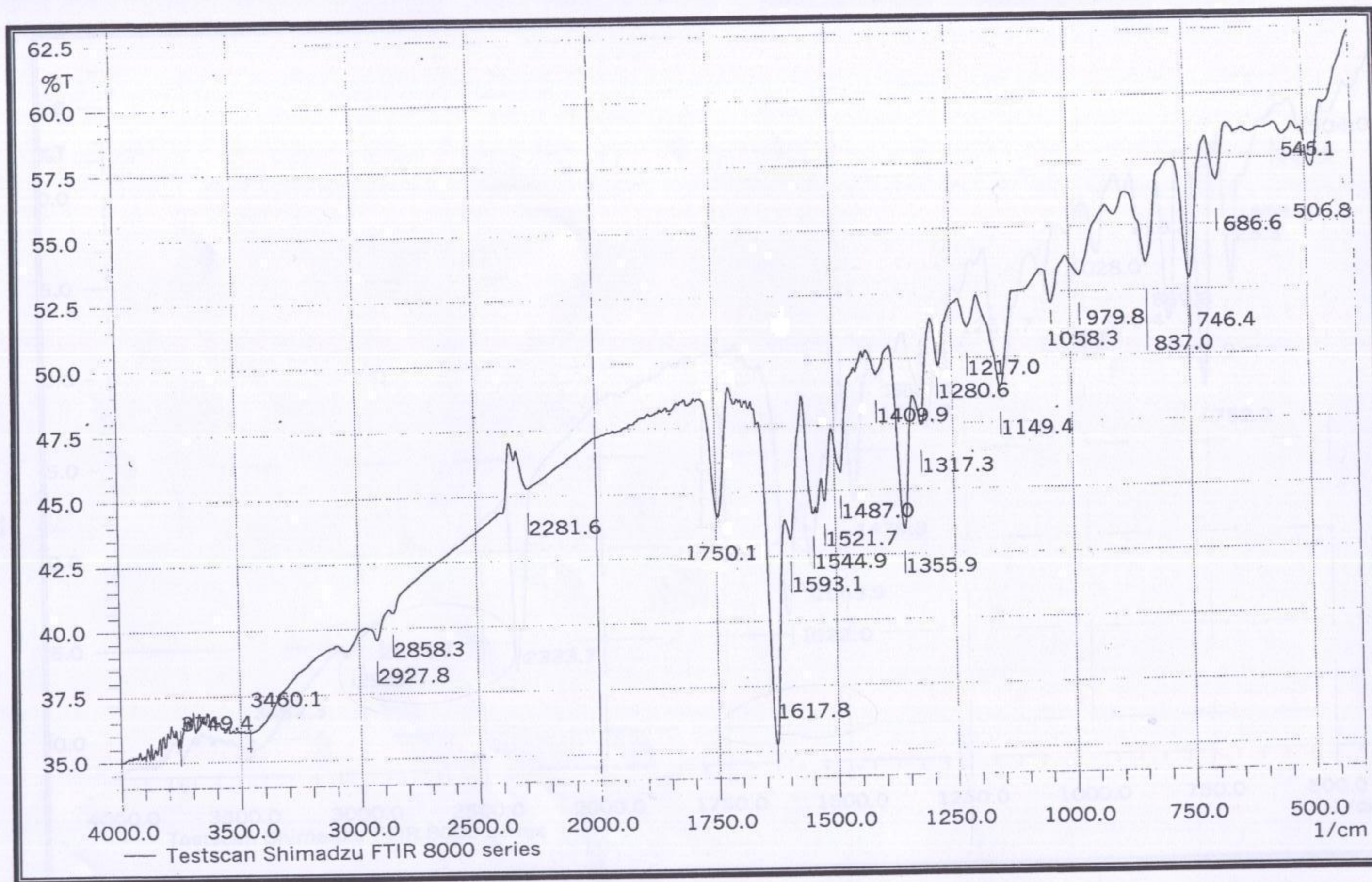
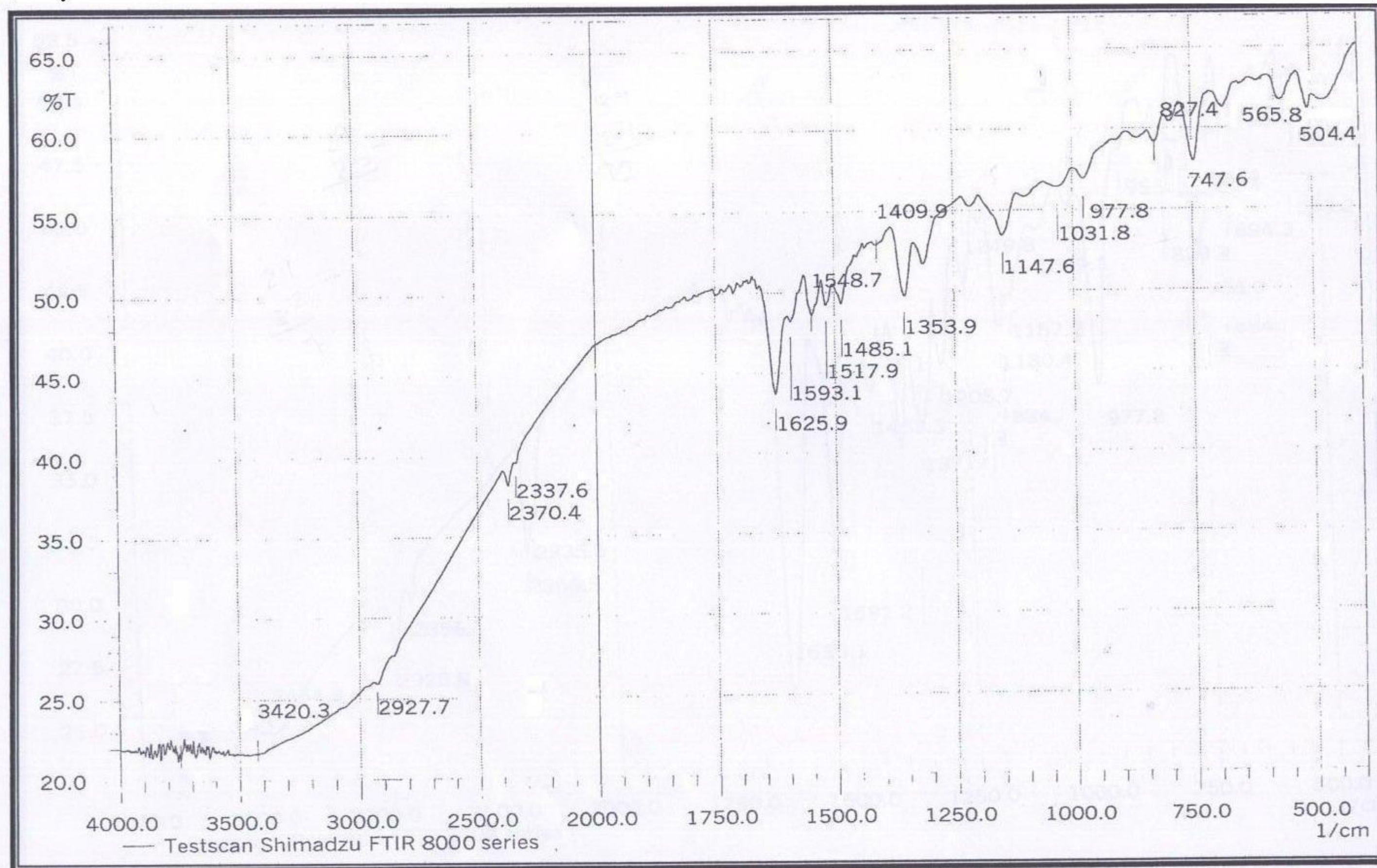


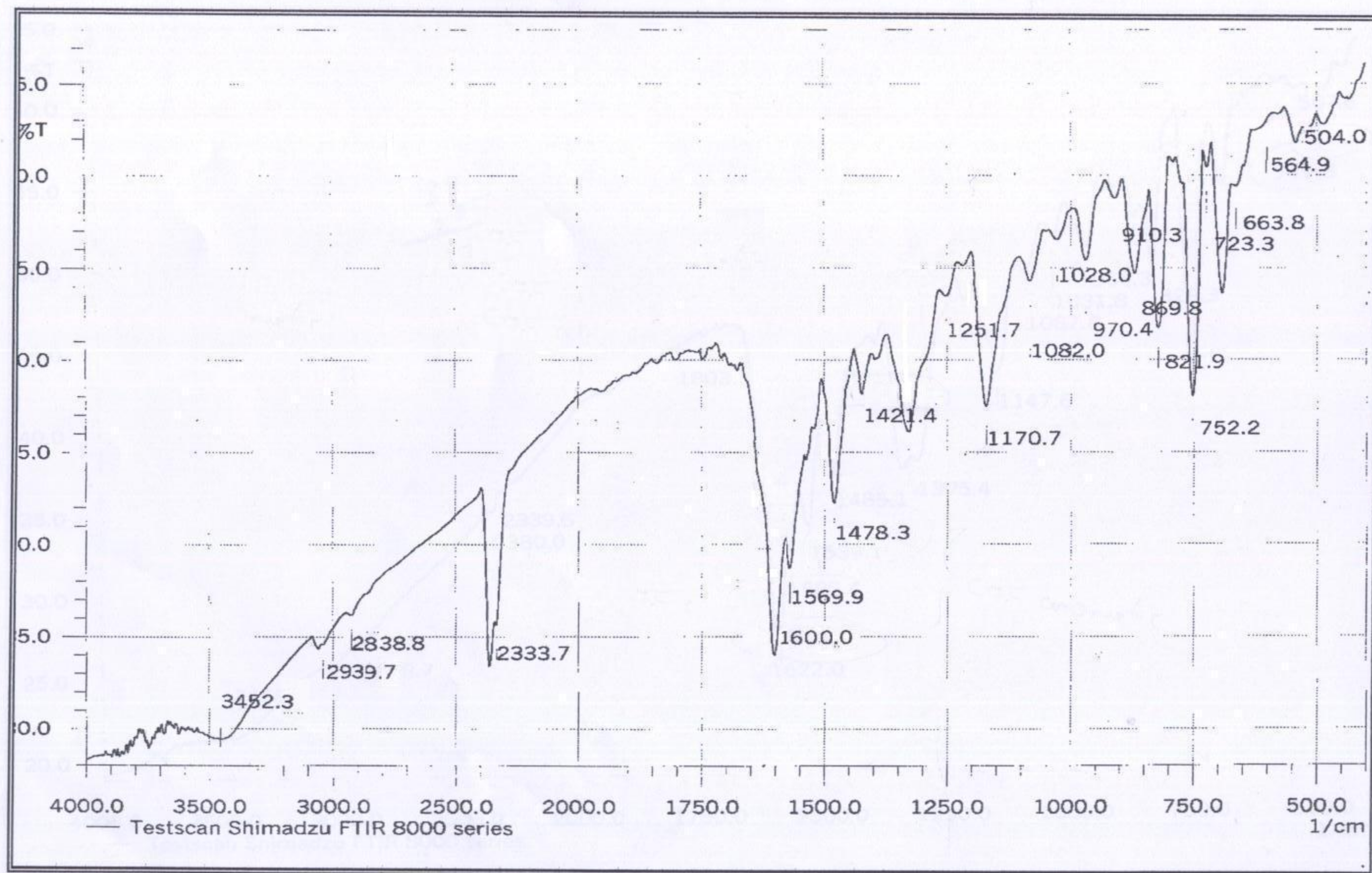
Fig(3-6) FT-IR spectra of Complex A(II)



Fig(3-7) FT-IR spectra of Complex A(III)



Fig(3-8) FT-IR spectra of Complex A(III)



Fig(3-5) FT-IR spectra of Complex A(I)

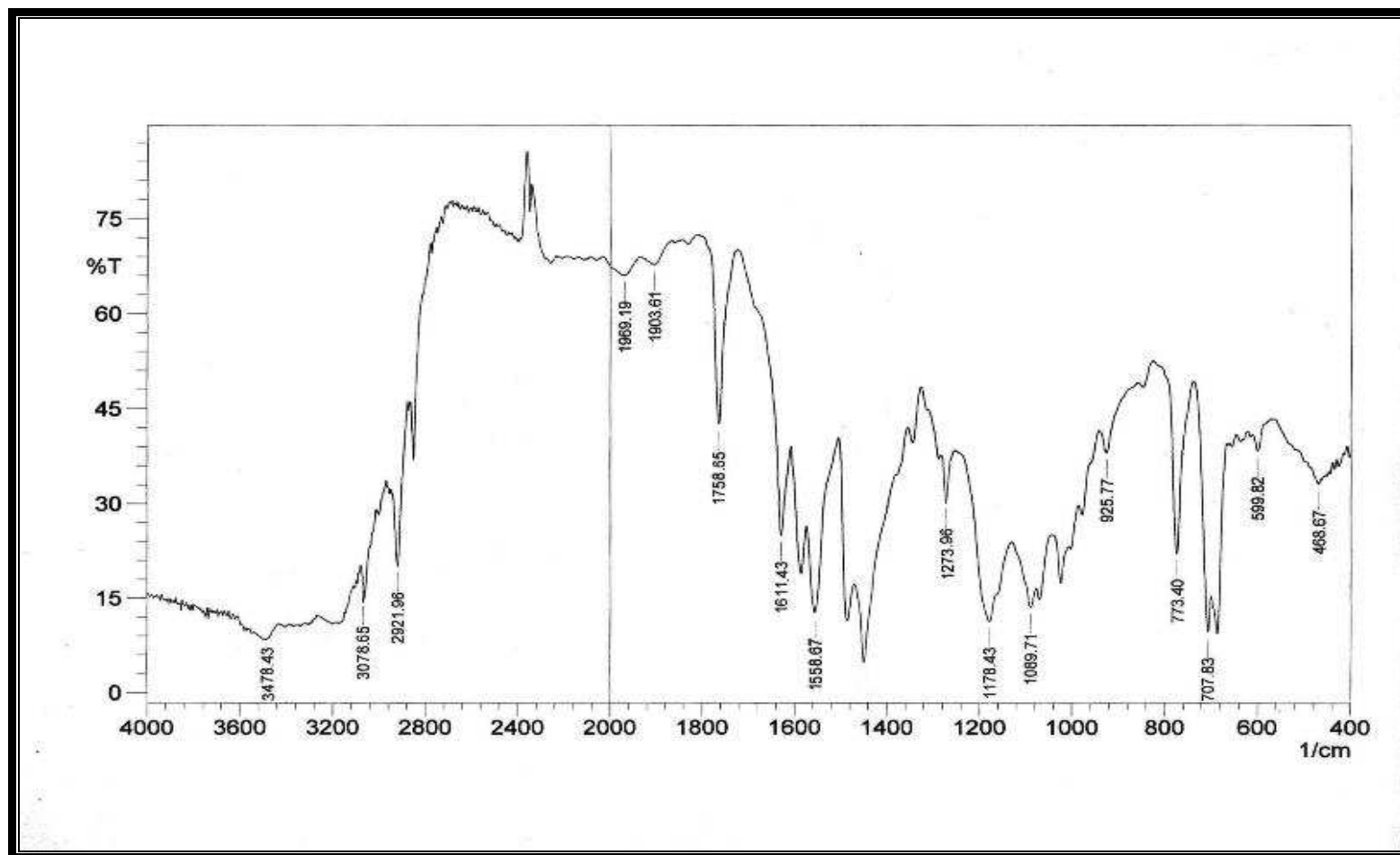


Fig (3-2) FT-IR Spectra of LII

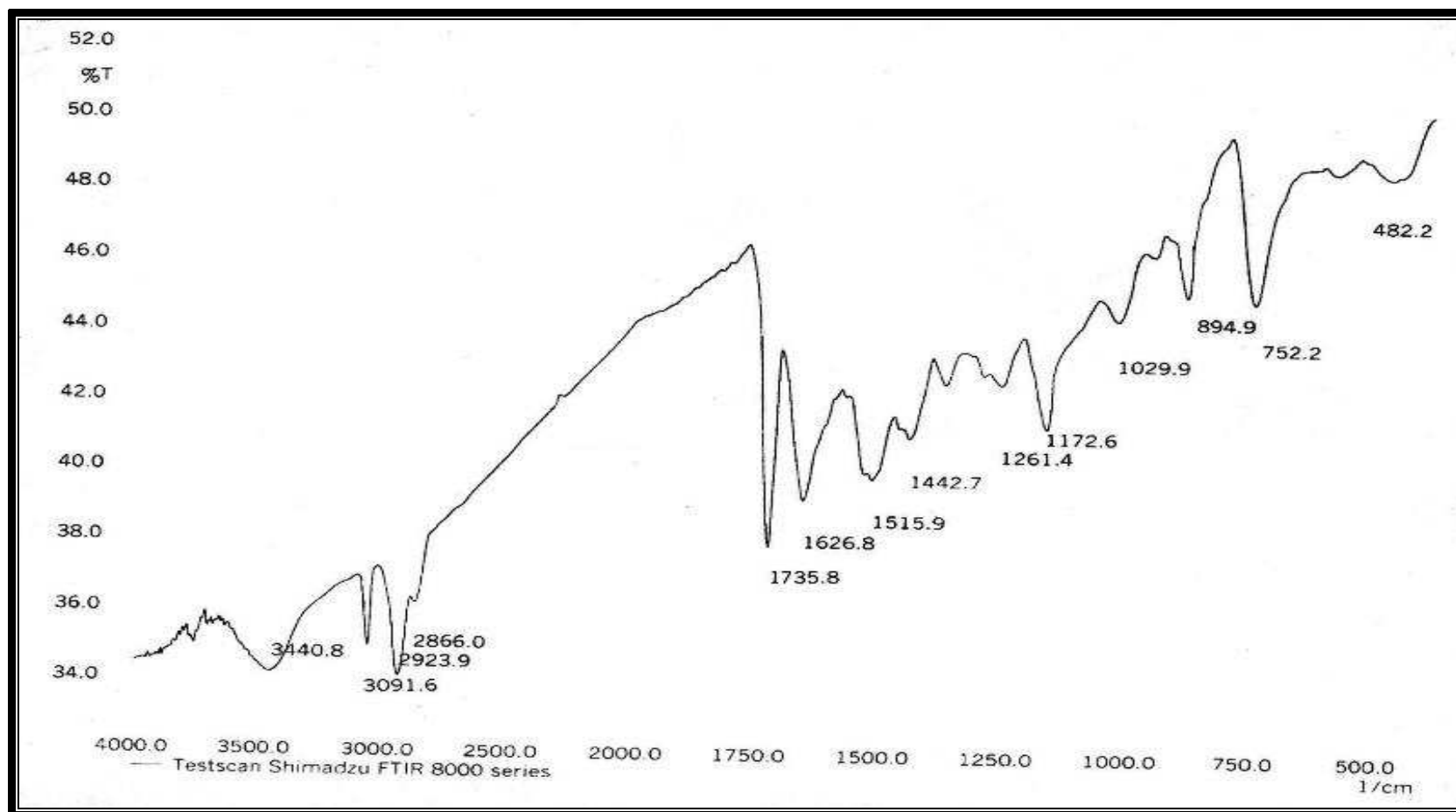


Fig (3-3) FT-IR spectra of LIII

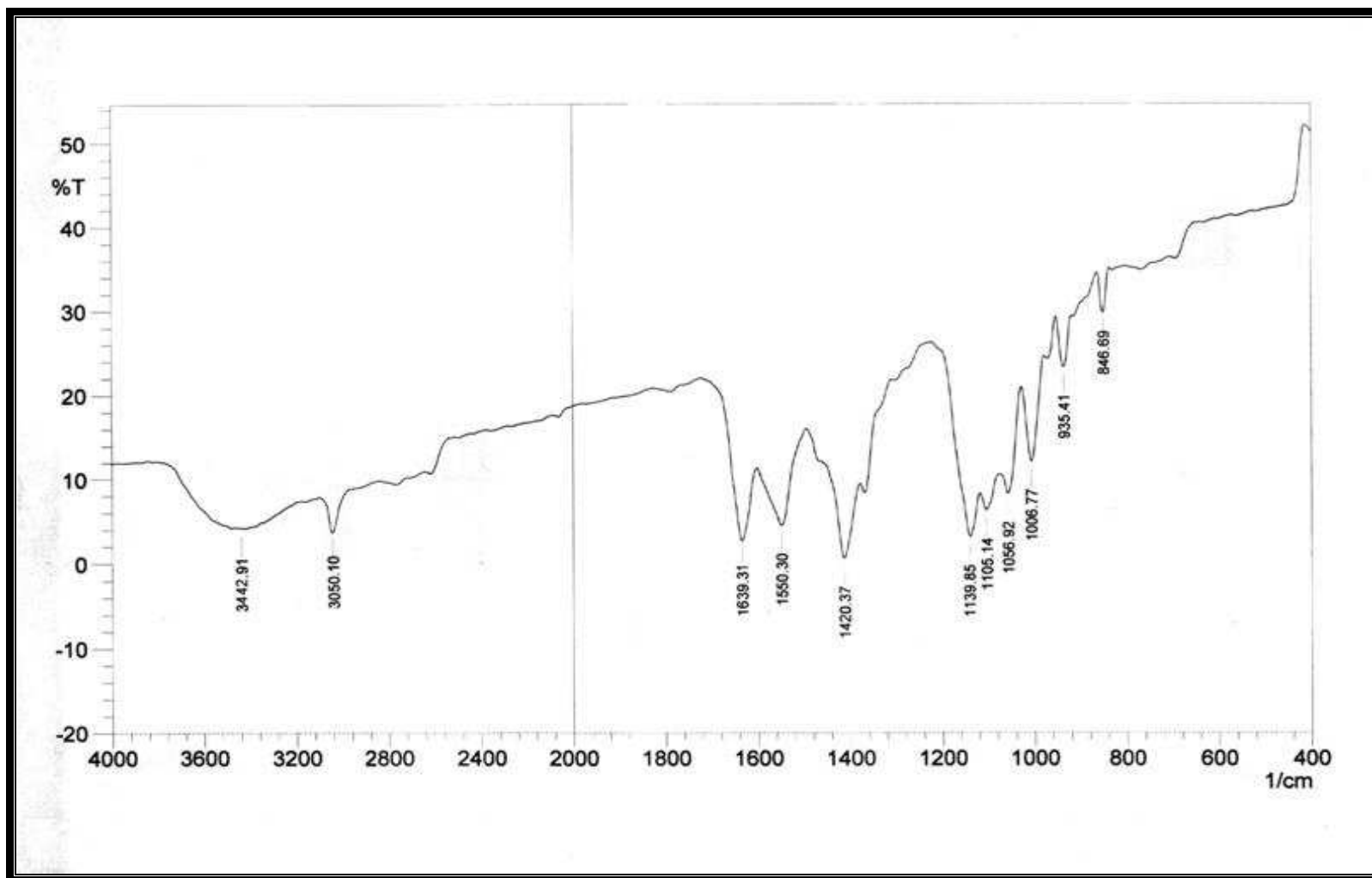


Fig (3-4) FT-IR spectra of LIII

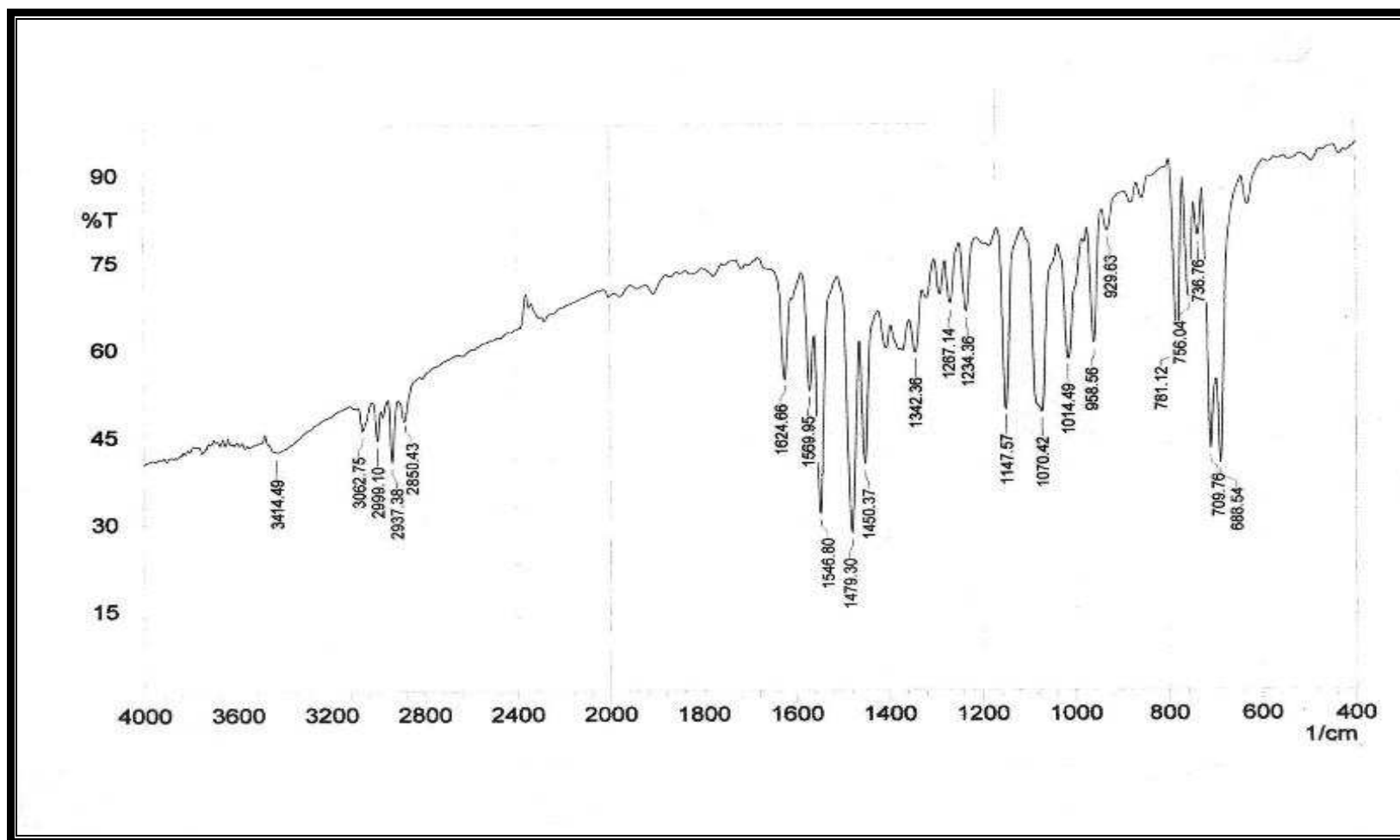


Fig (3-1) FT-IR of LI

Abstract:

Benzylidene compounds (Schiff bases), were prepared from the reaction of 2-hydroxy benzaldehyde with different primary amines, and elucidated by infrared spectroscopy.

Ferric sulfate di-hydrate salt was reacted with those Schiff bases which produced the corresponding ferric complexes.

These obtained complexes were elucidated by infrared spectroscopy and metal analysis.

The prepared compounds were tested for antibacterial activity.

The results obtained indicated that some of these compounds were more active than the others.

And the biological activity included two types of bacteria, gram positive bacteria(*Staphylococcus aureus*) and gram negative bacteria(*Escherichia*

الخلاصة:

تم الحصول على مجموعة من قواعد شيف من تفاعل الديهايد (٢- هيدروكسي بينز الديهايد) مع امين اولي (بارا- تولويدين، ميتا- امينو بينزويك اسيد، ٤-امينو اسيتو فينون، وميتا امينو فينول). وتم الكشف عن قواعد شيف باستخدام اشعة الطيف تحت الحمراء. الى قواعد شيف تم اضافة ايون الحديد الثلاثي، لتكوين معقدات قواعد شيف مع هذا الايون. وتم الكشف عن هذه المعقدات باستخدام اشعة الطيف تحت الحمراء وتحليل العناصر. تم قياس الفعالية البايولوجية للمركبات المحضرة ، والنتائج اظهرت ان بعض المركبات اكثر فعالية من غيرها. وتضمنت نوعين من البكتريا، الموجبة والسالبة للصبغة.

Introduction

Part One

Chemotherapy^{(1),(2),(3)}

1.1.1 What is Chemotherapy?

Is the use of chemical substances to treat disease. In its modern-day use, it refers primarily to cytotoxic drugs used to treat cancer.

In its non-oncological use, the term may also refer to antibiotics (antibacterial chemotherapy).

In that sense, the first modern chemotherapeutic agent was Paul Ehrlich's arsphenamine (fig(1-1)), an arsenic compound discovered in 1909 and used to treat syphilis.

This was later followed by sulfonamides (fig(1-14)) discovered by Domagk and penicillin (fig(1-2)) discovered by Alexander Fleming.

Other uses of cytostatic chemotherapy agents are the treatment of autoimmune diseases such as multiple sclerosis and rheumatoid arthritis and suppression of transplant rejections.

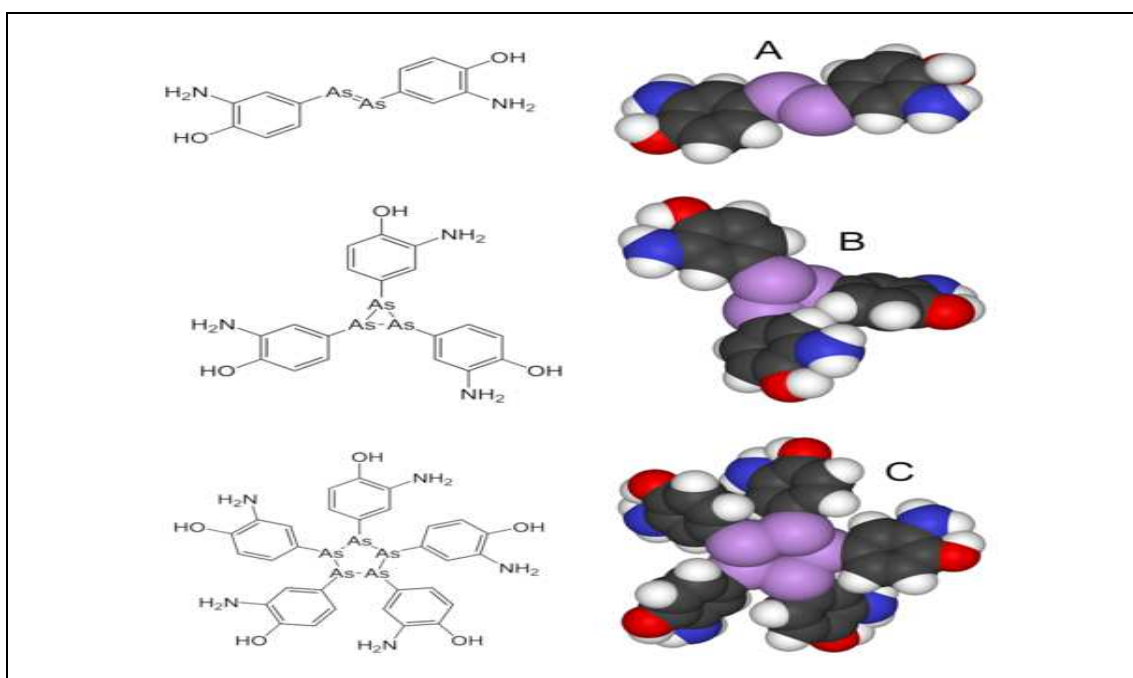
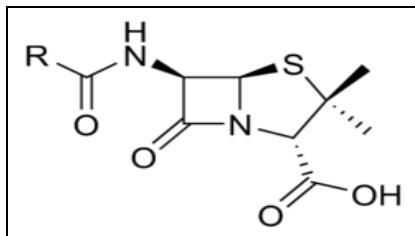


Fig.(1-1) Arsphenamine

Chapter One-Introduction

The structure was believed to be -A- until 2005, when new research suggested the true structure was in fact a mixture of the trimer -B- and the pentamer -C- .



Fig(1-2)
penicillin

Chemotherapy is used in a large scale in the cancer treatment.

The first drug used for cancer chemotherapy was not originally intended for that purpose.

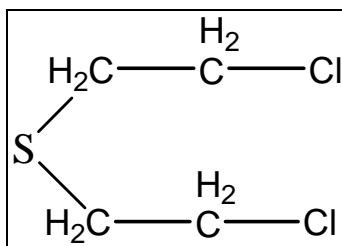
Mustard gas fig(1-3) was used as a chemical warfare agent during the 1st world war and was studied further during the second world war,

People were exposed to Mustard gas was later found to have very low white blood cell counts. It was reasoned that an agent that damaged the rapidly growing white blood cells might have a similar effect on Cancer.

So in 1940, several patients with advanced lymphomas (Cancers of certain white blood cells) were given the drug by vein, rather than by breathing the irritating gas.

There improvement, although temporary, was remarkable.

So this experiment led researchers to look for other substances that might have similar effects against Cancer.



fig(1-3)
Mustard gas

1.1.2 Types of Chemotherapy

The majority of chemotherapeutic drugs can be divided into:alkylating agents,antimetabolites,anthracyclines,topoisomerase inhibitors,monoclonal antibodies,and other antitumour agents.

All of these drugs effect cell division or DNA synthesis and function in some way.

Some newer agents don't directly interfere with DNA.These include the new tyrosine kinase inhibitor imatinib mesylate fig(1-4) which directly targets a molecular abnormality in certain types of Cancer(chronic myelogenous leukemia,gastrointestinal stromal tumors).

In addition some drugs may be used which modulate cell behaviour without directly attacking those cells.

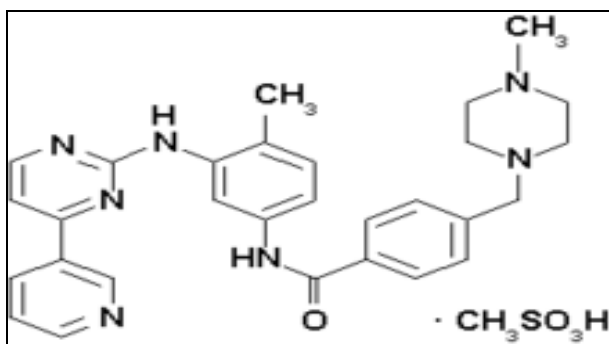


Fig.(1-4)imatinib mesylate

Two important types of chemotherapy are:-

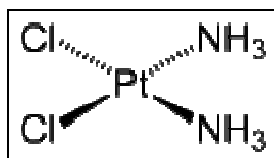
Chapter One-Introduction

1.1.2.1- Alkylating agents⁽⁴²⁾

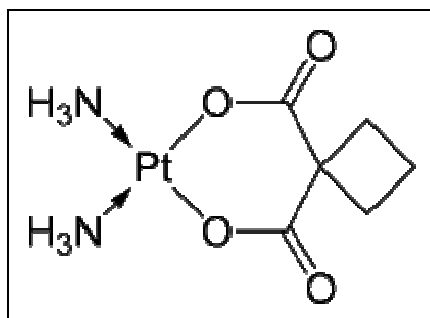
Alkylating agents are so named because of their ability to add alkyl groups to many electronegative groups under conditions present in cells.

Cis platin fig(1-5) and Carboplatin fig(1-6),as well as oxaliplatin fig(1-7) are alkylating agents.

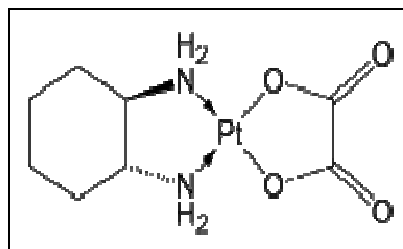
Other agents are mechloethamine,cyclophosphamide fig(1-8),chlorambucil fig(1-9).They work by chemically modifying a cell's DNA.



Fig(1-5)
Cisplatin



Fig(1-6)
Carboplatin



Fig(1-7)
Oxaliplatin

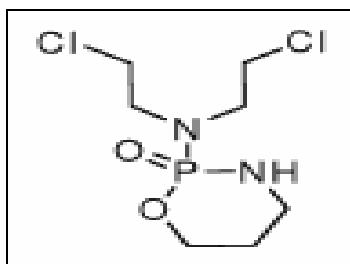
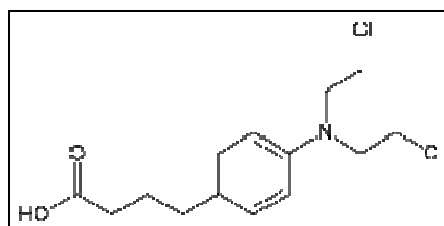


Fig.(1-8)cyclophosphamide



Fig(1-9)
Chlorabucil

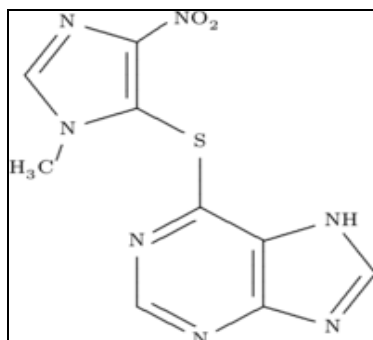
1.1.2.2-Anti metabolite:

An antimetabolite is a chemical with a similar structure to a substance(a metabolite) required for normal biochemical reactions,yet different enough to interfere with the normal functions of cells,including cell division.

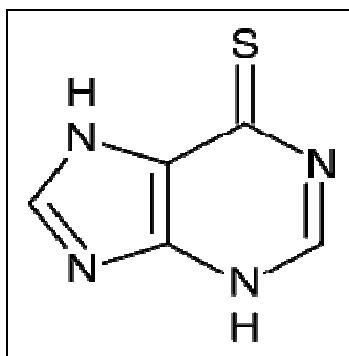
Antimetabolites can be used in cancer treatment,as they interfere with DNA replication and therefore cell division and the growth of tumors.Because cancer cells spend more time dividing than other cells,inhibiting cell division harms tumor cells more than other cells.

Anti-metabolite masquerade as purine(azathioprine,mercaptopurine)or pyrimidine which become the building blocks of DNA.

They prevent these substances becoming incorporated into DNA during the S phase of cell cycle,stopping normal development and division.



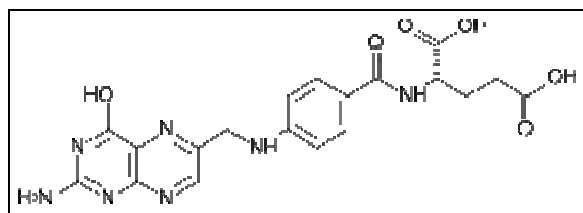
Fig(1-10)
Azathioprine



Fig(1-11)
Mercaptopurine

Generally, antimetabolite drugs⁽⁴¹⁾ include folic acid analogues, purine analogues and pyrimidine analogues.

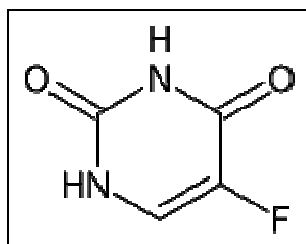
Methotrexate is a folic acid analogue, prevents the formation of tetrahydrofolate, essential for purine and pyrimidine synthesis.



Fig(1-12)
Folic acid

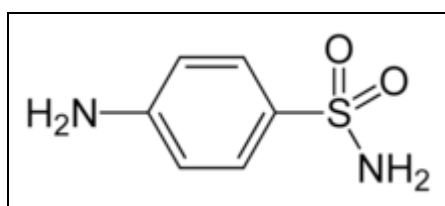
While purine analogues include azathioprine fig(1-10), mercaptopurine fig(1-11), thioguanine, fludarabine and pentostatin.

Pyrimidine analogues may include 5-fluorouracil, floxuridine and cytosine arabinoside.



Fig(1-13)
Fluorouracil

Antimetabolite may also be antibiotics, such as sulfanilamide drugs, which inhibit dihydrofolate synthesis in bacteria by competing with para-aminobenzoic acid.



Fig(1-14)
Sulfanilamide

1.1.3 Dosage of chemotherapy

Dosage of chemotherapy can be difficult: if the dose is too low, it will be ineffective against the tumor, while at excessive doses the toxicity (side-effects, neutropenia) will be intolerable to the patient).

This has led to the formation of detailed "Dosing schemes" which give guidance on the correct dose and adjustment in case of toxicity.

The BSA (body surface area) is usually calculated with a mathematical formula or a nomogram, using a patient's weight and height, rather than by direct measurement.

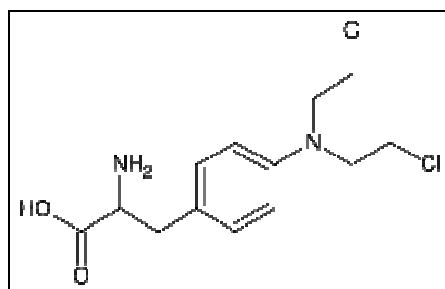
1.1.4 Delivery of chemotherapy

Most chemotherapy is delivered intravenously, although there are a number of agents that can be administered orally (e.g. melphalan, busulfan, capecitabine).

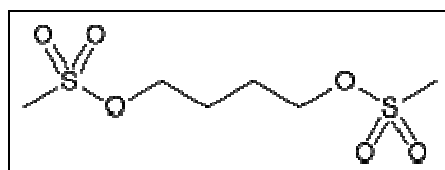
Chapter One-Introduction

Depending on the patient, the disease, the stage of disease, the type of chemotherapy, and the dosage.

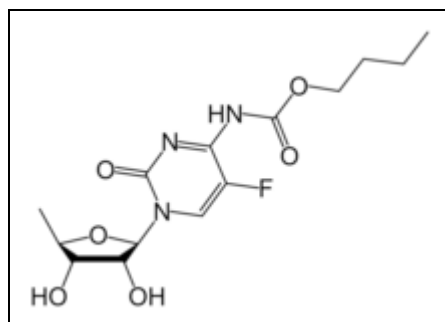
Intravenous chemotherapy may be given on either an inpatient or outpatient basis.



Fig(1-15)
Melphalan



Fig(1-16)
Busulfan



Fig(1-17)
Capecitabine

1.1.5 Side effects of chemotherapy⁽⁴⁰⁾

The treatment can be physically exhausting for the patient, current chemotherapeutic techniques have a range of side effects mainly affecting the fast-dividing cells of the body.

Chapter One-Introduction

Important side-effects include(dependent on the agent):-

- 1-Hair loss.
- 2-Nausea and vomiting.
- 3-Diarrhea or Constipation.
- 4-Anemia.
- 5-Malnutrition.
- 6-Depression of the immune system,hence(potentially lethal)infections and sepsis.
- 7-Hemorrhage.
- 8-Secondary neoplasms.
- 9-Cardiotoxicity.
- 10-Hepatotoxicity.
- 11-Nephrotoxicity.
- 12-Ototoxicity.
- 13-Death.

Chapter One-Introduction

Part two :Schiff bases.

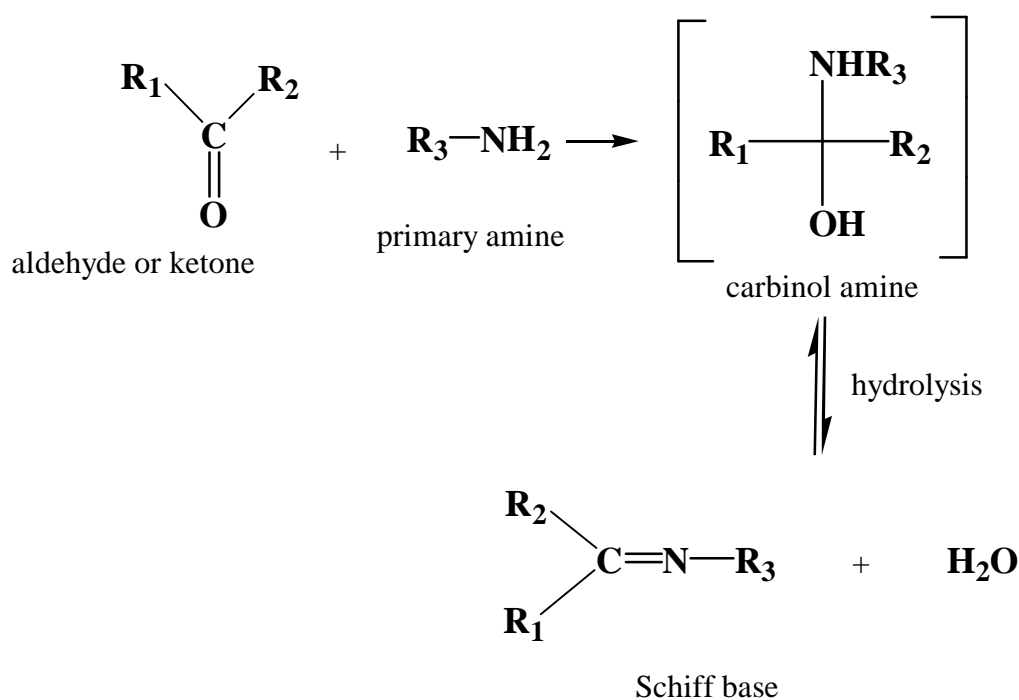
1.2.1 What are Schiff bases?:-

The term "Schiff bases" is using to define an organic compounds which contain the functional group(C=N).

They were firstly prepared by Schiff in the year 1864⁽⁴⁾.

Schiff bases have the general formula $R_1R_2C=NR_3$, when R_3 is a phenyl or alkyl group the Schiff base is then called an imine,which is very stable.⁽⁵⁾

Schiff bases can be obtained by condensation reaction between carbonyl compound(aldehyde or ketone)with a primary amine.



Chapter One-Introduction

These bases can also be prepared by refluxing of equimolar quantities of aldehyde or ketone with amine or by slow melting for 10 minutes and then isolating and purifying the product by recrystallization or sublimation under reduced pressure^(6,7).

Stabb⁽⁸⁾ prepared Schiff bases by removing water which is formed by condensation of aldehyde with the amine by reflux in benzene this is done by mixing the amine and the aldehyde in benzene and then the residual solution is distilled under vacuum.

1.2.2 Applications of Schiff bases:-

Schiff bases are used in a large scale in the industrial applications.

They are used in the synthesis of dyes and pigments⁽²³⁾.

Also in rubber accelerators, and in liquid crystals for electronics.

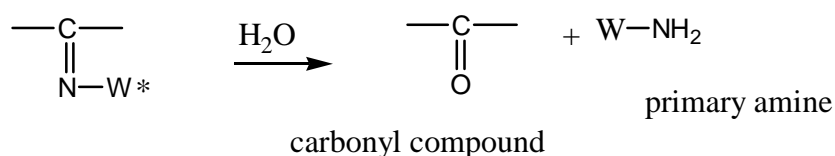
Schiff bases are used as substrates in the preparation of a number of industrial and biologically active compounds, via ring closure, cycloaddition and replacement reactions⁽³³⁾.

Moreover, they are also known to have biological activities such as antimicrobial^(34,35), antifungal^(36,37), and antitumor⁽³⁸⁾.

Finally, they are also employed as ligands for complexation of metal ions⁽³⁹⁾.

1.2.3 Some of the reactions of Carbon nitrogen double bond⁽⁹⁾:

- Hydrolysis of the carbon nitrogen double bond:



Compounds containing carbon-nitrogen double bonds can be hydrolyzed to the corresponding aldehydes or ketones.

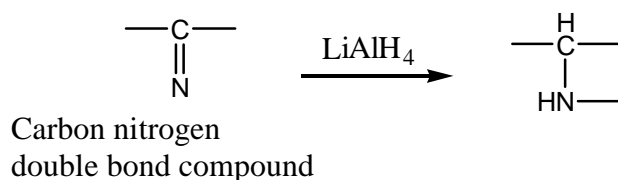
Chapter One-Introduction

For imines ($W^* = R$ or H) the hydrolysis is easy and can be carried out with water.

The hydrolysis of Schiff bases is more difficult and requires acid or basic catalysis.

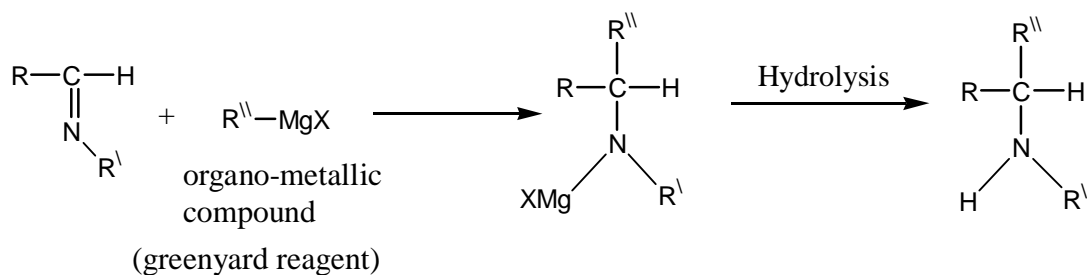
- Reduction of the carbon-nitrogen double bond:

Imines, Schiff bases, hydrazones, and other $C=N$ compounds can be reduced with $LiAlH_4$, $NaBH_4$, $Na-EtOH$, hydrogen and a catalyst, as well as with other reducing agents.

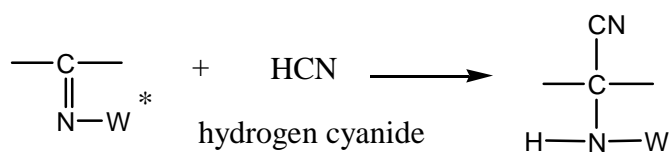


The addition of organometallic compounds to $C=N$ Compounds:

N-Hydro-C-alkyl addition:



The addition of HCN to $C=N$ Compounds:



$W^* = H, R, Ar, OH, NHA, \text{etc,}$

Chapter One-Introduction

HCN adds to imines, Schiff bases, hydrazones, oximes and similar compounds.

1.2.4 Complexation of ligands with metal ions:-

Chelating ligands⁽¹⁰⁾ are complex compounds consisting of a central metal atom attached to a large molecule, called a ligand, in a cyclic or ring structure.

Ligands that can attach to the same metal ion at two points are called bidentate ligand, while ligands that can attach to the same metal ion at more than two points are called polydentate ligands.

All polydentate ligands are chelating agents.

Chelates are more stable than nonchelated compounds of comparable composition, and the more extensive the chelation—that is, the larger the number of ring closures to a metal atom—the more stable the compound.

This phenomenon is called the chelate effect, the stability of chelate is also related to the number of atoms in the chelate ring.

The functional group $R_1HC=NR_2$ which has been called an imine, is particularly for binding metal ions via the N atom lone pair, to form polydentate chelating ligands, or macrocycles.

Ketones, of course, will also form imines of the type $R_1R_2C=NR_3$,

But the reactions tend to occur less readily than with aldehydes.

Bidentate Schiff bases have been among ligands that are extensively used for preparing metal complexes.

These ligands are described according to their donor set, N-donor Schiff bases, N,O-donor Schiff bases.

Tridentate Schiff bases may be generally considered as derived from the bidentate analogues by adding another donor group.

Chapter One-Introduction

These have been utilized as an ionic ligands having (N,N,O),(N,N,S),(N,N,O)and(N,S,O)donor sets.^(11,12).

In medical practice,chelating agents,particular salts of EDTA,are widely used for direct treatment of metal poisoning because they bind the toxic metal ions more strongly than do the vulnerable components of the living organism.

Chelating agents are also employed as extractants in industrial and laboratory separation of metals and as metal-ion buffers and indicators in analytical chemistry.

Also they are useful in stabilizing high oxidation states of metals.

Many commercial dyes and a number of biological substances including chlorophyll and hemoglobin,are chelate compounds.

Chapter One-Introduction

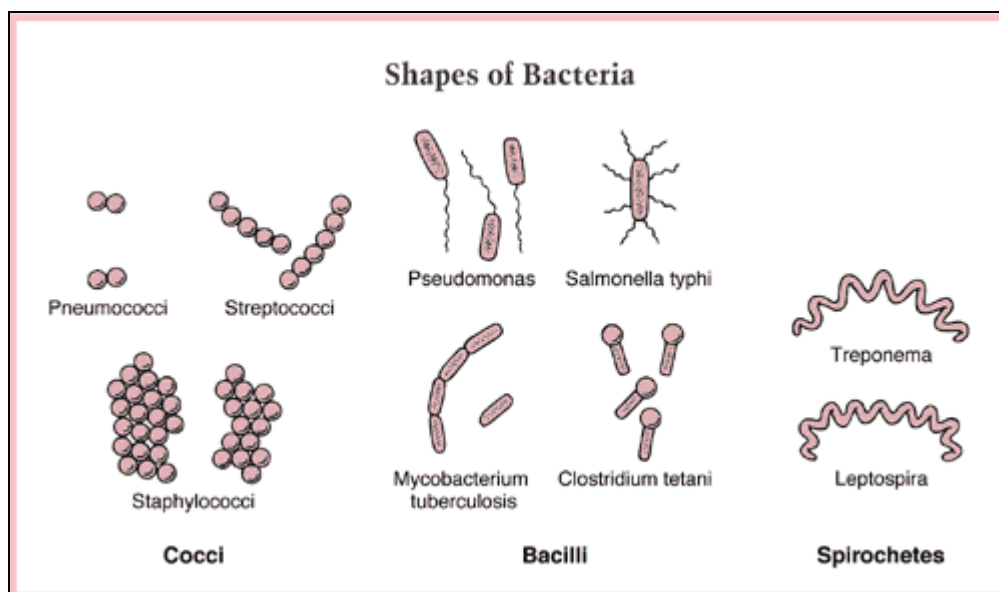
Part three

Bacteria

1.3.1 What are Bacteria?

Bacteria are the simplest and oldest form of life.⁽¹³⁾

Bacteria(singular:bacterium)are unicellular microorganisms.They are typically a few micrometers long and have many shapes including spheres,rods,and spirals.⁽²⁵⁾



fig(1-18)
shapes of bacteria

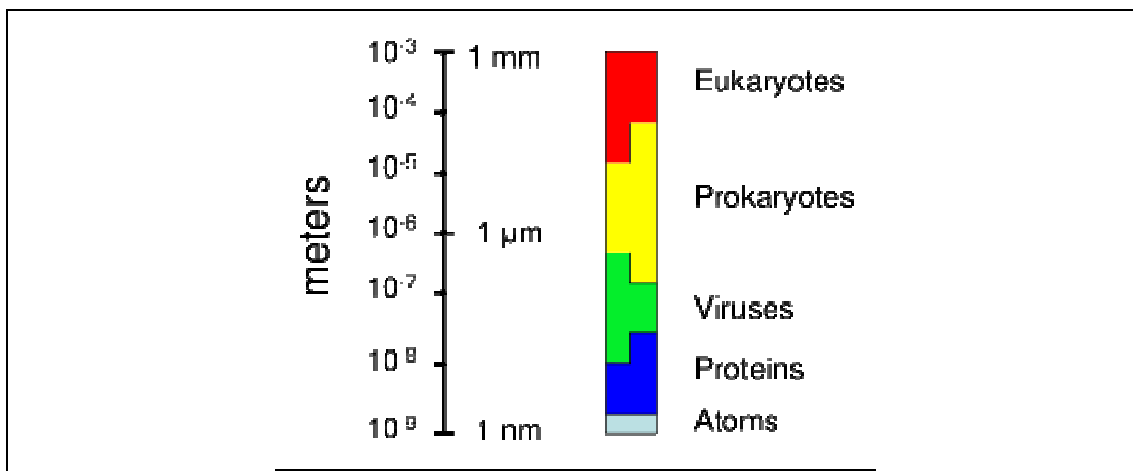
Bacteria are ubiquitous in every habitat on earth,growing in soil,acidic hot springs,radio active waste,⁽²⁶⁾sea water,and deep in the earth's crust.

Some bacteria can even survive in the extreme cold and vacuum of outer space.

There are typically 40 million bacterial cells in a gram of soil and a million bacterial cells in a milliliter of fresh water,in all,there are approximately five nonillion(5×10^{30})bacteria in the world.⁽²⁷⁾

Chapter One-Introduction

Also there are about 10 times as many bacterial cells as human cells in the human body, with large numbers of bacteria on the skin and in the digestive tract.⁽²⁸⁾



fig(1-19)

The range of sizes shown by Prokaryotes, relative to those of other organisms and biomolecules

Bacteria, unlike animals and other eukaryotes, do not contain a nucleus or other membrane-bound organelles.

They are just DNA and RNA encased in a hard cover, that they get their own category.⁽¹³⁾

1.3.2 Bacterial benefits:-

Some types of bacteria are harmless and some of them are beneficial.

Many bacteria species are found naturally in the human body, and in all other animal bodies.

Bacteria are instrumental in digestion, vitamin production, and other good work.

Chapter One-Introduction

When antibiotics are taken, the aim is to kill the "bad" bacteria that have caused the disease. However, the antibiotics also kill the "good" bacteria that the body relies on.

Bacteria are beneficial in other ways. Bacteria are what decompose and use up dead plant and animal matter. With no bacteria, the planet would be covered with dead plants and animals.

Certain species of bacteria that live on the roots of plants actually "fix" nitrogen from the air, convert it to plant food, and feed the plants with essential plant nutrients.⁽¹³⁾

Bacteria are important in processes such as waste water treatment, the production of cheese and yoghurt, and the manufacture of antibiotics and other chemicals.⁽²⁹⁾

1.3.3 Gram positive bacteria:-

Are those that retain a crystal violet dye during the gram stain process.⁽¹⁴⁾

Gram positive bacteria appear blue or violet under a microscope, while gram negative bacteria appear red or pink.

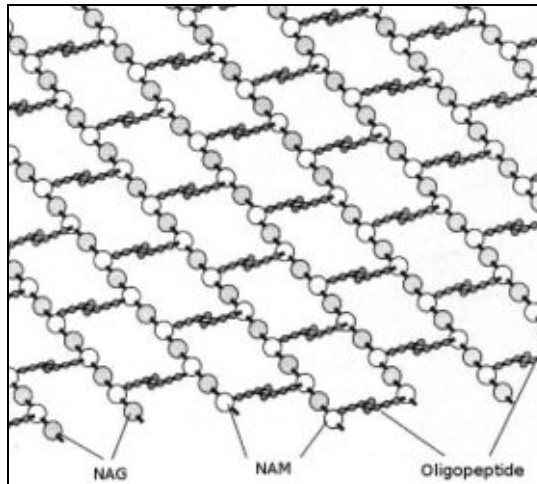
The gram classification system is empirical and largely based on differences in cell wall structure.⁽¹⁵⁾

The following characteristics are generally present in a gram positive bacteria:-⁽¹⁶⁾

Chapter One-Introduction

1-A very thick cell wall.(Peptidoglycan).

Peptidoglycan is a polymer consisting of sugars and amino acids.



Fig(1-20)

Peptidoglycan

Where NAG:N-acetyl glucoseamine,NAM:N-acetyl muramic acid.

2-If a flagellum is present,it contains two rings for support.(gram positive bacteria has only one membrane layer).

3-Teichoic acids and lipoteichoic acids are present,which serve to act as chelating agents,and also for certain types of adherence.

1.3.4 Gram negative bacteria:-

The following characteristics are displayed by gram negative bacteria:-

1-Cell walls only contain a few layers of peptidoglycan(which present in much higher levels in gram positive bacteria,it forms 90% of the dry weight of gram positive bacteria,but only 10% of gram negative bacteria)⁽²⁴⁾.

2-Cells are surrounded by an outer membrane of lipopolysaccharid.(also known as lipid A)outside the peptidoglycan layer.

3-Porins exist in the outer membrane,which act like pores for particular molecules.

Chapter One-Introduction

4-There is a space between the layers of peptidoglycan and the secondary cell membrane called the periplasmic space.

5-The S-layer is directly attached to the outer membrane,rather than the peptidoglycan.

6-If present,flagella have four supporting rings instead of two.

7-No teichoic acids or lipoteichoic acids are present.

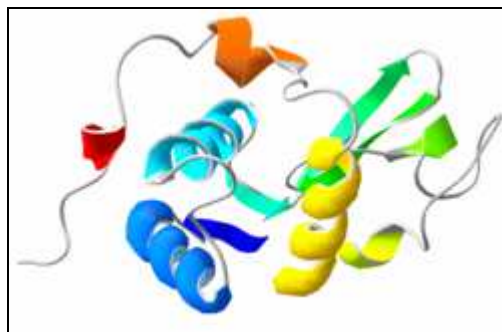
8-Lipoprotiens are attached to the polysaccharide backbone.

9-Most do not sporulate.

Both gram positive and gram negative bacteria may have a membrane called an S-layer.In gram negative,the S-layer is directly attached to the outer membrane,while in gram positive the S-layer is attached to the peptidoglycan layer.

The outer membrane in the gram negative bacteria is responsible for protecting the bacteria from several antibiotics,dyes,and detergents which would normally damage the inner membrane or cell wall(peptidoglycan).

The outer membrane provides these bacteria with resistance to lysozyme fig(1-22) and penicillin fig(1-2).



Fig(1-21)

Lysozyme

Lysozyme:is a 14.4 kilodalton enzyme,commonly refrrred to as the"body's own antibiotic"since it kills bacteria.It destroys bacteria cell walls by hydrolyzing the polysaccharids component of the cell wall.It is abundantly present in a number of secretion,such as tears.

Chapter One-Introduction

1.3.5 *Staphylococcus aureus* bacteria:

1.3.5.1-What are *Staphylococcus aureus* bacteria?

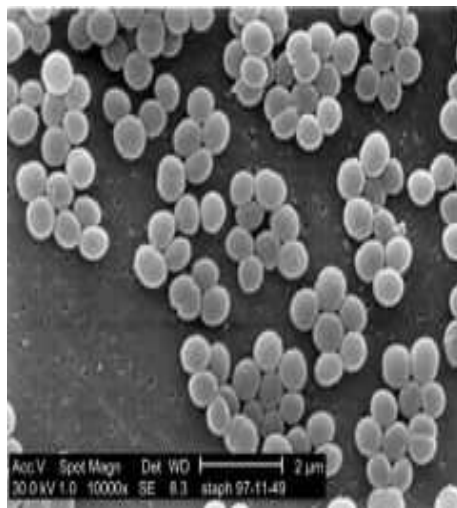
The most common cause of staph infections, is a spherical bacterium, frequently living on the skin or in the nose of a healthy person, that can cause a range of illnesses from minor skin infections.

S.aureus was discovered in Aberdeen, Scotland in 1880 by surgeon Alexander Ogston⁽¹⁷⁾.

Each year some 500,000 patients in American hospitals contract a staphylococcal infection.

S.aureus is a gram-positive coccus, which appears as grape-like clusters when viewed through a microscope and has largened, round, golden-yellow colonies, often when grown on blood agar plates⁽¹⁸⁾.

The golden appearance is the etymological root of the bacteria's name "golden" in latin.



Fig(1-22)
Stphyloccocus aureus bacteria
From an infected skin
200 x 217pixels.

Chapter One-Introduction

1.3.5.2-Role in disease:-

Occur as a commensal on human skin;it also occurs in the nose(in about 25% of the population)and throat and least commonly,may be found in the colon and in urine.

The finding of *S.aureus* under these circumstances does not always indicate infection and therefore does not always require treatment.

It can survive on domesticated animals such as dogs,cats and horses,and can cause bumblefoot in chickens.

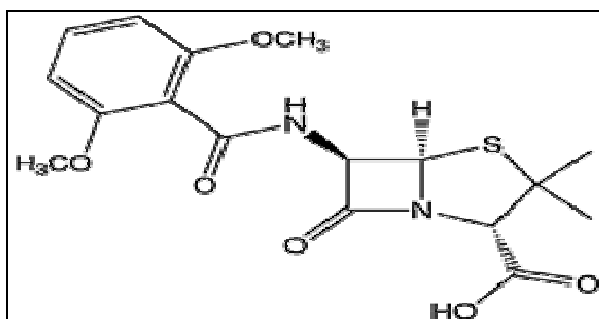
In infants *S.aureus* infection can cause a severe disease staphylococcal scaled skin syndrome(SSSS)⁽¹⁹⁾.

S.aureus infections can be spread through contact with pus from an infected wound,skin-to-skin contact with an infected person,and contact with objects such as towels,sheets,clothing,or athletic equipment used by an infected person.

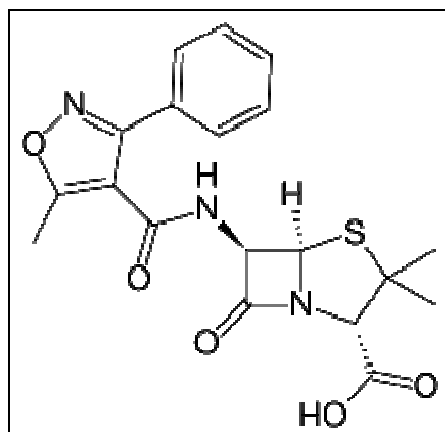
1.3.5.3- Mechanism of antibiotic resistance:-

Staphylococcus resistance to penicillin fig(1-2)is mediated by penicillinase(a form of β -lactamase)production:an enzyme which breaks down the β -lactam ring of the penicillin molecule.

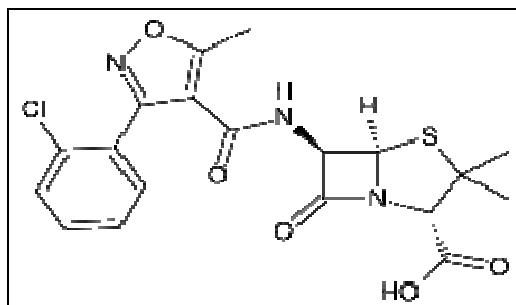
Penicillinase-resistant penicillins such as methicillin,oxacillin,cloxacillin,dicloxacillin and flucloxacillin are able to resist degradation by staphylococcal penicillinase.



Fig(1-23)
Methicillin



Fig(1-24)
Oxacillin



Fig(1-25)
Cloxacillin

1.3.6 *Escherichia coli* bacteria:-

1.3.6.1-What are *E.coli* bacteria?

Is one of the main species of bacteria living in the lower intestines of mammals, known as gut flora.

Discovered in 1885 by Theodor Escherich, a German pediatrician and bacteriologist⁽²⁰⁾, *E.coli* are abundant: the number of individual *E.coli* bacteria in the feces that a human excretes in one day averages between 100 billion and 10 trillion.

However, the bacteria are not confined to this environment and specimens have also been located, for example, on the edge of hot springs⁽²¹⁾.



Fig(1-26)

E.coli bacteria

As gram negative organisms, *E.coli* are unable to sporulate. Thus, treatments which kill all active bacteria, such as pasteurization or simple boiling, are effective for their eradication, without requiring the more rigorous sterilization which also deactivates spores. *E.coli* grow best in vivo or at the higher temperatures characteristic of such an environment, rather than the cooler temperatures found in soil and other environments.

1.3.6.2-Role in disease:-

E.coli can generally cause several intestinal and extra-intestinal infection such as urinary tract infections.

The enteric *E.coli* are divided on the basis of virulence properties into enterotoxigenic (ETEC, causative agent of diarrhea in humans, pigs, sheep, goats, cattle, dogs, and horses), enteropathogenic (EPEC, causative agent of diarrhea in humans, rabbits, dogs, cats and horses), enteroinvasive (EIEC, found only in humans), verotoxigenic (VTEC, found in pigs, cattle, dogs and cats), enterohaemorrhagic (EHEC, found in humans, cattle, and goats) and enteroaggregative *E.coli* (EAaggEC, found only in humans).

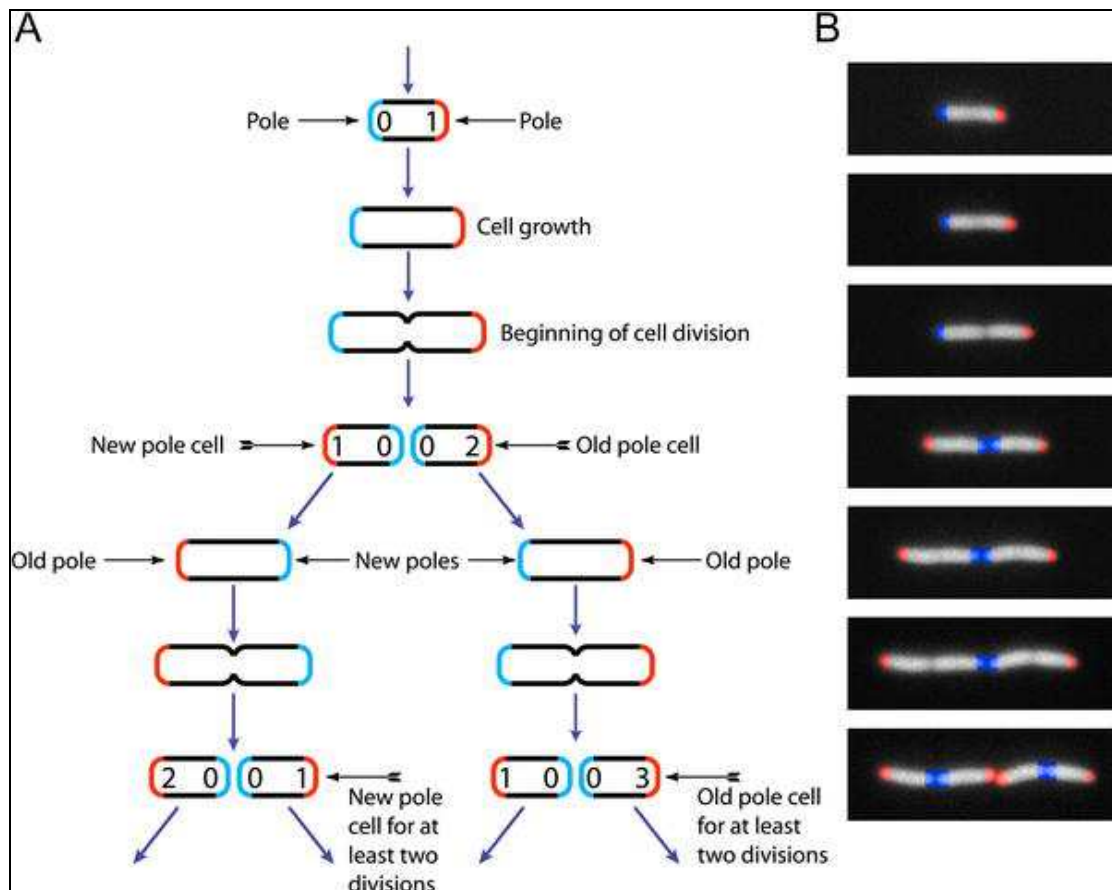
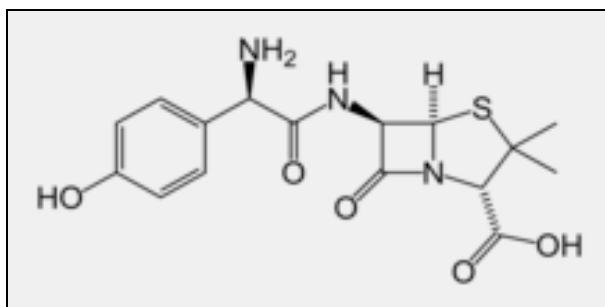


Fig.(1-27) Life cycle of *E.coli* bacteria.

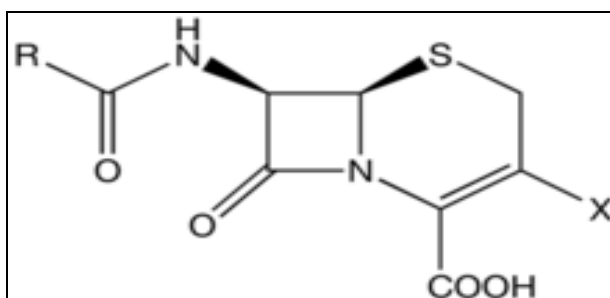
1.3.6.3-Antibiotic resistance:-

As gram negative organisms, *E.coli* are resistant to many antibiotics which are effective against gram-positive organisms, antibiotics which may be used to treat *E.coli* infection include (but are not limited to) amoxicillin as well as other semi-synthetic penicillins, many cephalosporins, ciprofloxacin, trimethoprim sulfamethoxazole.

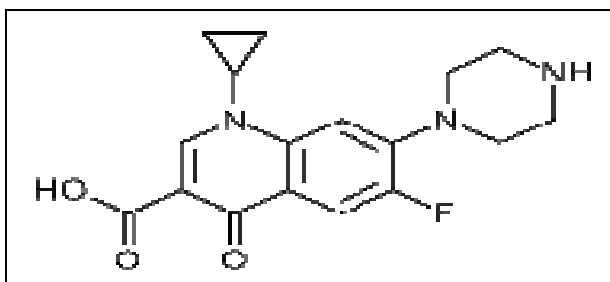
Not all antibiotics are suitable for every disease caused by *E.coli*.



Fig(1-29)
Amoxicillin



Fig(1-30)
Cephalosporins



Fig(1-31)
Ciprofloxacin

Antibiotic resistance is a growing problem. Some of this is due to overuse of antibiotics in humans, but some of it is probably due to the use of antibiotics as growth promoters in animals food⁽²⁹⁾.

Chapter One-Introduction

Aim of the work:

The aim of the work was to synthesize and characterize of four Schiff bases compounds and then using them as ligands in the preparation of ferric ion complexes.

And finally the biological activity of these compounds (ligands and complexes) were measured against both gram positive and gram negative bacteria.

Chapter Three-Results and Discussion

3.1 The physical properties of the prepared compounds:

The measurements of the melting points of the ligands and their complexes with the *Ferric* ion showed that the melting points of two of the complexes were higher than the melting points of the parent ligands, while two of them have a lower melting point than their parent ligand.

All reactions were carried out at room temperature under heating conditions using abs. ethanol as solvent. Recrystallization solvent also was absolute ethanol for all reactions.

Identification and study of these complexes were carried out by both metal analysis [The results are shown in table(3-1)] and Infra-red spectroscopy. According to these measurements the chemical formula of the prepared complexes have been suggested. As given in table (3-3).

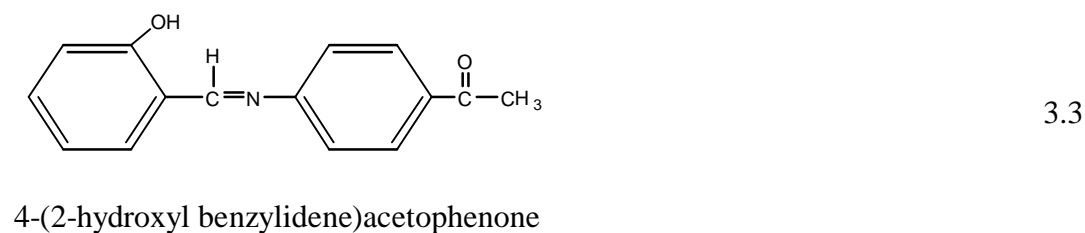
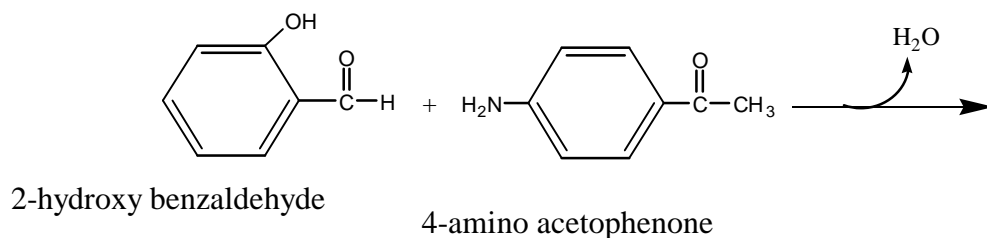
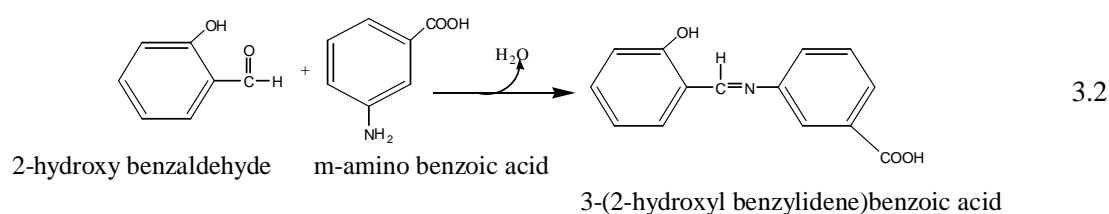
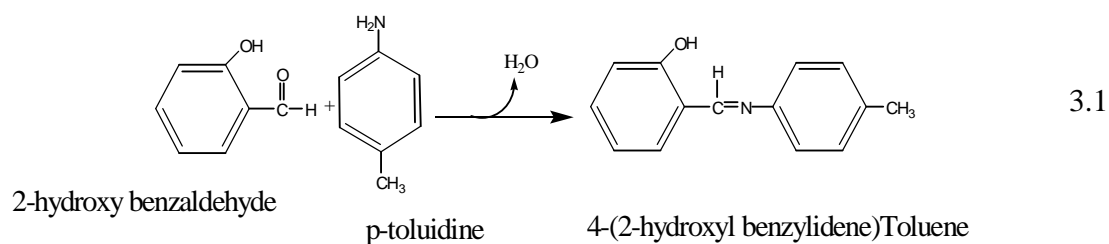
Table(3-1)
Physical properties for the prepared complexes

Complex	Melting pt. (°C)	Colour	Metal content	
			Calculated	Found
AI	(222-225)	Brown	11.9	12.8
AII	(275-278)	Light brown	11.8	11.2
AIII	(283-286)	Yellowish brown	10.9	10.7
AIII	(230-233)	Brown	13.6	13.9

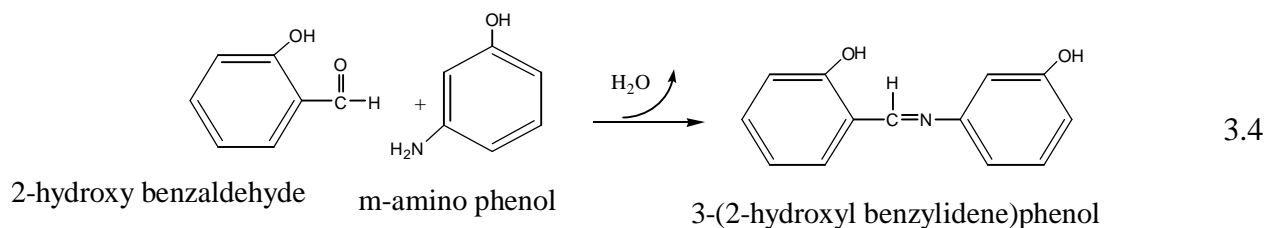
Chapter Three-Results and Discussion

3.2 Synthesis of ligands:

Schiff bases compounds were all prepared from the reaction of an aldehyde (2-hydroxy benzaldehyde) and a primary amine(p-toluidine,m-amino benzoic acid,4-amino acetophenone,and m-amino phenol).according to the following equations:respectively:

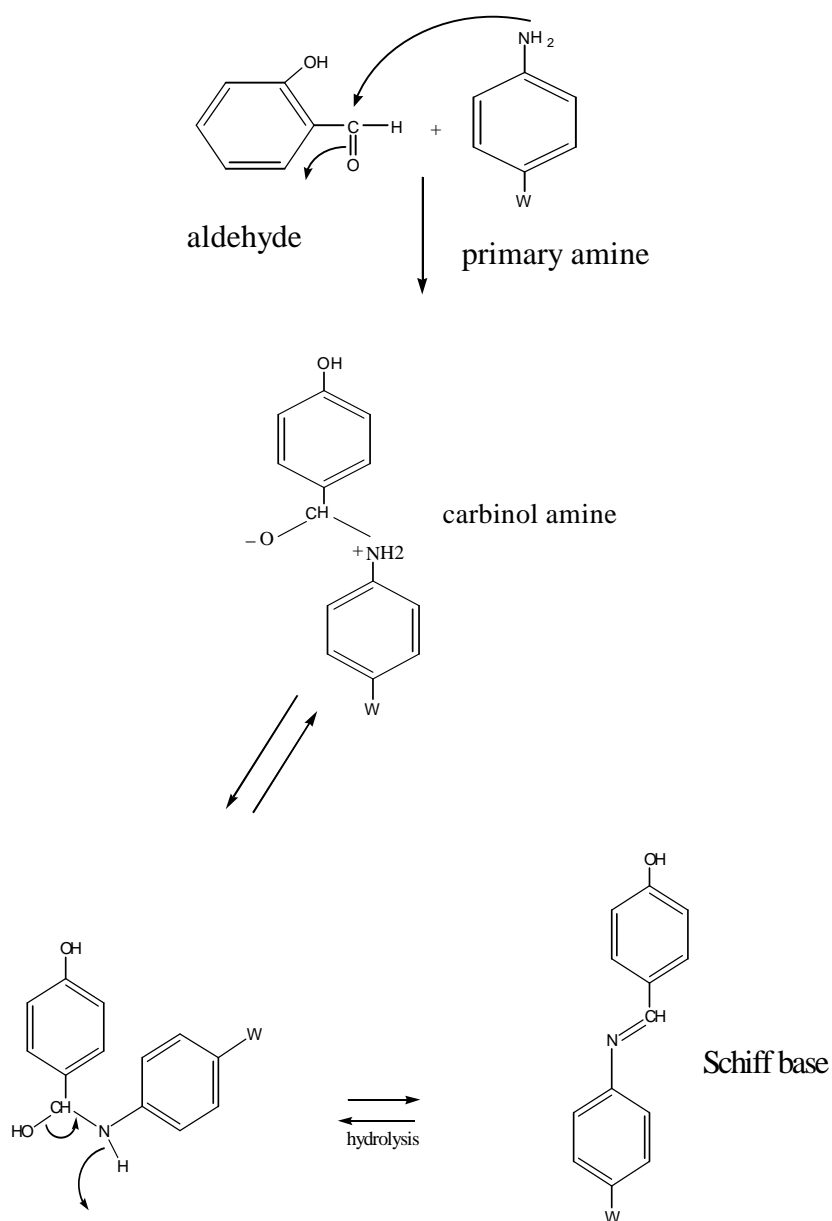


Chapter Three-Results and Discussion



All of these equations or reactions suggested to be according to the same mechanism⁽⁹⁾, Which is called Alkylimino-de-oxo-bisubstitution mechanism .

The reaction name is based on the IUPAC nomenclature for transformations.



Chapter Three-Results and Discussion

The reaction type is nucleophilic addition of the amine to the carbonyl compound followed by transfer of a proton from nitrogen to oxygen to a stable carbinolamine.(refers to the mechanism in the previous page).

With primary amines water is lost in an elimination reaction to an imine.

The reaction steps are reversible reactions and the reaction is driven to completion by removal of water.

3.3 Infra-red spectra:

The i.r.spectra were taken for the prepared complexes and compared with those of their respective ligands.The measurements were carried out for each compound in solid state as **KBr** disk in the range (4000-400) cm^{-1} .

All of the prepared ligands have the carbon nitrogen double bond($\text{C}=\text{N}$),it's absorption was occurred in the regions (1624,1611,1626,1639) cm^{-1} for ligands LI,LII,LIII,LIIII respectively.

The compounds containing ($\text{C}=\text{N}$) group show basic coordination behavior toward ferric ion coordinating via the nitrogen atom,this coordination shifts the stretching frequency of ($\text{C}=\text{N}$) group toward higher frequency in their complexes.⁽⁴³⁻⁴⁴⁾⁾.

3.3.1 FT-IR spectra of LI and it's ferric ion complex:

A- FT-IR spectra of LI:

The i.r spectra of the ligand Fig(3-1),table(3-2),showed the absence of the bands at $\sim 1735\text{cm}^{-1}$ and at $\sim 3315\text{cm}^{-1}$ due to the carbonyl $\nu(\text{C}=\text{O})$ and $\nu(\text{NH}_2)$ stretching vibration,and a strong new band appeared at 1624cm^{-1} assigned to the formation of the carbon nitrogen double bond. Showing that the amino and the aldehyde moieties of the starting materials are absent and have been converted into the imine group.

Chapter Three-Results and Discussion

A broad band appearing at 3414cm^{-1} has been assigned to the hydrogen bonded OH group in the ligand LI.

Also the bands appeared at $1546, 1479\text{cm}^{-1}$ assigned to the $\nu(\text{C}=\text{C})$ of aromatic ring, while bands at $2850, 2937$ and 2999cm^{-1} refer to the aliphatic $\nu(\text{C}-\text{H})$, and the band at 3062cm^{-1} to the aromatic $\nu(\text{C}-\text{H})$.

B- FT-IR spectra of AI:

The molecular formula of ferric ion complex (AI) includes four water molecules. Two of them may be coordinated to the metal and the other two were considered to be lattice water.

The presence of this number of water molecules expected due to the high tendency of ferric ion to bind to water through a strong bond which affected the I.r. spectrum of the complex⁽⁵⁴⁾, so the band at 3452 and 663cm^{-1} refer to the presence of both coordination and lattice H_2O molecules respectively.

The spectrum also shows the $\text{C}=\text{N}$ band to be shifted to a lower frequency by $(24)\text{cm}^{-1}$ indicating the interaction of the metal ion with the carbon-nitrogen double bond.

The weak band at 565 and 504cm^{-1} refer to $\nu(\text{Fe}-\text{N})$, $\nu(\text{Fe}-\text{O})$ bands respectively^(50,52).

Another bands appeared at $1170, 1082\text{cm}^{-1}$ refer to the sulphate group bonded to ferric ion^(50,51).

3.3.2 FT-IR spectra of LII and its ferric ion complex:

A- FT-IR of LII:

The I.r. spectrum of LII, Fig(3-2), table(3-2), shows the absence of the bands at $\sim 1735\text{cm}^{-1}$ and $\sim 3315\text{cm}^{-1}$ due to the carbonyl $\nu(\text{C}=\text{O})$ and $\nu(\text{NH}_2)$ stretching vibration. Showing that the amino and the aldehyde moieties of the starting materials are absent and have been converted into

Chapter Three-Results and Discussion

the imine group.

And the presence of the new band appeared at 1611cm^{-1} which refers to the $\nu(\text{C}=\text{N})$.

Also the spectrum shows a band at 3480cm^{-1} refers to the $\nu(\text{O}-\text{H})$ group in the ligand.

Bands at 2921,3078 refers to the $\nu(\text{C}-\text{H})$ of aromatic ring.

While the band appears at 1558cm^{-1} may refers to the $\nu(\text{C}=\text{C})$ of aromatic ring.

A broad band appearing at 1273 cm^{-1} may be assigned to the phenolic $\nu(\text{C}-\text{O})$ stretching mode.

B- FT-IR spectra of (AII):

The spectrum of this complex shows that the $\nu(\text{C}=\text{N})$ band was shifted to a lower frequency and appeared at 1600cm^{-1} , and the $\nu(\text{C}-\text{O})$ was shifted to a higher frequency and appeared at $(1315)\text{cm}^{-1}$, this indicating the participation of the nitrogen atom and phenolic oxygen in the complexation^(49,53).

The weak bands at 553 and 507cm^{-1} refer to the $\nu(\text{Fe}-\text{N})$ and $\nu(\text{Fe}-\text{O})$ band respectively^(50,52).

Other bands appeared at 1172 and 1142 cm^{-1} refer to the sulphate group bonded to ferric ion^(50,51).

Another bands at 3462 and 682cm^{-1} refer to the presence of both coordination and lattice H_2O molecules, this is expected to the ferric ion complex due to its high affinity for water, therefore the ligand cannot displace all the water molecules found in the coordination sphere of the metal ion⁽⁵⁴⁾.

3.3.3 FT-IR spectra of LIII and it's ferric ion complex:

A- FT-IR spectra of LIII:

The spectrum shows the appearance of the band at 1626 cm^{-1} which refers to the formation of carbon-nitrogen double bond.

Bands at $1442, 1515\text{ cm}^{-1}$ refer to the $\nu(\text{C}=\text{C})$ of the aromatic ring, while bands at $2923, 2866$ refer to the aliphatic $\nu(\text{C}-\text{H})$ and band at 3091 cm^{-1} refers to the $\nu(\text{C}-\text{H})$ of the aromatic ring.

Apperance of the band at 1261 cm^{-1} refers to the $\nu(\text{C}-\text{O})$.

Band at 3440 cm^{-1} has been assigned to the hydrogen bonded OH group in the ligand.

B- FT-IR spectra of (AIII):

The i.r. spectrum of this complex was characterized by the appearance of the band at 3749 cm^{-1} which could be attributed to the ethanol molecule in the structure.

And the band at 746 which attributed to the presence of coordination water.

The $\nu(\text{C}=\text{N})$ band was shifted to a lower frequency by $(9)\text{ cm}^{-1}$, this refer to the participation of the nitrogen atom in coordination. And $\nu(\text{C}-\text{O})$ absorption was shifted to 1280 cm^{-1} and this indicates the participation of phenolic oxygen in the complexation.

While bands at $545, 506\text{ cm}^{-1}$ erfer to $\nu(\text{Fe}-\text{N})$ and $\nu(\text{Fe}-\text{O})$ respectively, bands at $1149, 1058\text{ cm}^{-1}$ refer to the sulphate group bonded to ferric ion.

3.3.4 FT-IR spectra of LIII and it's ferric ion complex:

A- FT-IR of LIII:

The appearance of a band at 1639cm^{-1} refers to the formation of the carbon-nitrogen double bond.

Band at 1420cm^{-1} and 1550cm^{-1} assigned to the $\nu(\text{C}=\text{C})$ of the aromatic ring.

While, band at 3442cm^{-1} assigned to the hydrogen bonded OH group in the ligand.

B- FT-IR of (AIII):

The spectrum of this complex show the $\nu(\text{C}=\text{N})$ band to be shifted to lower frequency and appeared at 1625cm^{-1} , this indicates the participation of nitrogen atom in coordination.

The weak bands at 565cm^{-1} and 504cm^{-1} refers to the $\nu(\text{Fe}-\text{N})$ and $\nu(\text{Fe}-\text{O})$ bands respectively.

Other bands appeared at $1147, 1031\text{cm}^{-1}$ belongs to the sulphate group bonded to ferric ion.

Bands at $1409, 1593\text{cm}^{-1}$ refers to the $\nu(\text{C}=\text{C})$ of aromatic ring.

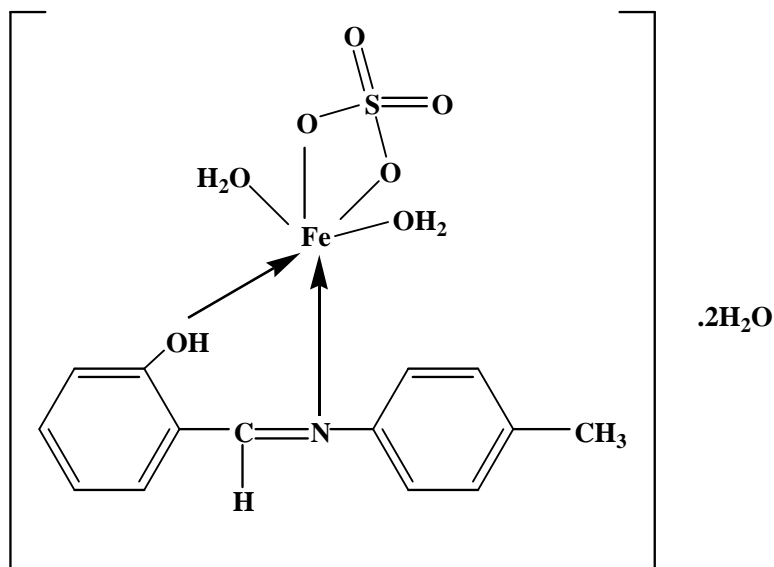
And bands at 3420 and 748cm^{-1} refers to both coordination and lattice H_2O molecules.

Table(3-2)
The most significant bands of FT-IR of the prepared
Ligands and Complexes

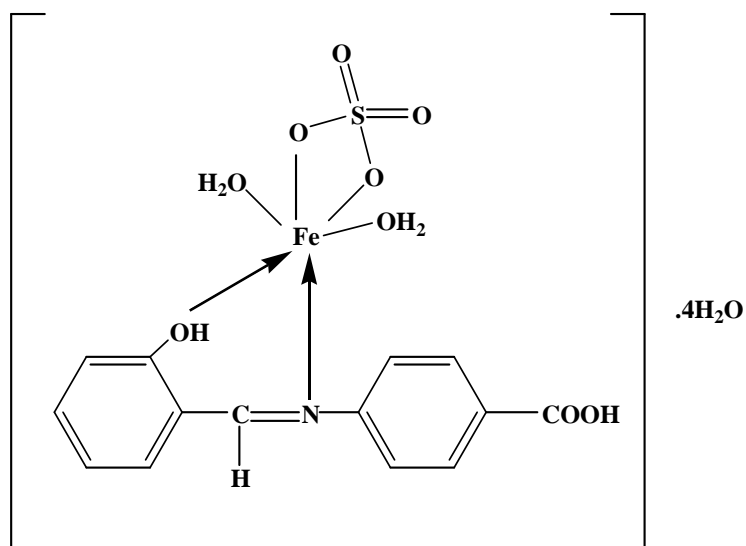
Symbol	ν (C=N)	ν (O-H)	ν (C-H)	ν (C-O)	ν (C=O)	ν (M-N)	ν (M-O)
LI	1624	3414	2850 2937	–	–	–	–
LII	1611	3480	2921	1273	1758	–	–
LIII	1626	3440	2923 2866	1261	1735	–	–
LIII	1639	3442	3050	–	–	–	–
AI	1600	3452	2838 2939	–	–	565	504
AII	1600	3462	2925 2850	1315	1751	553	507
AIII	1617	3460	2858 2928	1280	1750	545	506
AIII	1625	3420	2927	–	–	565	504

3.4 The structures of the Complexes:

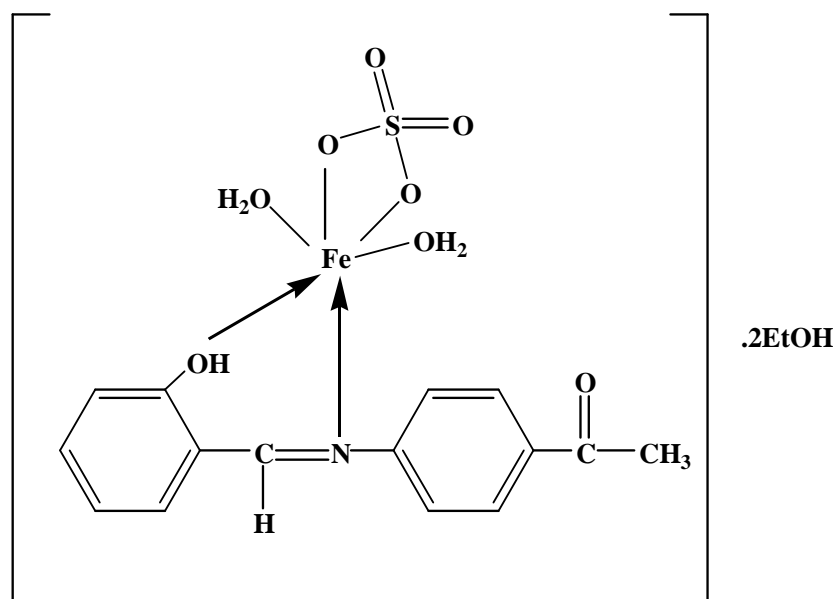
According to the results obtained by the FT-IR spectra and the results obtained by the Metal analysis, the following structures can be suggested for the prepared complexes, all of the structures were Octa hedral structures:



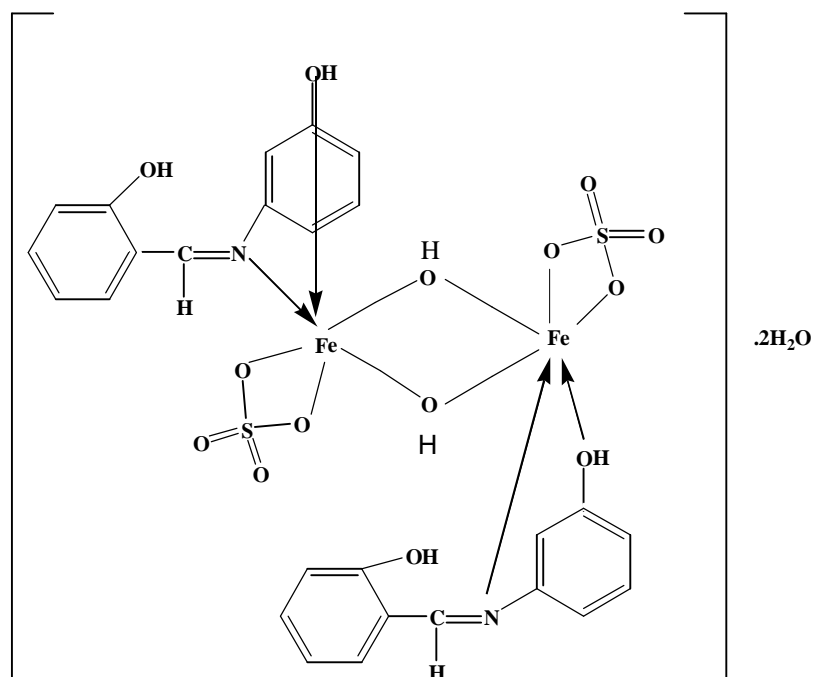
A(I) Complex



A(II) Complex



A(III) Complex



A(III) Complex

Chapter Three-Results and Discussion

Also according to these results, The following table for chemical formulas can be done:

Table (3-3)
Symbols, Formulas and Names of the prepared
Ligands and Complexes

Symbol	Chemical formula	Name
LI	$C_{14}H_{13}O$	4-(2-hydroxyl benzylidene) toluene.
LII	$C_{14}H_{11}NO_3$	3-(2-hydroxyl benzylidene) benzoic acid.
LIII	$C_{15}H_{13}NO_2$	4-(2-hydroxyl benzylidene) acetophenone.
LIII	$C_{13}H_{11}NO_2$	3-(2-hydroxyl benzylidene) phenol.
AI	$[Fe(LI)SO_4(H_2O)_2].2H_2O$	Di aquo sulfato[4-(2-hydroxyl benzylidene)toluene]iron(III). Dihydrate.
AII	$[Fe(LII)SO_4(H_2O)_2].4H_2O$	Di aquo sulfato[3-(2-hydroxyl benzylidene)benzoic acid]iron(III).Tetrahydrate.
AIII	$[Fe(LIII)SO_4(H_2O)_2].2EtOH$	Di aquo sulfato[4-(2-hydroxyl benzylidene)acetophenone]iron(III). Diethanol.
AIIII	$[Fe(LIIII)_2(SO_4)_2(OH)_2].2H_2O$	Di- μ -oxo[di hydroxo di-sulfato di bis 3-(2-hydroxyl benzylidene)phenol iron(III)].Di hydrate.

Chapter Three-Results and Discussion

3.5 Biological activity:

Two types of bacteria were chosen to study the effect of the synthesized compounds against them, the first one was the staphylococcus aureus bacteria as the gram positive bacteria, while the other was Escherichia coli as the gram negative bacteria.

And the following procedure was used for the two types:-

1-(0.005g) of the prepared compounds were taken.(of both ligands and complexes).

2-A- For the ligands they were dissolved by adding 1ml of distilled water, then adding 20 μ l of HCL(20%), then complete the volume to 2ml with distilled water.

B-For the complexes they were dissolved by adding 20 μ l of DMSO then complete the volume to 2ml with distilled water.

3- Adding about 50 μ l of the dissolved compounds to the holes were made in the Muller Hinton agar which contains the bacteria.

And the holes were 6mm. in diameter.

4- Put the Muller Hinton agar in 37°C for about 24 hours. Then reading the inhibition zones of the bacterial growth.

The results after 24 hours are shown below, in figures(3-9),(3-10),(3-11) and (3-12). And tables (3-4) and (3-5).

In figures (3-9) and (3-11), the numbers on the halls refers to:

Number 1: complex A(I), Number 2: complex A(II), Number 3: complex A(III) and Number 4: complex A(III).

While in figures (3-10) and (3-12), the numbers refers to:

Number 1: 4-(2-hydroxyl benzylidene)Toluene.

Number 2: 3-(2-hydroxyl benzylidene) benzoic acid.

Number 3: 4-(2-hydroxyl benzylidene)acetophenone.

Number 4: 3-(2-hydroxyl benzylidene)Phenol.

Chapter Three-Results and Discussion

Table(3-4)
Effect of Complexes on S.aureus and E.coli bacteria.

Complexes	Staphylococcus aureus	Escherichia coli
AI	+	+
AII	+++	+++
AIII	++	+
AIII	+++	+++

Table(3-5)
Effect of ligands on S.aureus and E.coli bacteria.

Ligands	S.aureus	E.coli
LI	—	—
LII	+	+++
LIII	—	+
LIII	+++	+++

The biological activity⁽⁴²⁾ for known antibiotic drugs against Staphylococcus aureus and E.coli are given below, which can be compared to the biological activity of the prepared compounds:-

Table (3-6)
Effect of Antibiotic drugs

Anti-biotic drugs	Staphylococcus aureus	Escherichia coli
Erythromycin	+++	-
Chloramphenical	+++	-
Tetracycline	+++	-
Ampicillin	+++	-
Fusidic acid	+++	-
Amoxicillin	+++	-
Neomycin	+++	++
Streptomycin	-	-

(-) No Inhibition.

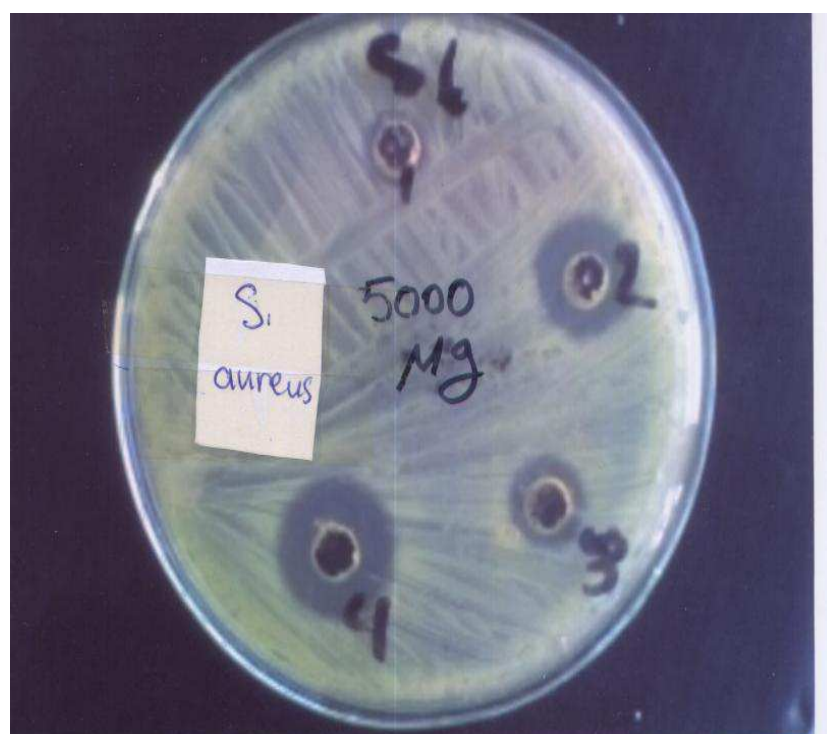
(+) Inhibition zone (8-10) mm.

(++) Inhibition zone (10-12) mm.

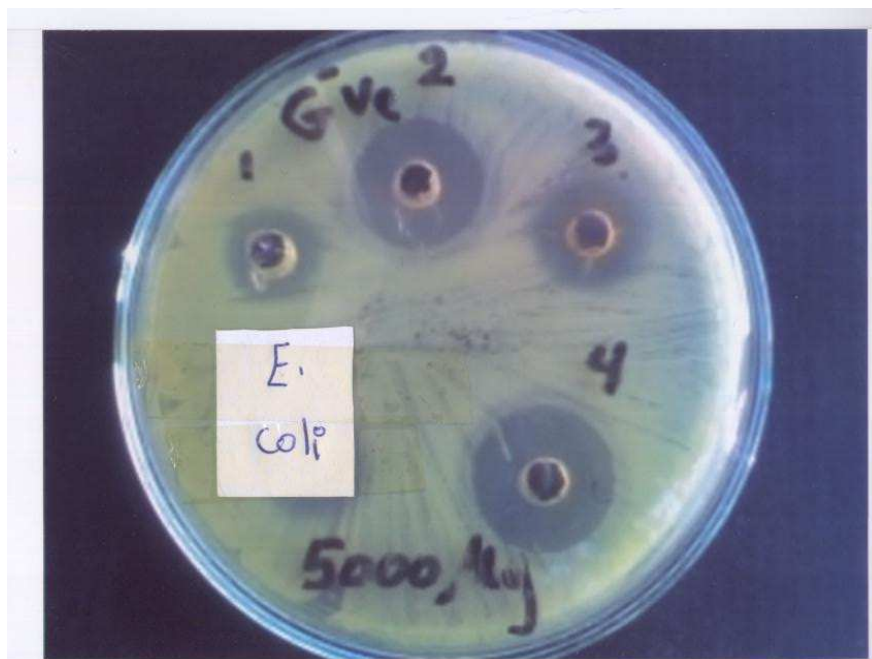
(++) Inhibition zone (>12) mm.



Fig(3-9) Effect of complexes on *S.aureus*.



Fig(3-10) Effect of ligands on *S.aureus*.



Fig(3-11) Effect of complexes on *E.coli* .



Fig(3-12) Effect of ligands on *E.coli* .

Chapter Three-Results and Discussion

Conclusion:-

The results obtained from measuring the inhibition zones of the bacterial growth for the *s.aureus* and *E.coli* bacteria showed that complexes A(II) and A(III) having the same inhibition zones against the *S.aureus* and *E.coli* bacteria.

While complexe A(I) also showed to has the same effect against the two types of bacteria, but it's inhibition zone was smaller than the inhibition zones of complexes A(II) and A(III).

Complex A(III) showed to has a larger inhibition zone against the *S.aureus* bacteria than it's inhibition zone against *E.coli* bacteria.

For the ligand 4-(2-hydroxyl benzylidene)toluene, it has no effect against the *S.aureus* and *E.coli* bacteria.

While 3-(2-hydroxyl benzylidene)benzoic acid showed to has a larger inhibition zone against *E.coli* rather than against the *S.aureus* bacteria.

4-(2-hydroxyl benzylidene)acetophenone showed to has an effect of (8-10)mm against *E.coli* bacteria, but it has no effect on the *S.aureus* bacteria.

Finally, 3-(2-hydroxyl benzylidene)phenol showed to has the same effect on both *s.aureus* and *E.coli* bacteria.

In general the complexes showed to have larger inhibition zones against the two types of bacteria than their corresponding ligands.

The mechanism of inhibition of the two types of bacteria was not studied but it might be one of the following:

1. Breaking of the bacterial cell wall.
2. Inhibition of DNA synthesis.
3. Inhibition of protein synthesis.

3.6 Suggestions for future work:

- 1-Other Schiff bases can be prepared instead of the Schiff bases of this work.
- 2-Or other salts can be used instead of the ferric sulfate di-hidrate salt,and then reacting it with the Schiff bases to form complexes.
- 3-The same prepared ligands and complexes in this work can be tested in vivo and it's selective toxicity can be measured.
- 4-Other types of bacteria can be used to measure the biological activity of the synthesized ligands and complexes.

Chapter Two-Experimental part

Chapter two Experimental part

2.1 Chemicals

Chemicals which have been used in the work are all listed below in table(2-1):-

Table(2-1)

Names,purity and source of chemicals used in the work

Chemical compound	It's purity(%)	Company
2-hydroxy benzaldehyde.	98	BDH
P-toluidine.	99.9	Fluka
m-amino benzoic acid.	98	Fluka
4-amino acetophenone.	99	Hyman limited
m-amino phenol.	99	Fluka
Absolute ethanol.	99.9	Hyman limited.
Hydrochloric acid.20%.	87.9	BDH
DMSO.	99	Fluka
Ferric sulfate dihydrate.	-	BDH

2.2 Techniques

2.2.1 Melting point:-

Melting points of all prepared compounds were recorded on hot stage

Gallen Kamp melting point apparatus.

2.2.2 Infrared spectrophotometer:-

The I.R spectra of the prepared compounds were recorded using *SHIMADZU* F.T.IR 8300 spectrophotometer Japan as *KBr* disk in the range(4000-600) cm^{-1} .

2.2.3 Metal analysis:-

The metal content of the complexes was measured using atomic absorption technique by *Pye unicam* of *Philips scientific instrument* which employed the hallow cathode lamp of *Pye unicam LTD.Cambridge*.

2.3.1 Preparation of ligands: **A-Preparation of 4-(2-hydroxyl benzylidene)Toluene:**

(0.57g,0.0040 mole)of 2-hydroxy benzaldehyde was mixed with (0.5g,0.004 mole)of p-toluidin,after dissolved in about(6 ml)of absolute ethanol,then the resulting solution of the mixed compounds was brought to reflux for about (3 hours).

The resulting product, after reflux, was cooled to room temperature and then filtered by using a filter paper,then the precipitate was washed with absolute ethanol so as to give a yellow product of about 70% yield, which has a melting point of 234°C .

B-preparation of 3-(2-hydroxyl benzylidene)benzoic acid:

(0.44g,0.0036 mole)of 2-hydroxy benzaldehyde,and(0.5g,0.0036 mole) of m-amino benzoic acid was mixed ,after dissolving the m-amino benzoic acid in a 10 ml solution of absolute ethanol,then the resulting solution was refluxed for about (5hours),when the red product was formed which was cooled to the room temperature,and filtered by a filter paper and finally washed with absolute ethanol to give about 68% yield,the melting point of the product was found to be 262°C.

C-preparation of 4-(2-hydroxyl benzylidene)acetophenone:

(0.45g,0.0036 mole)of 2-hydroxy benzaldehyde was mixed with (0.5g,0.0037 mole)of 4-amino acetophenone,after dissolved in about (8ml) of absolute ethanol and the resulting solution was brought to reflux for about(3 and a half hours).

The resulting product ,after reflux,was cooled to room temperature and filtered by using a filter paper , then the precipitate was washed

Chapter Two-Experimental part

with absolute ethanol to give an orange product product. With a percentage yield of 65% which has a melting point of 275°C.

D-Preparation of 3-(2-hydroxyl benzylidene)phenol:

(0.55g, 0.0045 mole) of 2-hydroxy benzaldehyde was mixed with (0.5g, 0.0045 mole) of m-amino phenol dissolved in 10 ml of absolute ethanol.

refluxed for about (4 hours), the resulting product was cooled to room temperature, and filtered, the precipitate was washed with absolute ethanol to give a yellow product of 72% yield, which has been found to have a melting point of 248°C.

In the preparation of the four ligands, when the final product was formed a recrystallization was done, by using a filter paper in a funnel, putting the product on the filter paper and adding the recrystallization solvent which was absolute ethanol in small quantities until the recrystallization was end.

Chapter Two-Experimental part

2.3.2-Preparation of the complexes:

All of the complexes were prepared according to the following procedure, except that there were some differences in the weights and number of moles of the ligands and the metal in each case, these differences are included in the table(2-2):-

Procedure:-

A suitable weights of the ligand was dissolved in (10 ml) of absolute ethanol, while the corresponding weights of the metal was dissolved in (2.5 ml) of absolute ethanol too.

Then they were mixed together and brought to reflux for about (1 to 2 hours), resulting product was cooled to the room temperature, and then it was filtered by using a filter paper, the precipitate was taken and washed with absolute ethanol to obtain a pure product of the complexes.

Table(2-2)
Number of moles and grams of ligands and metal in the
complexation reaction

Complex	X ₁	Y ₁	X ₂	Y ₂
AI	0.5g	0.00236	0.514g	0.00118
AII	0.5g	0.0020	0.452g	0.00103
AIII	0.5g	0.0020	0.455g	0.00104
AIII	0.5g	0.00234	0.511g	0.00117

Where:

X₁: grams of the ligand.

Y₁: number of moles of the ligand.

X₂: grams of the metal.

Y₂: number of moles of the metal.

Chapter Two-Experimental part

Contents:

Chapter One :Introduction :

1.1: Chemotherapy:

1.1.1 What is Chemotherapy?.....	1
1.1.2 Types of Chemotherapy.....	3
1.1.3 Dosage of Chemotherapy.....	7
1.1.4 Delivery of Chemotherapy.....	7
1.1.5 Side effects of Chemotherapy.....	8

1.2: Schiff bases :

1.2.1 What are Schiff bases?.....	10
1.2.2 Applications of Schiff bases.....	11
1.2.3 Some of the reactions of Schiff bases.....	11
1.2.4 Complexation of ligands with metal ions.....	13

1.3: Bacteria :

1.3.1 What are bacteria?.....	15
1.3.2 Bacteria benefits.....	16
1.3.3 Gram positive bacteria.....	17
1.3.4 Gram negative bacteria.....	18
1.3.5 What are Staphylococcus bacteria?.....	20
1.3.6 What are E. coli bacteria?.....	22

Chapter Two:Experimental part:

2.1 Chemicals.....	27
2.2 Techniques.....	27
2.3.1 Preparation of the ligands.....	28
2.3.2 Preparation of the complexes.....	30

Chapter Three:Results and discussion:

3.1 Physical properties of the prepared compounds.....	32
3.2 Preparation of the ligands	33
3.3 Infra-red spectra.....	35
3.4 Structures of the Complexes.....	49
3.5 Biological activity.....	52
3.6 Suggestions for future work.....	56

List of abbreviations:-

DNA: Deoxy ribonucleic acid.

RNA: Ribonucleic acid.

EDTA: Ethylene diamine tetra acetic acid.

DMSO: Di methyl sulfoxide.

S.aureus bacteria: *Staphylococcus aureus* bacteria.

E.coli bacteria: *Escherichia coli* bacteria.

List of figures:

<i>Number of Figure</i>	<i>It's name</i>
(1-1)	Arsphenamine
(1-2)	Penicillin
(1-3)	Mustard gas
(1-4)	Imatinib mesylate
(1-5)	Cis platin
(1-6)	Carboplatin
(1-7)	Oxalplatin
(1-8)	Cyclophosphamide
(1-9)	Chlorambucil
(1-10)	Azathioprine
(1-11)	Mercaptopurine
(1-12)	Folic acid
(1-13)	Fluorouracil
(1-14)	Sulfanilamide
(1-15)	Melphalan
(1-16)	Busulfan
(1-17)	Capecitabine
(1-18)	Shapes of bacteria
(1-19)	The range of sizes shown by prokaryotes, relative to those of other organisms and biomolecules

(1-20)	Peptidoglycan
(1-21)	Lysozyme
(1-22)	<i>S.aureus</i> bacteria
(1-23)	Methicillin
(1-24)	Oxacillin
(1-25)	Cloxacillin
(1-26)	<i>E.coli</i> bacteria
(1-27)	Life cycle of <i>E.coli</i> bacteria
(1-28)	Amoxicillin
(1-29)	Cephalsporins
(1-30)	Ciprofloxacin
(3-1)	FT-IR spectra of LI
(3-2)	FT-IR spectra of LII
(3-3)	FT-IR spectra of LIII
(3-4)	FT-IR spectra of LIII
(3-5)	FT-IR spectra of AI
(3-6)	FT-IR spectra of AII
(3-7)	FT-IR spectra of AIII
(3-8)	FT-IR spectra of AIII
(3-9)	Effect of complexes on <i>S.aureus</i>
(3-10)	Effect of ligands on <i>S.aureus</i>
(3-11)	Effect of complexes on <i>E.coli</i>
(3-12)	Effect of ligands on <i>E.coli</i>

List of tables:

<i>Number of table</i>	<i>It's name</i>
(2-1)	Names,purity and source of chemicals used in the work
(2-2)	No.of moles and grams of the ligands and ferric sulfate dehydrate salt in the complexation reaction
(3-1)	Physical properties for the prepared complexes
(3-2)	The most significant bands of FT-IR spectra of the prepared compounds

(3-3)	Symbols, formulas and names of the prepared ligands and complexes.
(3-4)	Effect of complexes on <i>S.aureus</i> and <i>E.coli</i>
(3-5)	Effect of ligands on <i>S.aureus</i> and <i>E.coli</i>
(3-6)	Effect of antibiotic drugs

References

- 1-Gralla R, de Wit R, Herrstedt J, Carides A, Ianus J, Guoguang-Ma J, Evans J, Horgan K "Antiemetic efficacy of the neurokinin-1 antagonist, aprepitant, plus a 5HT3 antagonist and a corticosteroid in patients receiving anthracyclines or cyclophosphamide in addition to high-dose cisplatin: analysis of combined data from two Phase III randomized clinical trials". Cancer **104** (4):864-8,(2005).
- 2- Tramer MR, Carroll D, Campbell FA, Reynolds DJ, Moore RA, McQuay HJ." Cannabinoids for control of chemotherapy induced nausea and vomiting".p22,Vol 34,(2001).
- 3- Tannock IF, Ahles TA, Ganz PA, Van Dam FS." Cognitive impairment associated with chemotherapy for cancer",p(45),Vol.51(2004).
- 4-A.A.H. Saeed,Journal of chemical and engineering data,vol.29 No.3,359(1984).
- 5-A.Jarrahpour,M.Zarei,Molbank,M 352 Open access publication,p89,Vol.45, (2004).
- 6-S.patai,"the chemistry of carbon-nitrogen double bond"John Wiley and sons,New York(1979).
- 7-A.A.H.Saeed,M.N.AL-Zagoumand,and M.H.Walton,"preparation of the carbon nitrogen double bond".p(34),Vol.50,(1980).
- 8-H.A.Staab,Ber."Preperation of Schiff bases",98(8),2681(1965).

References

- 9-J.March"advanced organic chemistry"3rd edition,John Wiley and sons,New York(1985).
- 10-F.P.Dwyer and D.P.Mellor,"chelating agents and metal chelates" Academic press,New York,P45,Vol67,(1964).
- 11-D.P.Freyberg,and G.M.Mockler,J.chem.soc.Dalton Trans,5,445(1976).
- 12-J.A.Goodiwn,and L.J.Wilson,Inorg-chem.,28,42(1989).
- 13-Joe.Richard. University of florida's lakewatch,"*Graduate student studies,Bacteria in lakes*",p34,Vol 78,(2003).
- 14-Ryan KJ,Ray CG(editors), Sherris McGraw Hill,Microbiology,4th edition,p.232.(2004).
- 15-Baron,Samuel" medical microbiology" 4th edition.
The university of Texas,medical branch of Galviston.(1996).
- 16-Madigan,Martinko J(editors)" Brock biology of microorganisms",11th edition;Prentice Hall.p20,Vol 48,(2005).
- 17-Ogston A. "*An abscesses classics in infections diseases*",p(23),Vol.45,(1984).
- 18-Ryan KJ,Ray CG(editors) " Sherris medical microbiology",4th ed. McGraw Hill,(2004).

References

- 19-Curran JP,Al-Salihi FL.,"*Meonatal staphylococcal scalded skill syndrome massive outbreak due to an unusual phage type*",p(22),Vol.12,(1980).
- 20-Michael A.Grant"Eunmeration of E.coli and the coliform bacteria"bacteriological analytical manual(8th)ed,p(30),Vol.20,(2003).
- 21-Peter Feng."*E.coli,CDC division of bacterial and mycotic diseases*".p(12),Vol (67),2007.
- 22-Johnson J,Kuskowski M,Menard M,Gajewski A, Xercavins M,Gran J.
"similarity between human and chicken E.coli isolates in relation to ciprofloxacin resistance status",P50,Vol 38,(2006).
- 23-Christie,Tim"*tests suggest E.coli spread through air*",P(34),Vol.65,(2001).
- 24-Salton MRJ,Kimks.'introduction to biological systems" Baron's medical microbiology,p(54),Vol 45,
University of Texas medical branch(1996).
- 25-"An introduction to biochemistry",Trudy Mckee and James R.Mckee
p34,Vol 50,(1996).
- 26-Fredrickson J,Zachara J,Balkwill D."Geomicrobiology of high-level nuclear waste contaminated vadose sediments at the hanford site",Washington state,p(65),Vol 72,(2004).

References

- 27-Whitman W,Coleman D,Wiebe W., "Prokaryotes:the unseen majority"John wiley and sons,(1998).
- 28-Sears C, "*A dynamic partner ship:celebrating our gut flora*",P(12),Vol 25,(2005).
- 29-Ishige T,Honda K,Shimizu S.,"Whole organism biocatalysis",p87,88,Vol.23.(2005).
- 30-Frampton,E.W.(WHO:world health organization), mortality data accessed 20 January 2007.
- 31-Izumi,Yoshio,and Isozumi, "Modern Japanese medical history and the European influence",p34,Vol.16.(2001).
Keio journal of medicine.
- 32-Taggi A.E.,Hafez A.M..Wack H.,Young B,Ferroris D,Lectka T, " The Development of the first catalysed reaction of ketens and imines"
J.American chem.. Soc (54),vol.25.(2002).
- 33-Karia F.D.,Parsania P.H.,"Synthesis,biological and thermal properties of some Schiff bases". Asian J.chem,(32),Vol.21.(1999).
- 34-More P.G.,Bhalvankar R.B.,Pattar S.C.,"Synthesis and biological activities of Schiff bases of amino thiazoles".J.Indian chem..Soc (2001).
- 35-Pandya S.N.,Sriram D,Nath G.,De Clercq E. "Synthesis and antimicrobial activity of schiff and Mannich bases of istain and it's derivatives with pyrimidine"p46,Vol.25,1999.

References

- 36-Baseer M.A.,Jadhav V.D.,Phule R.M.,Archana Y.V., Vibhute Y.B.
"Synthesis and antimicrobial activity of some new Schiff bases, Orient
J.chem,p(55),Vol(19). 2000.
- 37-Singh W.M.,Dash B.C. "Synthesis of some new Schiff bases
containing thiazole and oxazole nuclei and their fungicidal activity",
p(54),vol.(34),(1988).
- 38-Hodnett E.M., and Dunn W.J. "Structure-antitumour activity
correlation of some Schiff base". J.Med.Chem.(22-24),Vol.12(1970).
- 39- Kimpharmzh,"Chem.Abst".110,173068(1989).
- 40-*American cancer Society*, <http://www.Cancer.org>.
- 41-"The organic chemistry of drug design and drug action",(2nd.ed.)
R.B.Silverman,P(25),Vol.67,2004.
- 42-Ahmed Sabeeh,M.Sc. Thesis,Al-Nahrain University(1997).
- 43-R.Padmaja,Shukla and M.Akilesh Jaiswal. **J.Indian chem..Soc.LX.**
546,(67),Vol 51.(1983).
- 44-P.S.PrabhuandS.S.Dodulad,**J.Indianchem.Soc.LX,(71)**,Vol.56,
(1983).
- 45-V.K.Agrawal,R.P.MaheshandSingh,**J.Indianchem.Soc.**(34),Vol.46
(1981).
- 46-A.Abl Ali and B.shaubani,Acta. Chem.. Slov.,47,363(2000).
- 47-R.M. Silverstein,G.C.Bassler and T.C. Morrill,"Spectrometric
identification of organic chemistry" John wilely and sons,(1981).
- 48-B.Stuart,W.George and P. McIntyre,"Modern infrared spectroscopy"
New York,p(45),Vol.89,(1996).

References

- 49-H.L.Singh,M.SharmaandA.K.Varshney,Metorg.Chem.p(45),Vol.95,
(1999).
- 50-K.Nakamoto "Infrared and Raman Spectra of
InorganicandCoordination Compounds"4th. Ed.Wiely int.New
York,p45,Vol.87,(1986).
- 51-K.Nakamoto,J.Fujita,S.Tunaka and M.Kobayashi,J.Am.Chemical Soc.
P54,Vol. 16.(1957).
- 52-A.Ouchi,T.Takeuchi and I.Taminage,Bull Chem.Soc.Japan 43,2840-
2844 (1970).
- 53-M.Vazquez,M.R.Bermejo,M.Foundo,A.Garcia-Deibe,A.M.Gonzalez
and R.Pedrid,Appl.Organomet.Chem,(45),Vol.67,(2002).
- 54-F.A.Cotton and G.Wilknson,"Advanced inorganic chemistry" John
Wiely and sons.4th.ed.(1980).

CHAPTER THREE
RESULTS AND DISCUSSION

REFERENCES

CHAPTER TWO
EXPERIMENTAL PART

CHAPTER ONE

INTRODUCTION