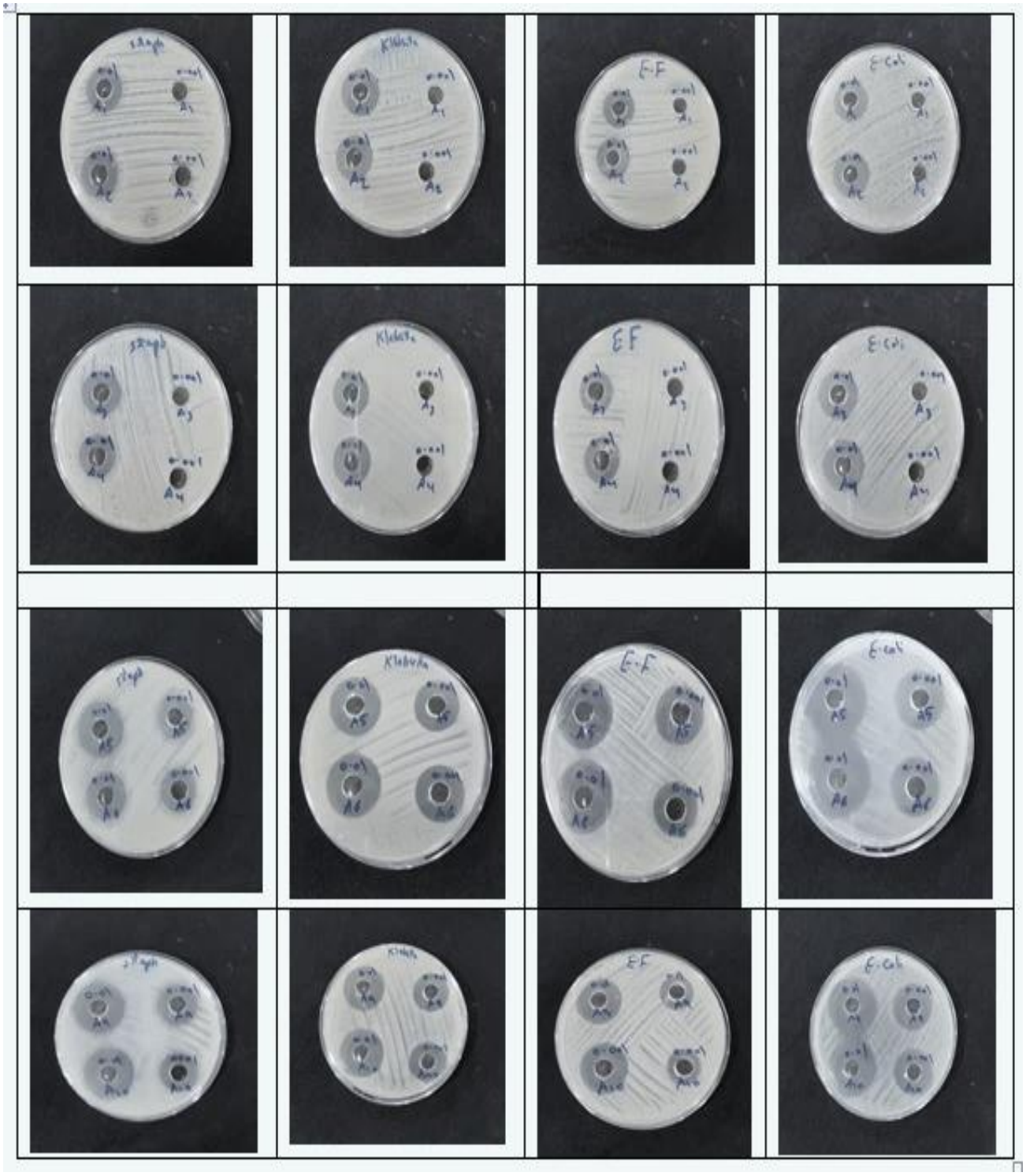


Photo. 1: bio—Evaluation of Bacteria

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