Article

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Synthesis, Identifications and Study Inhibitory anti-Cancer Activity for Some New Heterocyclic Compounds from Derivatives Coumarine

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Abstract

In this research paper, our work included the synthesis of some new heterocyclic organic derivatives compounds {penta, hexa, hepta} rings membered by using Schiff Base reaction methods. These cyclic derivatives have given good results, in anti-cancer Activity, and can be prepared there are compounds in three steps.

First step:-\ It involves the preparation of some heterocyclic penta-cyclic derivatives; it is contained from Imidazolidine (five ring members).

Second step:-\ It includes the preparation of some new heterocyclic hepta derivate containing from 1, 3- Oxazepine and Oxazapane (hepta ring saturated and unsaturated members)

Third step:-\ involved the study inhibitory of activity anticancer of some compounds synthesis from this line. The compounds were analyzed and characterized using spectrum photometers by {FT-IR, 1HNMR}

KEYWORD: **Synthesis, Heterocyclic derivatives, Schiff Base, anti -Cancer.**

INTRODCTIONY

Heterocyclic compounds are a very big family and have class of organic compounds is at one of heteroatom (i.e. atom than carbon) in the system cyclic general atoms. [(1).]

In fact, so many natural products and many drugs contain heterocyclic rings.

As the flowers and plans has gets many colors the heterocyclic compounds same things colors [(2)]

Heterocyclic compounds are given this name, because the ring contains one or more heteroatoms that do not belong to carbon atoms of the original rings [(3).]

Medicinal chemistry field, which has died on the classical branches of chemistry, in particular organic chemistry, physics, and some research of biological activity. In this study, the limited number of synthesis derivatives of these compounds provides a cornucopia for this chemical system, (90%) of newly man-factored medicines drugs including heterocyclic and it is the linkage between chemical and biological wild. At that much scientific insight, discovery, and application is taking place of the file, the structure products chemically. Once these compounds have therapeutically significant molecular sections, the pharmacophores. Most of these treatments are of the same category for the heterocyclic compounds play a vital role in the cyclic system chemical many, drugs have a positive effect on the ill human cells to take a successful path of treatment. [(4).] The cell line are vitro is a model system are lung and colorectal cancer cell lines are now the most important cells used in basic medical research and pharmacy discovery, so much valuable digital data results given by the cancer cells were prepared at the Stethoscope Health Hospital in cancer types. [(5)] Authenticated cancer cell lines preserve most of the research in the genetics field are most originate under the right setting and with all the necessary controls, [(6)] Comparing genomic data results from more types of cancer cell lines has verified these conclusions are observed examining tumor tissue equivalents cells in the { THE CANCER GENOME ATLAS (TCGA)} database[(7).] According to the latest statistics and recent global medical surveys, the second cause of death is cancer. The most difficult obstacle is the lack of a real response of the infected cells to the treatments, which leads to confusion in the drug-infected person [(8).] Many studies have practical proof the

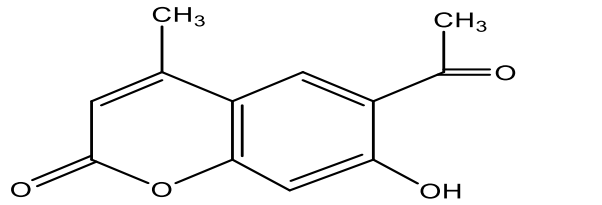
activity biological of Oxazapane and Imidazolidine compounds the possibility of obtaining new drugs that serve humanity and get rid of cancer types [9].

METHODS AND MATERIAL

The solid reactants and liquid solvents are that using in this research study were important from international companies such as {SEGMA, B.H.D, and FLUKA}. All reactions were observed completed by (TLC) (MERCK grad) thin layer chromatography Solvents are purified beforehand. The purified derivatives and Ethanol abs and Benzene dry mixture as mobile phase. The melting points were measured in open capillaries, with the help of (Stuart) melting point (SMP30, England) melting point apparatus uttered in Infrared spectra (FT-IR) were recorded on ShimadusSpectrophotometer by using (KBr pellets) and the are results uttered in the unit of (cm-1) (HNMR) spectra of the derivatives were recorded on Bruker (Avance III, Bruke{r 400-4000} MHz NMR) Spectrophotometer using TMS as an interior standard and the values results are showed in unit of a (ppm) in university of Basra

GENERAL PROCEDURES FOR SYNTHESIS OF

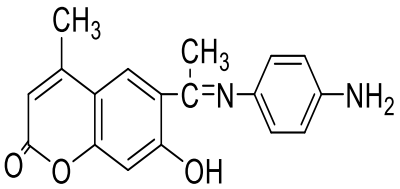
{(6-acetyl-7-hydroxy-4-methyl-2*H*-Coumarine -2-one. {(AA)} [10, 11, 12, 13]



6-acetyl-7-hydroxy-4-methyl-2*H*-chromen-2-one

We preparation the main compounds (AA) by reflux by taking weight (8.80gm 0.05mol) from 7-methyl-4-methyl Coumarine,dissolved in absolute ethanol (50ml) in glass flask with a capacity of (250ml) put mixture on magnetic stirrer to completed solubility , next that add the weight of acetic acid anhydride (6ml) . Than install the capacitor the reflux while (30hr), monitor the reaction used (TLC) and solvents (ethanol $_{\text{abs; benzene dry}}$ 1; 4) , used iodine to showing the result .The precipitate result found was filtered , washed and re - recrystallized form Ether . Physical properties of the product are listed in Table (1).

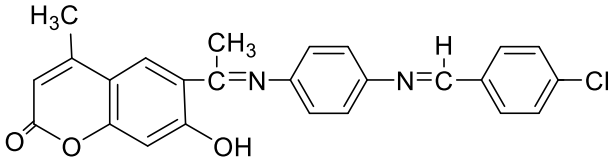
Synthesis by Schiff Base for compound {-6(1-((4-aminophnyl) imio) ethyl)-7-hydroxy-4-methyl-2H- Coumarine -2-one)} {(AA1)}



6-(1-((4-aminophenyl)imino)ethyl)-7-hydroxy-4-methyl-2H-chromen-2-one

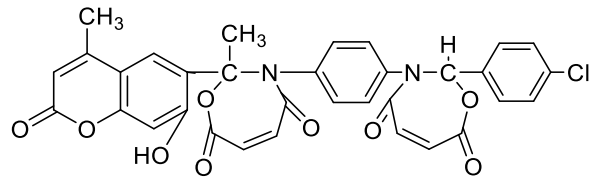
The preparation of the compounds (AA1) by reflux by taking weight (1.53gm 0.007mol) from (AA) compounds, dissolved in absolute ethanol (50ml) in a glass flask with a capacity of (250ml) put the mixture on a magnetic stirrer to complete solubility, next that add the weight of a p- Amino aniline (1.12gm 0.007mol). Then install the capacitor the reflux while (30hr), monitoring the reaction (TLC) and solvents (ethanol: benzene 1:4), using iodine to show. The precipitate product is dried and can filtered, washed, and re-recrystallized from Acetone. Physical properties of the product are listed in table (1)

(Synthesis of compound (-chlorophenyl) -4,7-diox-4,-dihy-1,3)) -oxazepin-3(2H)-yl)phenyl)-2-(7-hydroxy-4,6-dimethyl-2-oxo-2H-6-Couromen-6-yl)-2-methyl-2,3-dihydro-1,3-oxazepine-4,7-dione.)) {AA2}



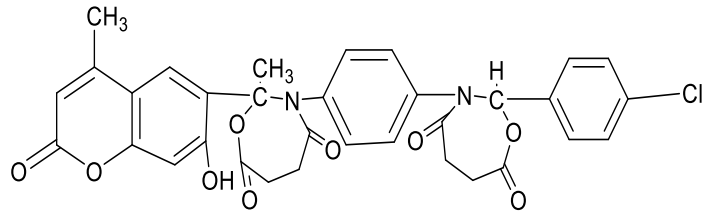
The preparation of the compounds (AA2) by reflux by taking weight (2.15gm 0.007mol) from (AA1) compounds, dissolved in absolute ethanol (50ml) in a glass flask with a capacity of (250ml) put mixture on a magnetic stirrer to complete solubility, next that add the weight of a P-chlorobenzldehyde (0.983gm 0.007mol). Then install the capacitor for the reflux while (30hr), monitor the reaction us (TLC) and solvents ((ethanol $_{abs}$: benzene $_{dry}$ 1:4), and use iodine to show. The precipitate product result found was filtered, washed, and recrystallized from Ether. The physical properties of the product are listed in table (1).

3)-4-)-2-)- Synthesis of compound (chlorophenyl)-4,7-dioxo-4,7-dihydro-1,3-oxazepin-3(2H)-4-yl)phenyl)-2-(7-hydroxy-4,6-dimethyl-2-oxo-2H-6l5-chromen-6-yl)-2-methyl-2,3-dihydro-1,3-oxazepine-4,7-dione{AA3}



The preparation the compounds (AA3) by reflux by taking weight (0.429gm 0.001mol) from (AA1) compounds ,dissolved in absolute ethanol (50ml) in glass flask with a capacity of (250ml) put mixture on magnetic stirrer to completed solubility , next that add the weight of a Maleic unhydered (0.196gm 0.002mol). Than install the capacitor the reflux while (30hr), monitor the reaction us (TLC) and solvents (ethanol $_{abs}$: benzene $_{dry}$ 1:4) , used iodine to show .The precipitate product dried and can filtered , washed and recrystallized form Toluene . Physical properties of the product are listed in table (1)

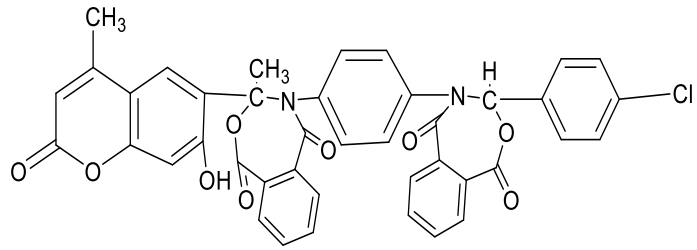
Synthesis of compound (chlorophenyl)-4,7-dioxo-4,7-dihydro-1,3-oxazepin-3(2H)-4-yl)phenyl)-2-(7-hydroxy-4,6-dimethyl-2-oxo-2H-6l5-chromen-6-yl)-2-methyl-2,3-dihydro-1,3-oxazepine-4,7-dione{AA4}



The preparation the compounds (AA4) by reflux by taking weight (0.429gm 0.001mol) from (AA1) compounds ,dissolved in absolute ethanol (50ml) in glass flask with a capacity of (250ml) put mixture on magnetic stirrer to completed solubility , next that add the weight of a Succinic unhydered (0.200gm 0.002mol). Than install the capacitor the reflux while (30hr), monitor the reaction us (TLC) and solvents(ethanol $_{abs}$: benzene $_{dry}$ 1:4) , used iodine to show .The precipitate product found was filtered , washed and re- recrystallized form Toluene, Physical properties of the product are listed in table (1).

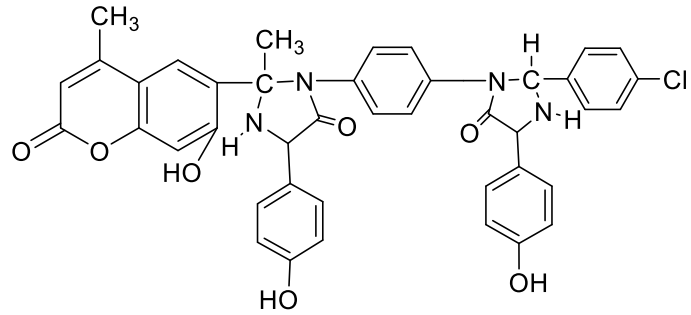
Synthesis of compound (chlorophenyl)-4,7-dioxo-4,7-dihydro-1,3-oxazepin-3(2H)-4-yl)phenyl)-2-(7-hydroxy-4,6-dimethyl-2-oxo-2H-6l5-chromen-6-yl)-

2-methyl-2,3-dihydro-1,3-oxazepine-4,7-dione{AA5}

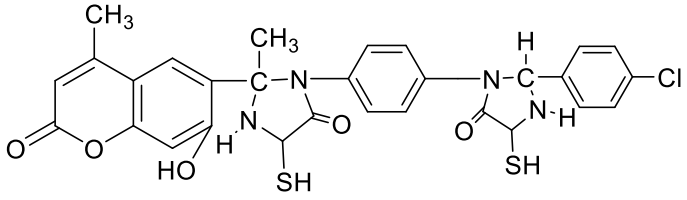


The preparation the compounds (AA5) by reflux by taking weigh (0.480gm 0.001mol) from (AA1) compounds ,dissolved in absolute ethanol (50ml) in glass flask with a capacity of (250ml) put mixture on magnetic stirrer to completed solubility , next that add the weight of a Phathalic unhydered (0.298gm 0.002mol). Than install the capacitor the reflux while (30hr), monitor the reaction us (TLC) and solvents((ethanol $_{abs}$: benzene $_{dry}$ 1:4) , used iodine to showing the dot (ethanol $_{abs}$: benzene $_{dry}$ e to show .The result of reaction work dried and can filtered , washed and recrystallized form Ether , physical properties of the product are listed in table(1)

Synthesis of compound (chlorophenyl)-4-(4-hydroxyphenyl)-5-oxoimidazolidin-1-yl) methyl) phenyl)-2-(7-hydroxy-4-methyl-2-oxo-2H-chromen-6-yl)-5-(4-hydroxyphenyl)-2-methylimidazolidin-4-one {AA6}



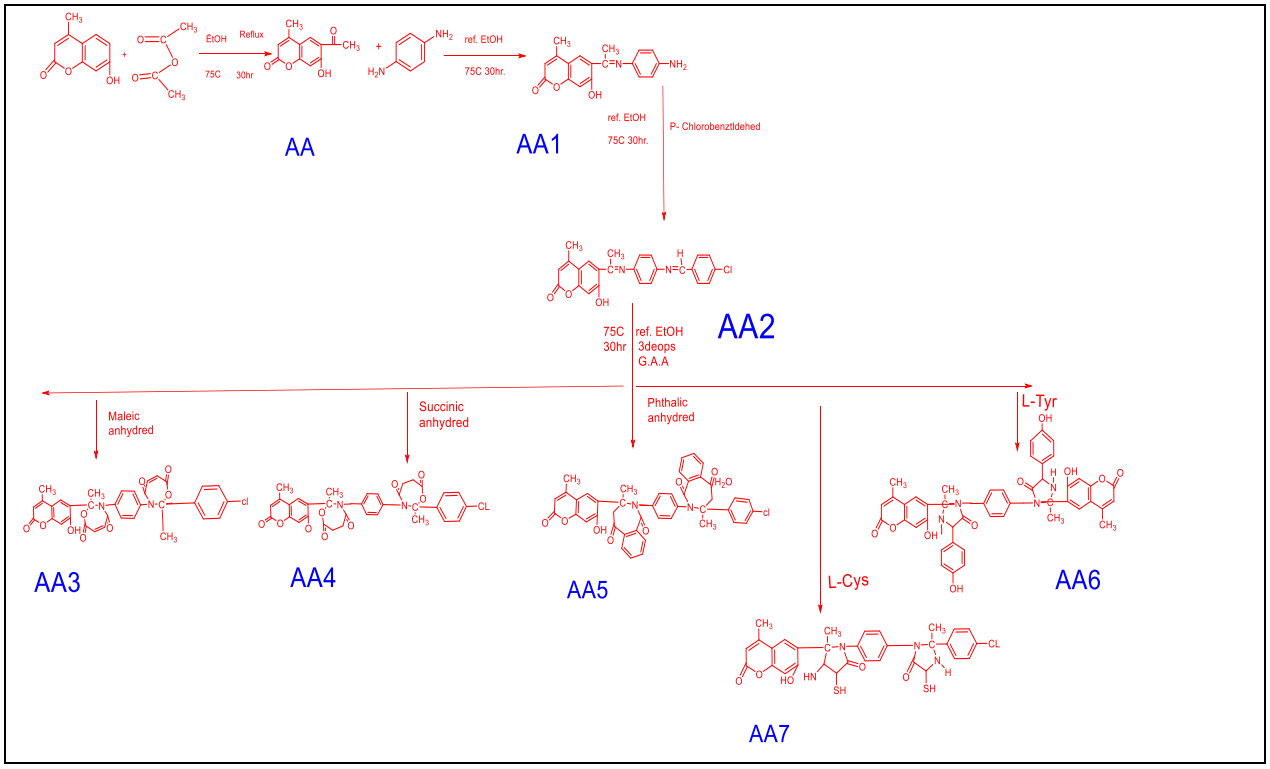
-Synthesis of compound (chlorophenyl)-4-mercapto-5-oxoimidazolidin-1-yl) methyl)phenyl)-2-(7-hydroxy-4-methyl-2-oxo-2H-chromen-6-yl)-5-mercapto-2-methylimidazolidin-4-one{ AA7}



The preparation this compounds (AA7) by reflux by taking weight (0.480gm 0 l) from (AA1) compounds , dissolved in absolute ethanol (50ml) in a glass flask with a capacity of (250ml) putting mixture on a magnetic stirrer to complete solubility, next that add the weight of an Amino acid{ L-Cytosine} (0.480gm 0,002 mol). Then install the capacitor for the reflux (30hr), monitor the reaction (TLC) and solvents (ethanol $_{abs}$: benzene $_{dry}$ 1:4) , and use iodine to show. The precipitate results product found was filtered, washed, and recrystallized from Ether. These physical properties of the product are listed in table (1).

Inhibitory activity of anti-cancer assay

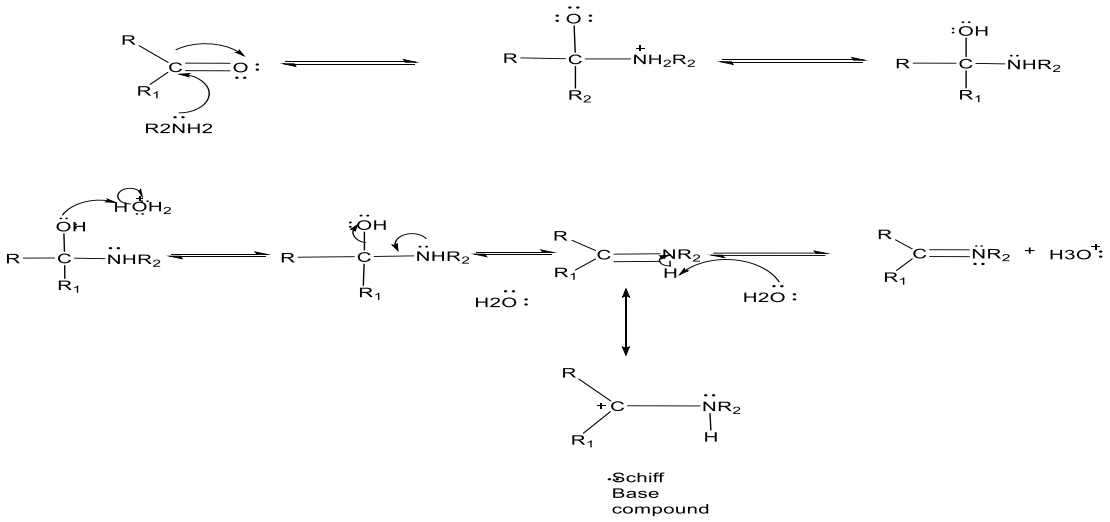
The inhibitory activity of anti-cancer of heterocyclic compounds { AA, AA1} have good results for the study Colorectal Cancer (CaCo-2), this type of Cancer is more common than another type, so that this study taking important point for it to show the differences results between clean human cells (HdFn) and infected cells and using these compounds in range concentrated between (500-31.1µg\ml) under (37ºC) and (24hr) times , The fact which this study gives studies contributes ideas to the synthesis and manufacture of successful drugs from derivatives of these modern compounds [14,15] ,tests on infected and healthy cells for these therapeutic derivatives have shown that they do not negatively affect healthy cells at rather have all the effect on infected cells [16,17] , using of (MTT) dye facilitates clarification and study and makes the results more realistic and credible to the researcher. There are tables and pictures and data shown this study and results.



Scheme (1) –Pathway suggests compounds prepared from this research study

Results & discussion

The research proofs , could synthesis and identifications of these derivatives , has get excellent results on compounds prepared for the first time , all these derivatives comes from re compound action methods Schiff Base methods are important intermediate products , they have many differences drug pharmacy field and inhibitorical activity ,in this research can showing two ways in this research ,the first one it's about prepared and identificated some new derivatives compounds form main Coumarine derived (7-Hydroxy -4-methyl Coumarine) with used {FT-IR and H^1MR}and study the physical properties, with yield for them products .



Scheme
(-2) Mechanism of Schiff Base

Table (- 1-) Physical properties of synthesized derivatives

NO	M.F	M.Wt	M .p C	Color	Time	Name of compound	Rf	Yield %
AA	$C_{12}H_{10}O_4$	218	176-178	White	30 hr	**(6-acetyl-7-hydroxy-4-methyl-2*H*-Coumarine -2-one.**	0.91	90
AA1	$C_{18}H_{16}N_2O_3$	308	189 - 190	White	30 hr	**{-6(1-((4-aminophnyl) imio) ethyl)-7-hydroxy-4-methyl-2H- Coumarine -2-one)}**	0.95	80
AA2	$C2_7$ H_{24}CL N_2O_3	459	190 - 192	Grey	30hr	**(-chlorophenyl)-4,7-diox-4,-dihy-1,3)) -oxazepin-3(2H)-yl)phenyl)-2-(7-hydroxy-4,6-dimethyl-2-oxo-2H-6-Couromen-6-yl)-2-methyl-2,3-dihydro-1,3-oxazepine-4,7-dione.))**	0.78	95
AA3	$C_{34}H_{26}$ CL N_2 O_9	642	177 – 179	Yellowish	30 hr	**Synthesis of -)- 2-)-4)-3 compound (chlorophenyl)-4,7-dioxo-4,7-dihydro-1,3-oxazepin-3(2H)-4-yl)phenyl)-2-(7-hydroxy-4,6-dimethyl-2-oxo-2H-6l5-chromen-6-yl)-2-methyl-2,3-dihydro-1,3-oxazepine-4,7-dione**	0.89	90

AA4	$C_{34}H_{25}$ CL N_3O_4	641	175 - 177	Light yellow	30hr	**(chlorophenyl)-4,7-dioxo-4,7-dihydro-1,3-oxazepin-3(2H)-4-yl)phenyl)-2-(7-hydroxy-4,6-dimethyl-2-oxo-2H-6l5-chromen-6-yl)-2-methyl-2,3-dihydro-1,3-oxazepine-4,7-dione**	0. 97	70
AA5	$C_{41}H_{27}$ CL N_2 O_9	727	178 - 180	Light yellow	30 hr	**(chlorophenyl)-4,7-dioxo-4,7-dihydro-1,3-oxazepin-3(2H)-4-yl)phenyl)-2-(7-hydroxy-4,6-dimethyl-2-oxo-2H-6l5-chromen-6-yl)-2-methyl-2,3-dihydro-1,3-oxazepine-4,7-dione**	0. 77	88
AA6	C_{30} $H2_7$CL N_4 O_5 S_2	623	197 – 200	Black	30 hr	**(chlorophenyl)-4-(4-hydroxyphenyl)-5-oxoimidazolidin-1-yl) methyl) phenyl)-2-(7-hydroxy-4-methyl-2-oxo-2H-chromen-6-yl)-5-(4-hydroxyphenyl)-2-methylimidazolidin-4-one {AA6}**	0. 88	67
AA7	$C_{42}H_{35}$ CL N_4 O_7	734	198 - 200	Black	30 hr	**(chlorophenyl)-4-mercapto-5-oxoimidazolidin-1-yl)methyl)phenyl)-2-(7-hydroxy-4-methyl-2-oxo-2H-chromen-6-yl)-5-mercapto-2-methylimidazolidin-4-one{ AA7}**	0. 88	76

Results and discussion

The assignment of FT-IR for compounds [18, 19, and 20]

FT-IR spectrum of (AA) appeared absorption band

. of ,(OH) (3155.54cm^{-1}) (CH) aromatic 2850 cm $^{-1}$ (-CH) aliphatic (2650 cm^{-1} ,), (C=O) ester (1683.88 cm $^{-1}$),(C=C) (1452.40 cm $^{-1}$),(C-O) 1062.78 cm $^{-1}$

.The { FT-IR} spectrum derivative (AA1) appeared absorption band of free amine group (NH2) which was in main compounds at (NH2)(3266.70-3069.90) cm $^{-1}$,(OH) 3155.54cm $^{-1}$

(C-H) aromatic(3062.96cm $^{-1}$) (C-H) aliphatic(2908.56 cm^{-1} ,) ,(C=N)1620 cm^{-1} , (C=O) ester (1703.14 cm $^{-1}$),(C=C) at 1508.33 cm $^{-1}$,(C-O) (1240.23 cm $^{-1}$),(C-H) bending at 1463.97 cm $^{-1}$,(C-Cl) at 740.67 cm $^{-1}$. The rest of the vibrations of the beans to these effective groups of the prepared compounds are shown in the following table -2.

Comp NO.	Lactone υ (C=O)cm^{-1}	Lactam C=O) cm^{-1} υ	Aromatic υ(C=C)	Aromatic υ (C-H) cm^{-1}	Aliphatic υ (C-H) cm^{-1}	(OH) υ cm^{1-}	C-N)υcm^{-1}	C-O) υcm^{-1}
AA3	1685.79	1593.20	1514.12	3142.04	2596.19	3354.21	1381.03	1139.93
AA4	1705.07	1620.21	1510.26	2908.65	2360.87	3356.14	1384.89	1228.88
AA5	1708.93	1616.35	1508.33	3068.75	2360.87	3439.08	1388.75	1240.23

Comp NO.	OH)cm^{-1} υ (	υ (C-H) aromatic cm^{-1}	υ (C-H) aliphatic cm^{-1}	C=O) Ketone υ(cm^{-1}	O-C=O) ester υ (cm^{-1}	N-C=Oamide cm^{-1} υ(	N-H) (cm^{-1} υ	C-O) cm^{1-} υ(	C=C) alkene cm^{-1} υ(	C-CL) (cm^{-1} υ
AA6	3354.21	3057.17	2908.65	1705.07	1618.28	1508.41	3288.70	1141.88	1486.76	738.74
AA7	3402.43	3163.28	2933.73	1681-93	1598.99	1510.26	3200.70	1134.14	1448.54	750.31

Table (-2-) Vibrations for prepared compounds.

HNMR spectra for derivatives

The H^{1} –NMR spectrum of compound (AA) exhibited single at (2.5ppm) for proton solvent DMSO-d6 {di methyl sulfoxide} , and appeared single for acetyl group at (2ppm) in main compound, and exhibited single for methyl group to new derived at (2.3ppm) ,with single at (6ppm) belong to alkene ring Coumarine ,with exhibited single for hydroxyl group at (10ppm) ,and hydroxyl group for aromatic ring at (6.7ppm).

The H^{1} –NMR spectrum of compound (AA1) exhibited single at (2.7ppm) for proton solvent DMSO-d6 {di methyl sulfoxide} ,and appeared single for acetyl group at (2ppm) in main compound ,and exhibited single for methyl group to new

derived at (2.3ppm) ,with single at (5.5ppm) belong to alkene ring Coumarine ,with exhibited single for hydroxyl group at (10ppm) ,and hydroxyl group for aromatic ring at (6.7 -7.6ppm)., and exhibited single foe amine proton at(6.3ppm).

The H^1 –NMR spectrum of compound (AA2) exhibited single at (2.5ppm) for proton solvent DMSO-d6 {di methyl sulfoxide} ,and appeared single for acetyl group at (2ppm) in main compound ,and exhibited single for methyl group to new derived at (2.3ppm) ,with single at (6ppm) belong to alkene ring Coumarine ,with exhibited single for hydroxyl group at (10ppm) ,and hydroxyl group for aromatic ring at (6.7ppm).

The H^1 –NMR spectrum of compound (AA3) exhibited single at (2.5ppm) for proton solvent DMSO-d6 {di methyl sulfoxide} ,and appeared single for acetyl group at (2ppm) in main compound ,and exhibited single for methyl group to new derived at (2.3ppm) ,with single at (6ppm) belong to alkene ring Coumarine ,with exhibited single for hydroxyl group at (10ppm) ,and hydroxyl group for aromatic ring at (6.7ppm).

The H^1 –NMR spectrum of compound (AA4) exhibited single at (2.7ppm) for proton solvent DMSO-d6 {di methyl sulfoxide} ,and appeared single for acetyl group at (2ppm) in main compound ,and exhibited single for methyl group to new derived at (2.3ppm) ,with single at (5.5ppm) belong to alkene ring Coumarine ,with exhibited single for hydroxyl group at (10ppm) ,and hydroxyl group for aromatic ring at (6.7 -7.6ppm)., and exhibited single foe amine proton at(6.3ppm).

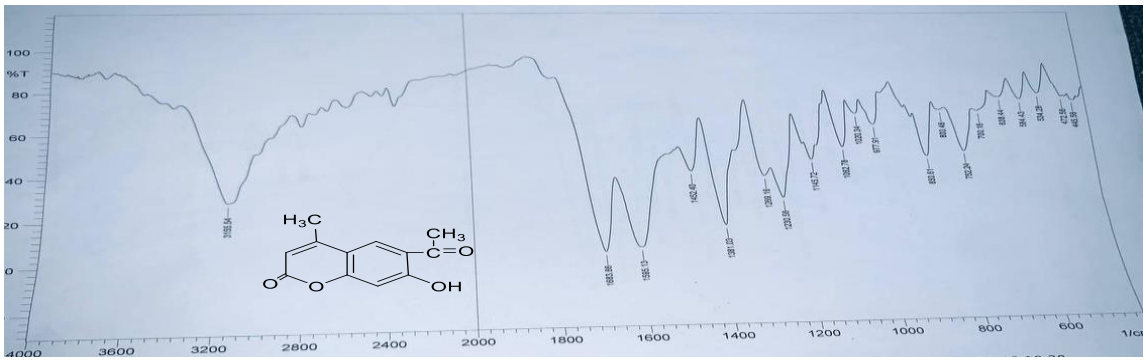
The H^1 –NMR spectrum of compound (AA5) exhibited single at (2.7ppm) for proton solvent DMSO-d6 {di methyl sulfoxide} ,and appeared single for acetyl group at (2ppm) in main compound ,and exhibited single for methyl group to new derived at (2.3ppm) ,with single at (5.5ppm) belong to alkene ring Coumarine ,with exhibited single for hydroxyl group at (10ppm) ,and hydroxyl group for aromatic ring at (6.7 -7.6ppm)., and exhibited single foe amine proton at(6.3ppm)

The H^1 –NMR spectrum of compound (AA6) exhibited single at (2.7ppm) for proton solvent DMSO-d6 {di methyl sulfoxide} ,and appeared single for acetyl group at (2ppm) in main compound ,and exhibited single for methyl group to new derived at (2.3ppm) ,with single at (5.5ppm) belong to alkene ring Coumarine

,with exhibited single for hydroxyl group at (10ppm) ,and hydroxyl group for aromatic ring at (7.9ppm)., and exhibited single foe amine proton at(4.6-7ppm).

Biological activity

The development of inhibitory of anti-Cancer for two derivatives compounds prepared in this research have a specially importance in the treatments of effective colorectal Cancer (CaCo-2) [21] . The important results that the effectiveness of this study which two both best in the derivatives{ (AA) &(AA1)} , can considered them involved to organic heterocyclic rings compounds they have acetate same and amine groups , so these compounds showed high effective in low concentration between {(31.1 -500) µg\ml}. The results also showed that these compounds are effectively. In this study used (MTT) test {3-(4, 5) –dimethyl thiazol-2yl) -2,5dimethyl tetrazolium bromide} was chosen to examine cell vitality on infected cells and is very safe for healthy cells. The tables below show the mechanism of the final results of the test using concentrations from the highest value, which is {(500 – 31.1) µg\ml} found that what is known as the half inhibitory concentration *(IC50*) In the case of the derivative{ AA}, the descriptive inhibitory concentration for infected cells was(CaCo-2 141.1 gu/ml, while for healthy cells (HdFn=279.gu/ml) and for{ AA1} for infected cells it was equal to(CaCo-2= 122.6 gµ\ml) and for healthy cells it was(HdFn= 176.2.gµ\ml) These are promising results as they gave a good response to the infected cells to the derivative and did not affect Healthy cells



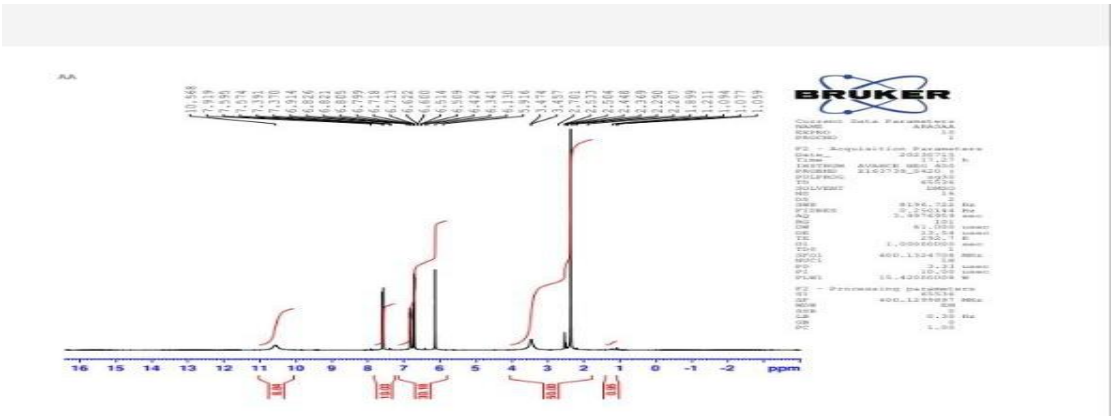
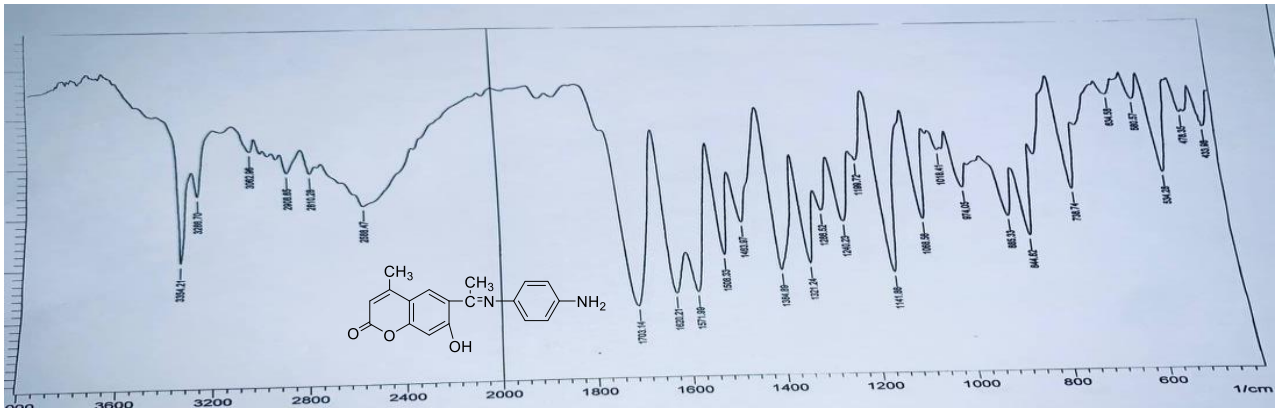


Figure (3) HNMR of{AA}



Figure(5) FT-IR of {AA1}

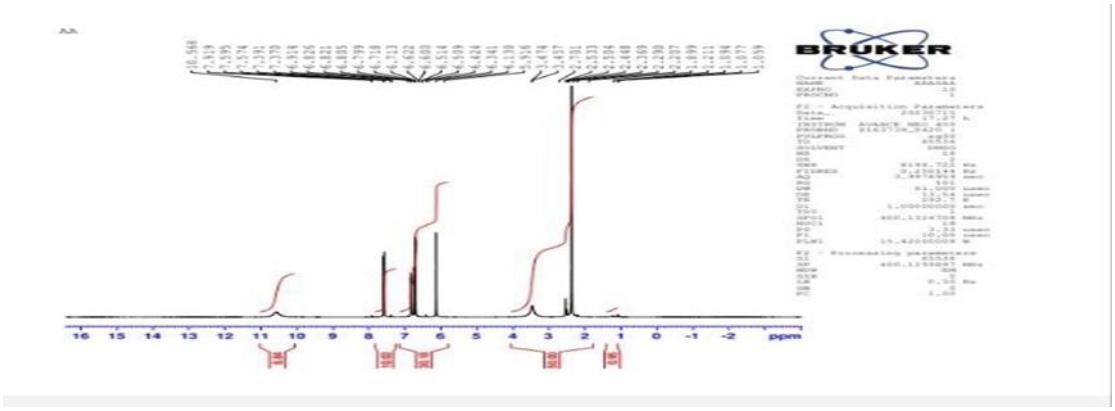


Figure (6) HNMR of {AA1}

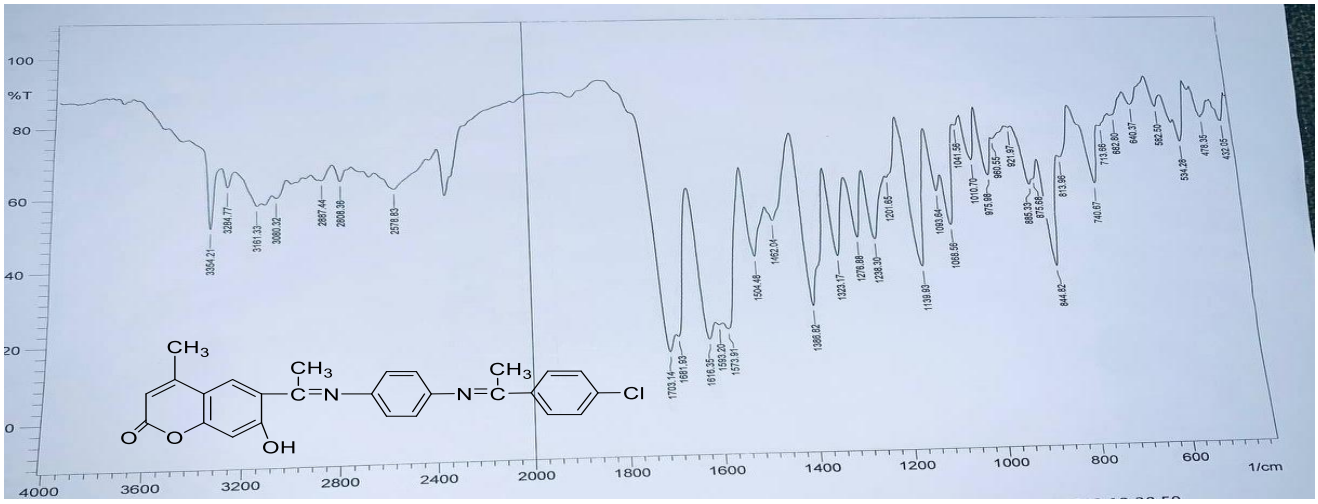


Figure (7) FT-IR of {AA3}

Figure (6) FT-IR of {AA2}

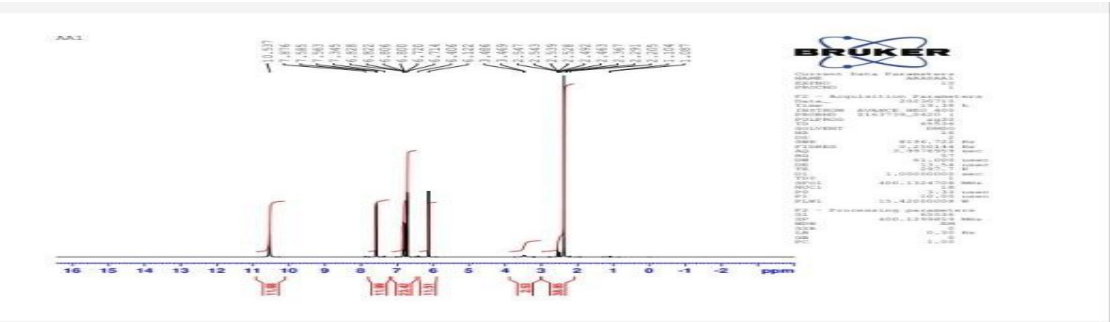


Figure (7) HNMR of {AA2}

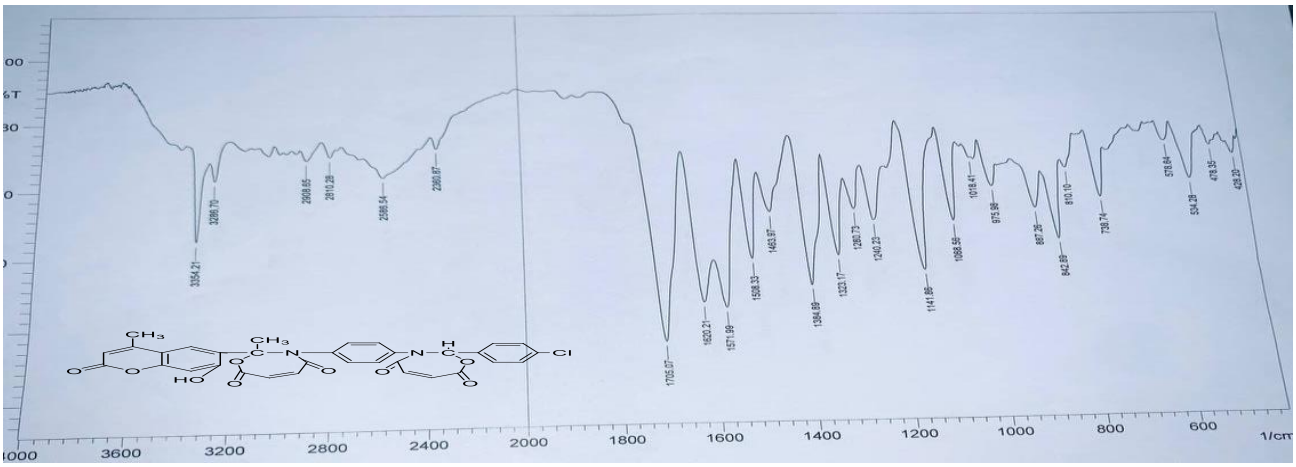


Figure (8) FT-IR of {AA3}

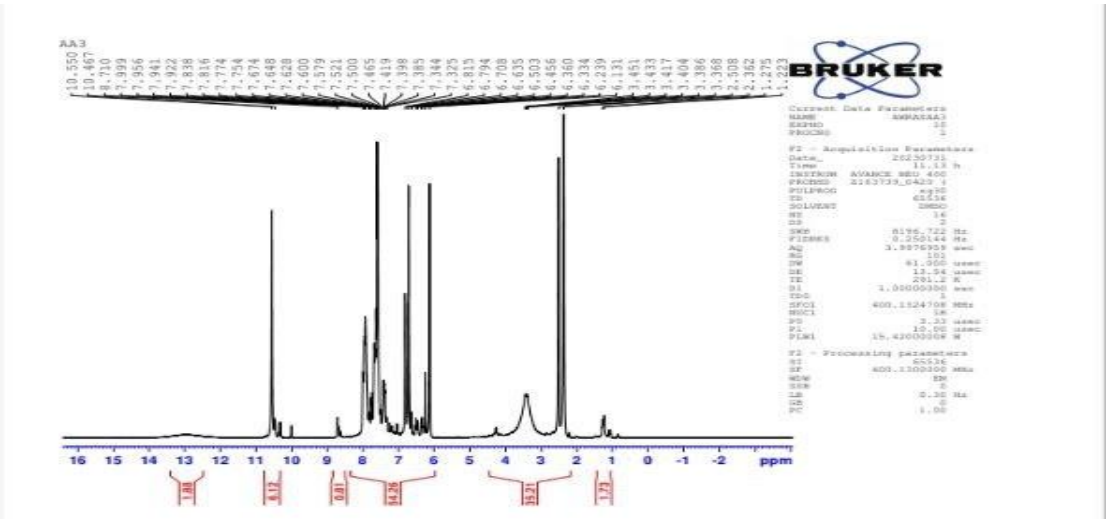


Figure (9) HNMR of {AA3}

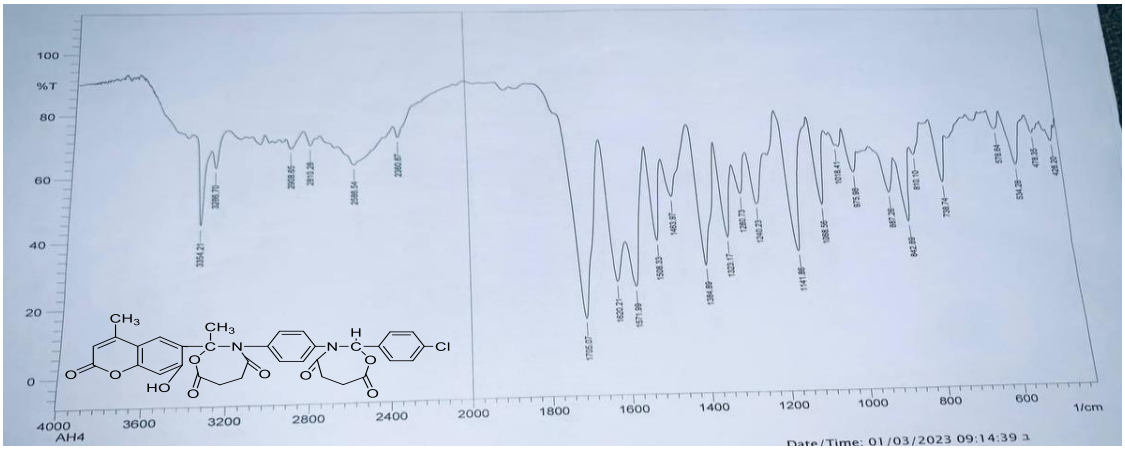


Figure (10) FT-IR of {AA4}

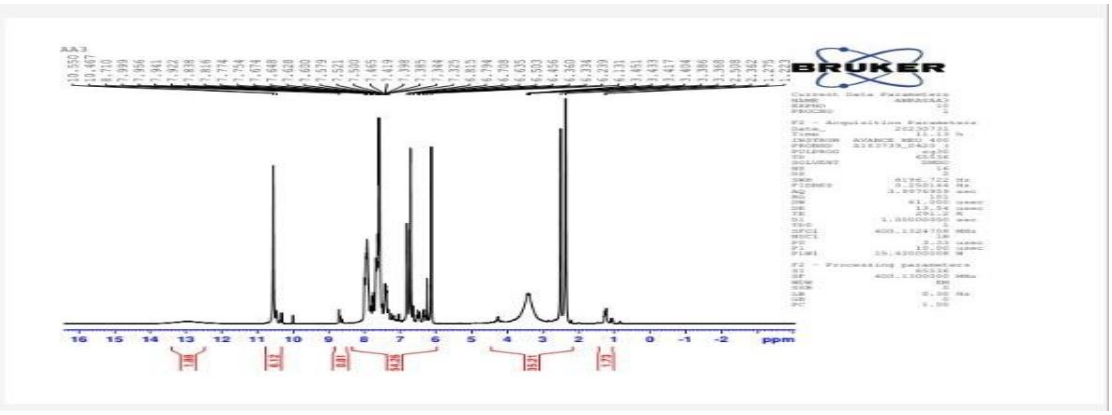
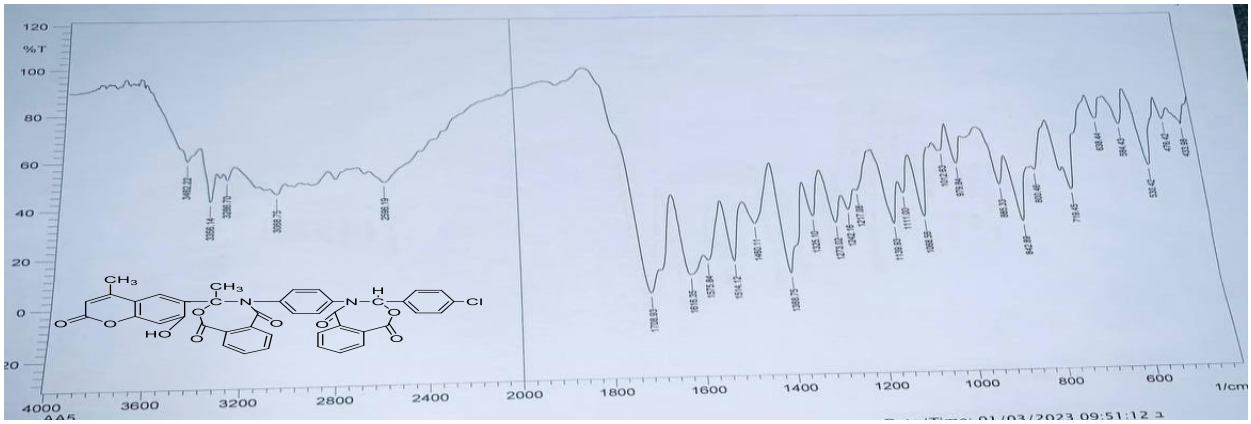


Figure (11) HNMR of {AA4}



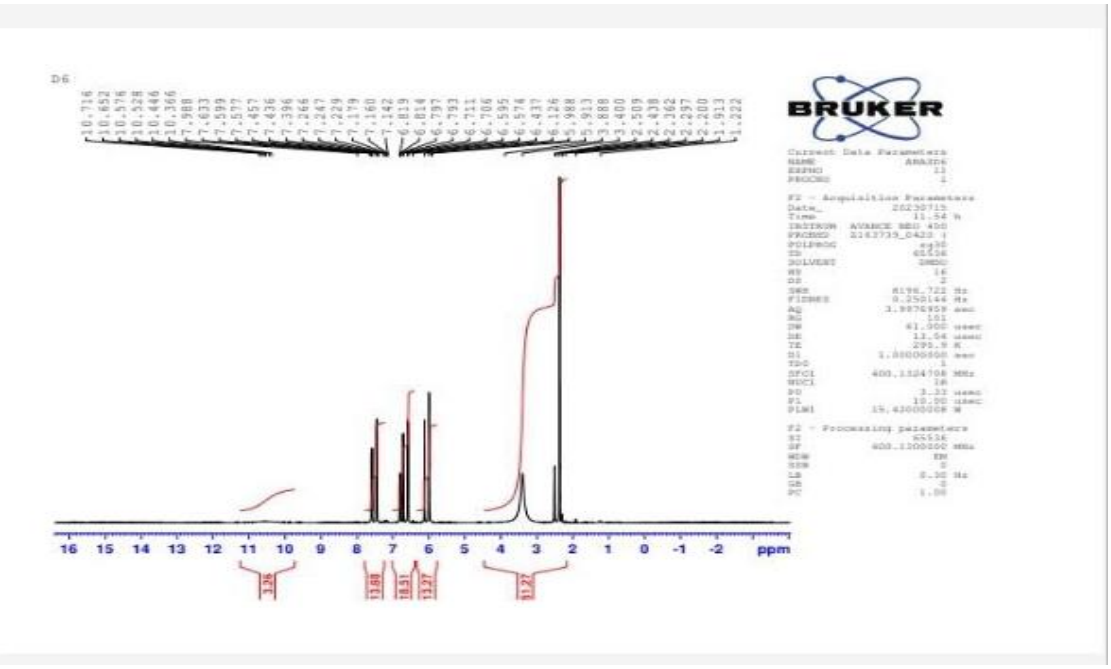


Figure (13) HNMR of {AA5}

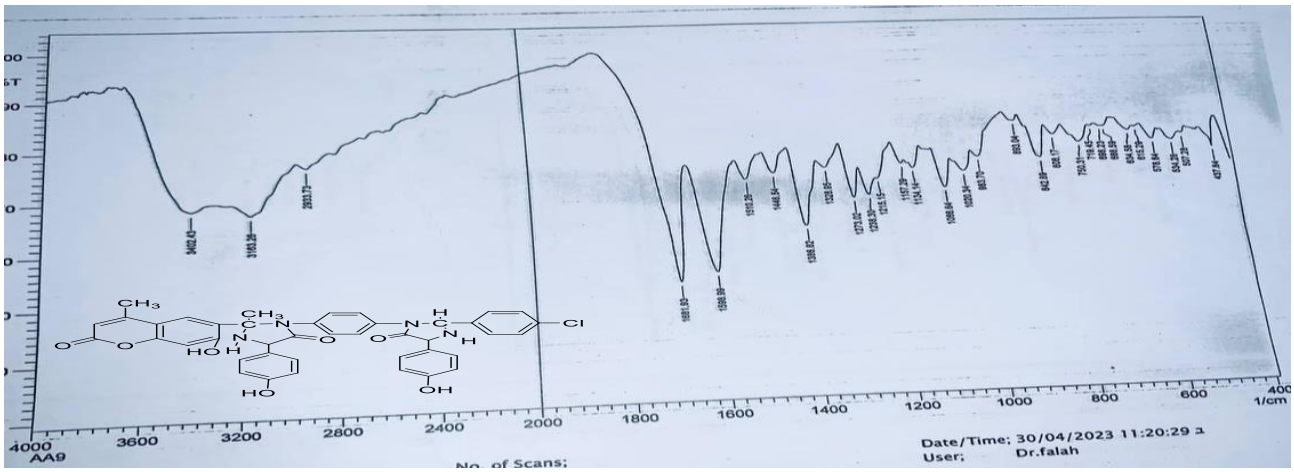


Figure (14) FT-IR of {AA6}

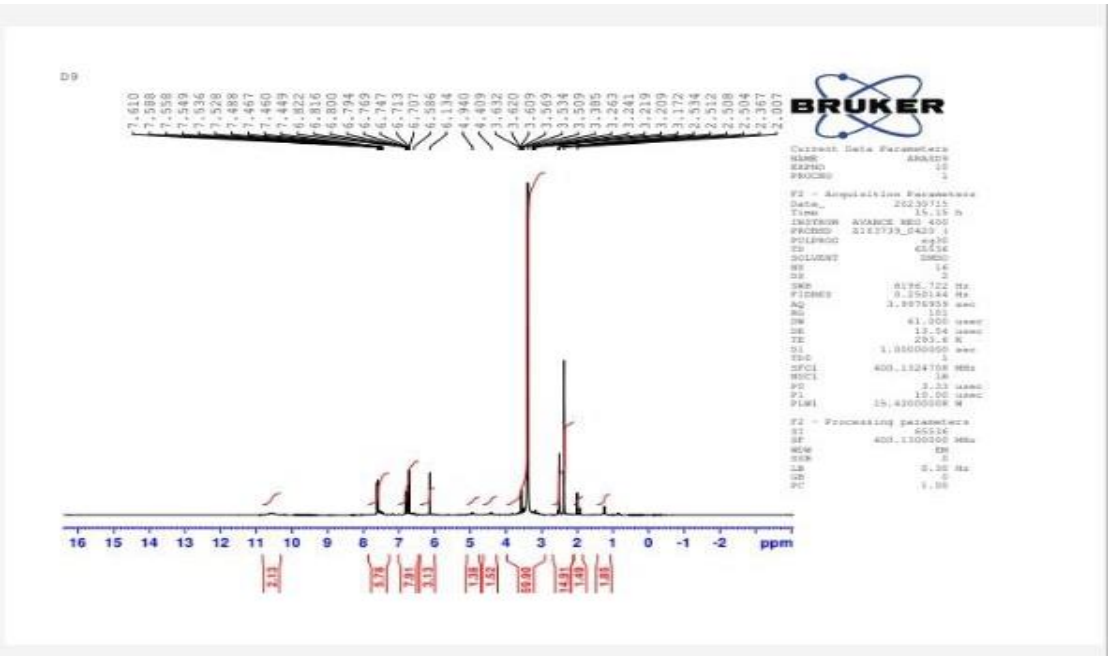


Figure (15) HNMR of {AA6}

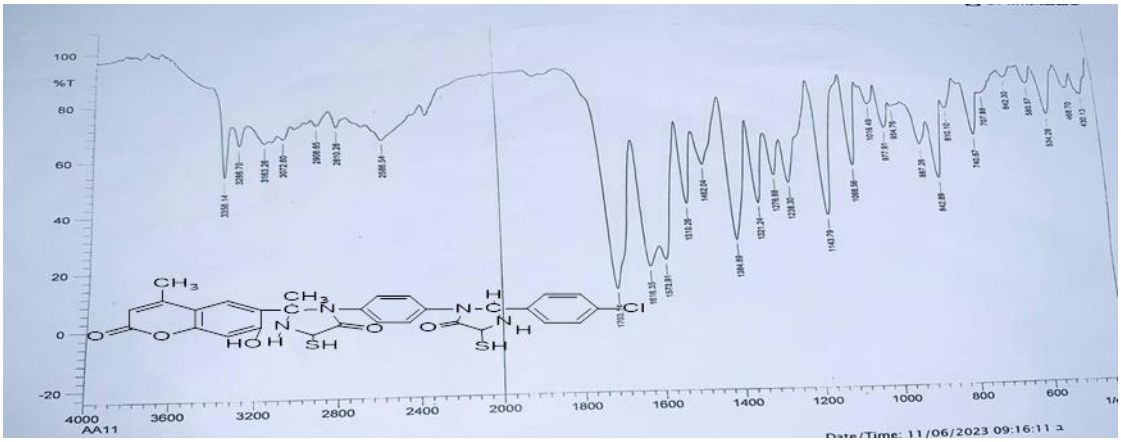


Figure (`16) FT-IR OF {AA7}

Table-3- the effect of com.{AA} on (CaCo-2) line and (HdFn) for same concentrations with using (MTT) under time (24hr) and (37ºC)

Conc. µg\ml	Inhibition%(HdFn) cell line	Inhibition%(CaCo-2) cell line
500	26.852	60.031
250	15.977	50.231
125	7.716	29.205
62.2	3.555	10.262
31.1	3.704	99.322
IC_{50}= 297		IC_{50}=141.7

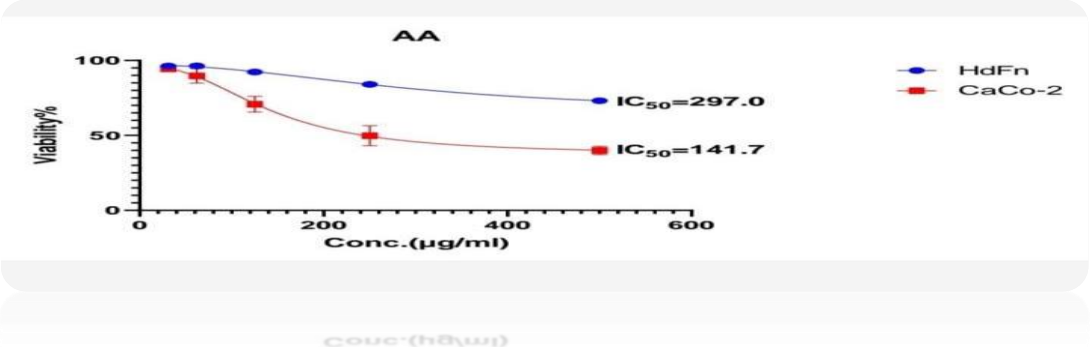


Figure (11) the relationship between the percentage of inhibition healthy (HdFn) and infected (CaCo-2) cells for com. {AA}

Table (-4-) statistical values for (CaCo-2) for com {AA}.

Does (µg\ml)	Mean	SD	No. of Values
500	39.969	2.754	3
250	49.768	6.655	3
125	70.795	5.264	3
62.2	89.737	4.823	3

31.1	**94.367**	**0.678**	**3**
Total	**344.636**	**20.174**	**15**

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Table (-5-) the effect of com.{AA1} for (CaCo-2) line and (HdFn) for same concentrations with using (MTT) under time (24hr) and (37ºC)

Conc. µg\ml	**Inhibition%(HdFn) cell line**	**Inhibition%(CaCo-2) cell line**
500	**32.381**	**51.351**
250	**26.929**	**93.043**
125	**22.145**	**26.081**
62.2	**17.246**	**12.963**
31.1	**6.674**	**6.482**
IC $_{50}$= 176.2		***IC $_{50}$=122.6***

Table (-6-) statistical values for (CaCo-2) for com {AA1}.

Does (µg\ml)	Mean	SD	No. of Values
500	**48.649**	**0.481**	**3**
250	**60.957**	**2.431**	**3**
125	**73.919**	**1.342**	**3**
62.2	**87.037**	**3.062**	**3**
31.1	**93.518**	**0.417**	**3**
Total	**364.081**	**7.733**	**15**

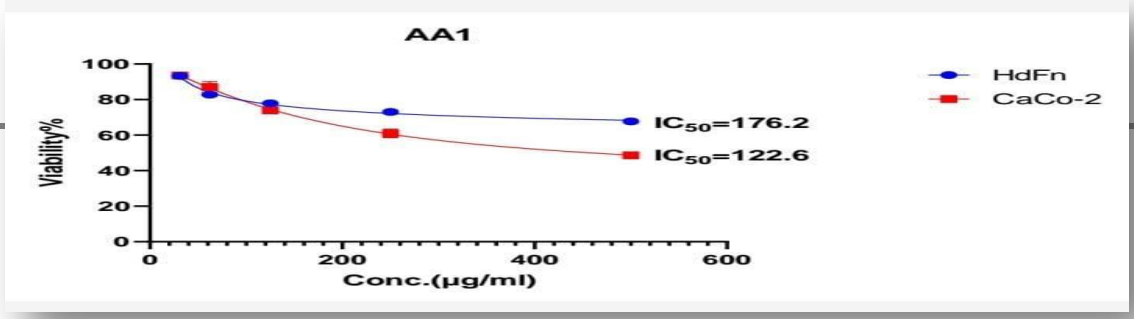

Figure (12) the relationship between the percentage of inhibition healthy (HdFn) and infected (CaCo-2) cells for com. {AA1}.

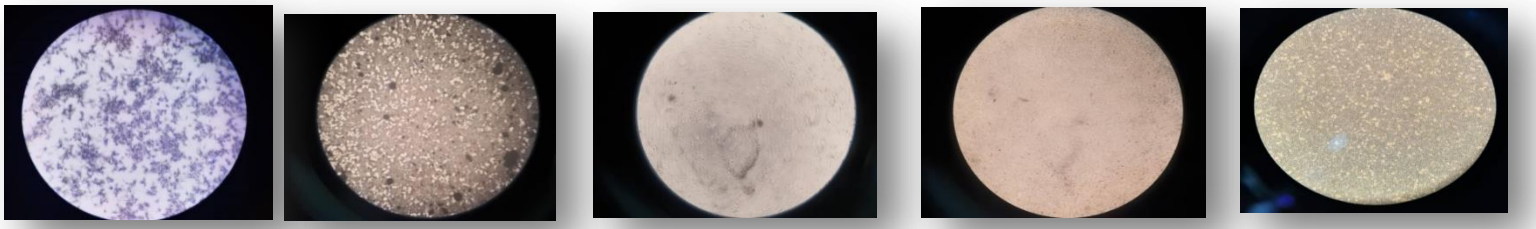

Figure (13) Cancer cells are treated {AA} at different concentrations after adding (MTT).

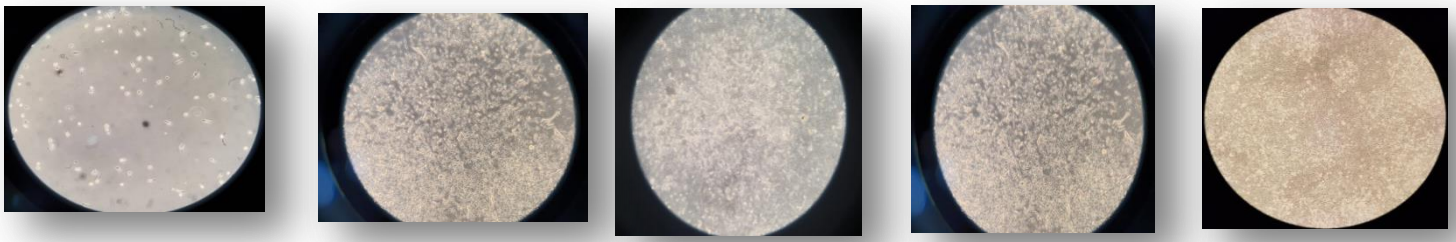

Figure (14) Cancer cells were treated with {AA1} at different concentrations after adding (MTT).

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