Shendi University

Faculty of Graduate Studies and Scientific Research

Synthesis, Characterization and Biological Activity of Some Mannich Bases and their Metal Complexes

تحضير وتوصيف والنشاط البيولوجي لبعض قواعد مانخ ومعقداتها الفلزية

By

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إستهلال

بسم الله الرحمن الرحيم

{لَا يُكَلِّفُ اللَّهُ نَفْسًا إِلَّا وُسْعَهَا لَهَا مَا كَسَبَتْ وَعَلَيْهَا مَا اكْتَسَبَتْ رَبَّنَا لَا تُؤَاخِذْنَا إِنْ نَسِينَا أَوْ أَخْطَأْنَا رَبَّنَا وَلَا تَحْمِلْ عَلَيْنَا إِصْرًا كَمَا حَمَلْتَهُ عَلَى الَّذِينَ مِنْ قَبْلِنَا رَبَّنَا وَلَا تُحَمِّلْنَا مَا لَا طَاقَةَ لَنَا بِهِ وَاعْفُ عَنَّا وَاغْفِرْ لَنَا وَارْحَمْنَا أَنْتَ مَوْلَانَا فَانْصُرْنَا عَلَى الْقَوْمِ الْكَافِرِينَ (286)} صدق الله العظيم

(سورة البقرة الاية:(286))

Dedication

To my

parents,
brothers, Sisters

Acknowledgements

Praise to Allah Almighity for given me the strength and health to complete this work .

I would like to express my immense gratitude and appreciation to my supervisor Dr. Mohammed Sulieman Ali Eltoum for this helpful suggestion and close supervision through the study.

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Abbreviation list

MBB: Morpholinobenzoylbenzamide

MBA: Morpholinobenzoylacetamide

MSA: Morpholinosalicylacetamide

DMSO: Dimethyl sulphoxide

IR: Infra-red Spectroscopy

UV/Visible: Ultra violet and visible spectroscopy

CBC : Covalent bond Classification

NVE : Number of valence Electron

T.B: Tuberculosis

HIV: Human immune deficiency virus

NTA: Nitrile tri acetic acid

EDTA: Ethylene di amine tetra acetic acid

DTPA: Diethylene tri amine penta acetic acid

MLCT: Metal-to-Ligand Charge Transfer

LMCT: Ligand to Metal Charge Transfer

CNMR:Carbon-13Nuclear magnetic resonance

HNMR: Hydrogen-1Nuclear magnetic resonance

MSB: Morpholinosalicylylbenzohydrazide

XRD: X-ray diffraction

SEM: Scanning electron microscope

Abstract

Copper Cu(II),Cobalt Co(II) and Zinc Zn(II) ion complexes of the ligands morpholinbenzoyl benzamide(MBB),morpholinobenzoylacetamide (MBA) and morpholinosaliccylacetamide (MSA) were prepared and different analytical techniques such as Ultra Violet and visible Spectroscopy (UV/vis) and Infra-Red Spectroscopy (IR) were used to characterize the products obtained. The obtained result of the complexes indicate the existence of bidentate nature of ligands, which undergo coordination to metal ions with oxygen, nitrogen donor atom .The antimicrobial activity of the ligands morpholinobenzoylbenzamide(MBB), morpholinobenzoylacetamide(MBA) and morpholinosalicylacetamide(MSA) and its Co (II), Cu (II) and Zn (II) complexes were conducted against various microbes such as Gram Positive species *Staphlococcus aureus*, *Enterococcus fecalis,Bacillus cerus* and Gram negative *Escherichia coli, Salmonella typhi* ,and *Pseudomonas,* effects of the investigated compounds have been tested by the disc diffusion method. A comparative study of inhibition values of the ligands and their complexes indicated that the biological activity of the ligands alone and with its complexes, some ligands had lower activity than their complexes form and other have higher than complexes. some complexes have higher activity in comparison with ligand activities some complexes had lower activity and other complexes showed no activity against some type of bacteria .

ligands like(MBB) had no activity against *Salmonella typhi*, *Escherichia coli* and *Staphlococcus aureus*, *Enterococcus fecalis*.(MBA) had no activity against *Pseudomona*s, *Salmonella typhi, Staphlococcus aureus*, *Enterococcus fecalis,Bacillus cerus*.

المستخلص

معقدات أيونات النحاس(II) ,الكوبالت(II) ,الزنك(II) مع اللواقط morpholinbenzy benzamide (MBB), morpholinobenzylacetamide (MBA) and morpholino saliccylacetamide (MSA).

تم تحضيرها وتحليلها بتقنيات مختلفة مثل جهاز الاشعة فوق البنفسجية والمرئية وجهاز الاشعة تحت الحمراء استخدمت لتشخيص الناتج المتحصل عليه. المعقدات الناتجة تشير الى وجود لواقط ثنائية المنح والتي تمنح عن طريق مواقع ذرات الاوكسجين والنيتروجين.النشاط المضاد للميكروبات للواقط ومعقداتها من النحاس والكوبالت والزنك اجريت ضد ميكروبات مختلفة مثل بكتريا موجبة مثل *Staphlococcus aureus, Enterococcus fecalis,Bacillus cerus* وبكتريا سالبة مثل *Escherichia coli* ,and *Pseudomonas Salmonella typhi* تم التحقق من تأثيرالمركبات اختبرت بطريقة الانتشار القرصي.واشارت الدراسة مقارنة بقيم التثبيط بين قواعد مانخ ومعقداتها أن بعض اللواقط اقل نشاط من المعقدات المتكونة وبعضها اعلى من المعقدات. بعض المعقدات لهانشاط عالي مقارنة مع اللاقط وبعض المعقدات لها نشاط اقل واخرى ليس لها نشاط ضد بعض انواع البكتريا.

أن اللاقط (MBB) لم يعطي نشاط مع بكتريا *Salmonella typhi,Escherichia coli* and *Staphlococcus aureus, Enterococcus fecalis* واللاقط (MBA) لم يعطي نشاط مع بكتريا *Pseudomonas, Salmonella typhi, Staphlococcus aureus, Enterococcus fecalis ,Bacillus cerus*.

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CHAPTER ONE

Introduction and Literature review

Chapter One

Introduction and Literature Review

1.General Introduction of Coordination compounds:

Coordination Compounds are molecules or ions in which a central atom has ligands (atoms or molecules) attached to it, and the number of bonds to the central atom (its coordination number) is not equal to the valence. Coordination compounds may be charged or uncharged. The central atom may be any element, but it is usually a metal atom. Every central metal atom has a charge, also known as the oxidation state. The charge is usually zero or positive, but it can be negative. Coordination numbers can range from 2 to 12, and they usually exceed its oxidation state. Coordination compounds are often called metal complexes or simply complexes[1].

1.1. Coordination Complex

a coordination complex consists of a central atom or ion, which is usually metallic and is called the coordination centre, and a surrounding array of bound molecules or ions, that are in turn known as ligands or complexing agents[2,3]. Many metal-containing compounds, especially those of transition metals, are coordination complexes[4].The central atoms or ion and the donor atoms comprise the first coordination sphere. Coordination refers to the "coordinate covalent bonds" between the ligands and the central atom. Some metal complexes are formed virtually irreversibly and many are bound together by bonds that are quite strong[5][6].

1.2. The Chemistry of Transition Elements:

The IUPAC definition[3] defines a transition metal as "an element whose atom has a partially filled d sub-shell, or can give rise to cations with an incomplete **d** sub-shell". Many scientists describe a "transition metal" as any element in the d-block of the periodic Table, which includes groups 3 to 12 on the periodic Table[7][8]. In actual practice, the f-block lanthanide and actinide series are also considered transition metals and are called "inner transition metals" .Cotton and Wilkinson [9] expanded the brief IUPAC definition by specifying which elements are included. As well as the elements of groups 4 to 11, they add scandium and yttrium in group 3 which have a partially filled d sub shell in the metallic state. These last two elements are included even though they do not seem to possess the catalytic properties which are so characteristic of the transition metals in general. Lanthanum and actinium in Group 3 are however classified as lanthanides and actinides respectively. English chemist Charles Bury (1890-1968) first used the word transition in this context in 1921, when he referred to a transition series of elements during the change of an inner layer of electrons (for example n=3 in the 4th row of the periodic table) from a stable group of 8 to 18, or from 18 to 32 [10-12].

1.3. Characteristic properties of Transtion Element:

There are a number of properties shared by the transition elements that are not found in other elements, as aresults of the partially filled d shell. These include:

1- the formation of compounds whose colour is due to d-d electronic transitions.

2 - The formation of compounds in many oxidation states, due to the ,relatively, low energy gap between different possible oxidation states [13].

3- The formation of many paramagnetic compounds due to the presence of unpaired d electrons[14].

The transition elements are dense, heavy, high melting and boiling points. The high density is accounted by the, relatively, small atomic radius e.g.: in the first transition series the largest atom is that of scandium with an atomic radius ($1.44x10^{-11}$pm), which is appreciably smaller than that of the calcium atom ($1.74x10^{-11}$pm). The high melting and boiling points are due to strong inter-atomic bonding which involve the participation of both 4s and 3d electrons. Along a particular transition series there is little variation in atomic radii with a slight contraction from (1.22×10^{-11} to $1.15x10^{-11}$pm). This ,partially, explains why these elements are used in the production of alloysteels[15][16].The majority of transition metal ions are coloured. However, hydrated $Sc^{3+}$and Zn^{2+}ions are non transitional since they have respectively nine and ten 3d electrons. These ions are colour less. The colour of a particular transition metal ion depends upon the nature of the ligands (either neutral molecules such as water which contains lone pairs, or negative ions) bonded to the ion. The pale blue hydrated copper (II) ion

changes to dark blue in the presence of ammonia and to green if sufficient chloride ions are added. Copper (II) chloride solution is, therefore, either blue or green depending upon the relative concentration of water molecules and chloride ions [17].

$$[Cu(H_2O)_6]^{2+} + 4CL^- \rightarrow [CuCL_4]^{2-} + 6H_2O$$

Pale Blue Green

The variable oxidation states displayed by transition elements are primarily due to the fact that successive ionization energies of a transition metal atom increase gradually. Metals, which have only one oxidation state, have a noticeable break in the values of successive ionization energies. The ionization energies of a transition metal atom such as vanadium, however, increase more gradually without any distinct breaks,

$$\xrightarrow{V\,648}\ V^{+}\xrightarrow{1367}\ V^{+2}\xrightarrow{2858}\ V^{+3}\xrightarrow{4634}\ \cdots\cdots\text{KJ/mole}$$

Except for scandium, which has exclusively an oxidation state of (+3), the first transition series elements show- an oxidation state (+2) when both 4s electrons are involved in bonding. For oxidation states greater than (+2), 3d electrons are used in addition to 4s electrons. In general the lower oxidation states are reducing and metal gives, predominately, basic oxides (MnO) (+2) and the higher oxidation states are oxidizing and metal gives ,predominately, acidic oxides (+7). The catalytic activity of transition metals and their compounds is associated with their variable oxidation states. Catalysis at a solid surface involves the formations of : bonds between the reactant molecules and the surface atoms of catalyst ,the first transition series elements have 3d electrons in addition to the 4s electrons which can be

utilized in bonding. This has the effect of increasing the concentration of the reactant at the catalyst surface, also of weakening the bonds in the reactant molecules, i.e. the activation energy is lowered[18].Most substances are,weakly, repelled by a strong magnetic field (diamagnetic), while some are, weakly, attracted by it (paramagnetic). If the force of attraction is very large the substance is said to be ferromagnetic e.g. iron, cobalt and nickel.The main compound of the transition metal form is a complex compound. A complex ion is one that contains a central ion or atom linked to other atoms, ions or molecules which are called ligands. Ligands attached to the central metal by more than one point of attachment are called chelating ligands and these ligands are called multidentate, and their complexes are called chelates, the ligand directly bound to the metal are said to be in the inner coordinating sphere, the ions that balance out of the charge remaining-on the complex after the coordination number of the central metal has been "satisfied" are said to be outer sphere ions[17].

1.4.The ligand:

In coordination chemistry, a ligand is an ion or molecule (functional group) that binds to a central metal atom to form a coordination complex. The bonding with the metal, generally, involves formal donation of one or more of the ligands electron pairs. The nature of metal–ligand bonding can range from covalent to ionic. Furthermore, the metal–ligand bond order can range from one to three. Ligands are viewed as Lewis bases, although rare cases are known to involve Lewis acidic "ligand”[19][20].ligands are most conveniently, classified according to the number of potential donor atoms which they contain and are known as uni- bi- ter- quadric- quinqi- and sexi-dentate [21]. the CBC method seeks to classify a molecule according to the

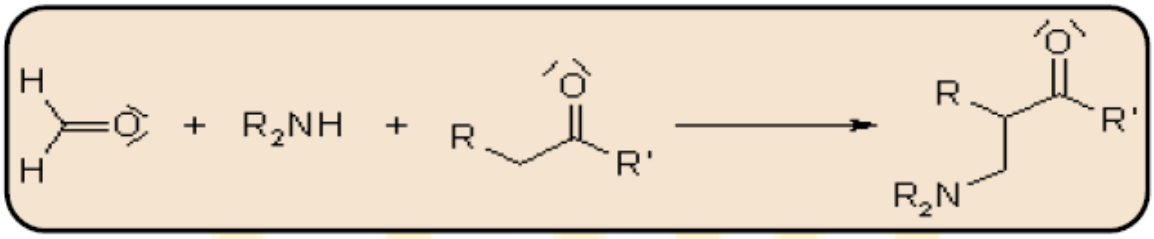
nature of the ligands around the central element of interest. The method is based on the notion that there are three basic types of interaction by which a ligand may bond to a metal center and the ligand is classified according to the nature and number of these interactions. The three basic types of interaction are represented by the symbols L, X, and Z, which correspond respectively to 2-electron, 1-electron and 0-electron neutral ligands and are clearly differentiated according to a molecular orbital representation of the bonding[22]. Another type of ligand worthy of consideration is the LX ligand which as expected from the used conventional representation will donate three electrons if NVE (Number of Valence Electrons) required. Example is alkoxy ligands (which are regularly known as X ligand too). L ligands are derived from charge-neutral precursors and are represented by amines, phosphines, CO, N_2, and alkenes. X ligands are ,typically, derived from anionic precursors such as chloride but includes ligands where salts of anion do not really exist such as hydride and alkyl. Thus, the complex $IrCl(CO)(PPh_3)_2$ is classified as an MXL_3 complex. The oxidative addition of H2 to $IrCl(CO)(PPh_3)_2$ gives an $18e^-$ ML_3X_3 product, $IrClH_2(CO)(PPh_3)_2$. $EDTA^{4-}$ is classified as an L_2X_4 ligand, as it features four anions and two neutral donor sites [23].

1.5. Mannich bases as ligand:

Carl Ulrich Franz Mannich (March 8, 1877 in Breslau – March 5, 1947 in Karlsruhe) was a German chemist. From 1927 to 1943 he was Professor for pharmaceutical chemistry at the University of Berlin. His areas of expertise were keto bases, alcohol bases, derivatives of piperidine, papaverine, lactones and also Digitalis-glycosides.The Mannich reaction was named after his discovery of the mechanism in 1912[24].Mannich visited High

school in Weimar and later on in Berlin where he left without reaching the school graduation. He took an internship at a pharmacy in Berlin instead. From 1898, he studied in Marburg and Berlin and received his doctorate in 1903 in Basel. In 1905 he did his matriculation examination and made the state examination for food chemistry. 1907 he completed his habilitation at the University of Berlin in 1910 after which he was appointed to an extraordinary Professor. From 1911 till 1917 Mannich became extraordinary Professor for Pharmaceutical Chemistry in Göttingen and went., (1920) to Frankfurt.Between 1927 and 1943 Mannich was Professor of Pharmaceutical Chemistry at the University of Berlin[25].Mannich is well known for his discovery of a special form of amino alkylation which was named after him Mannich reaction[24].Synthetic organic chemistry is one of the most developing, expanding and successful branches of science. During the last fifteen years, synthetic organic chemistry has seen enormous growth, not only in terms of development of new methodologies for construction of carbon-carbon and carbon-hetero atom bonds but also in terms of development of new strategies, reagents, catalysts, transformations and technologies. From the survey of existing literature. it appears that Mannich bases have played a vital role in the development of synthetic organic chemistry. It is well known, from the literature, that compounds containing amide moiety as a functional group have been found to possess donor properties and exhibit a wide range of biological activities[26].Mannich bases, beta-amino ketones carrying compounds, are the end products of Mannich reaction[27,28]. Mannich reaction is a nucleophilic addition reaction which involves the condensation of a compound with active hydrogen with an amine (primary or secondary) and formaldehyde (any aldehyde)Scheme1.1[29].

1.6. Mannich reaction:

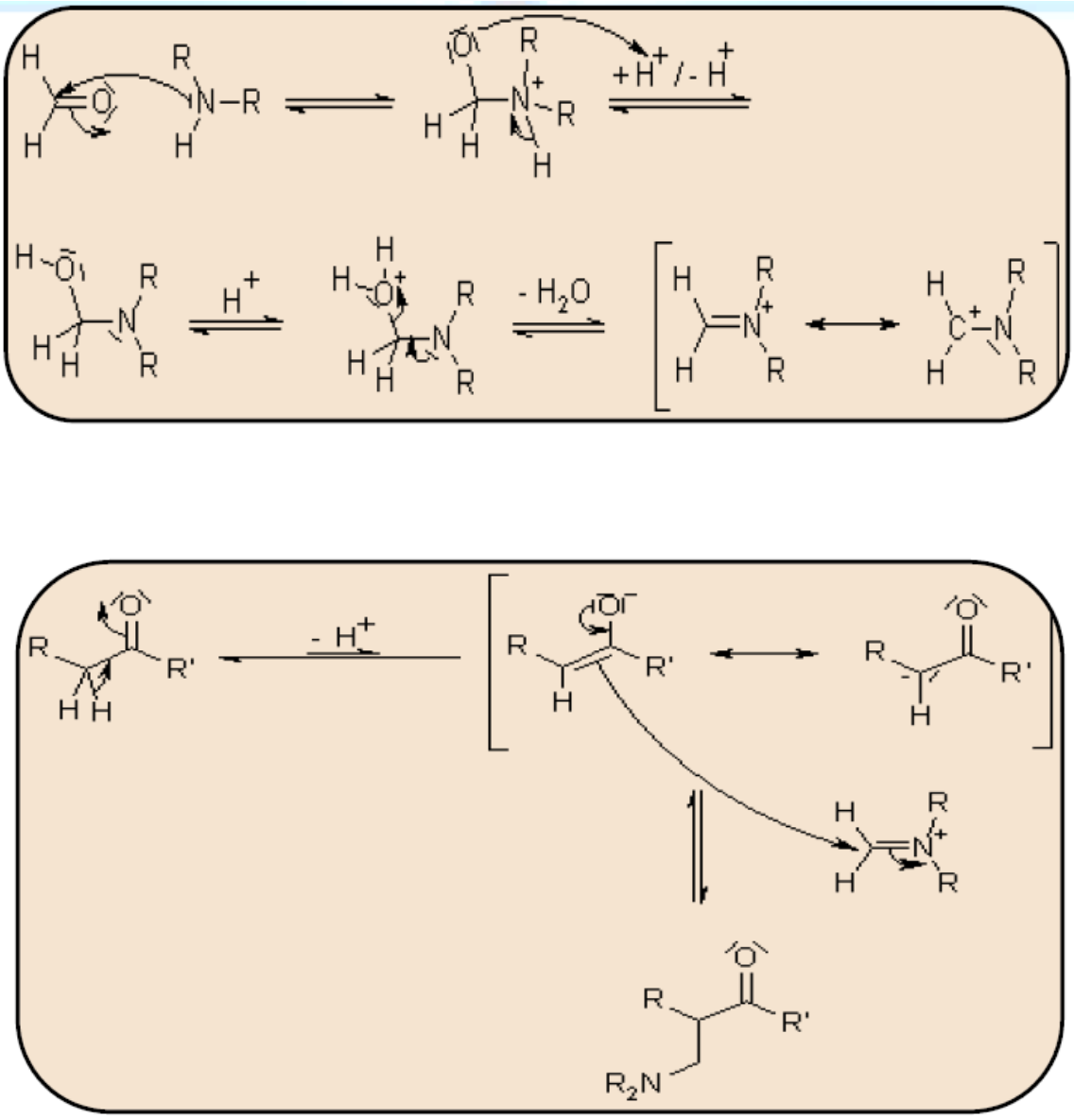


Scheme 1.1Mannich reaction

In 1912, Carl Mannich has investigated this reaction Scheme1.1. Today, due to its wide range of biological activities, much interest has been focused on this reaction. Mostly, they are found to be antineoplastic, analgesic and antibiotic agents. Mannich bases are also employed as an intermediate in industrial chemical synthesis Mannich bases containing bridged N-atom exhibit pronounced biological activities. The study of Mannich reaction attracted a great deal of attention to the chemists because it plays a vital role owing to their wide range of pharmacological and industrial applications. Mannich bases are also employed as intermediate in chemical synthesis. Mannich base derivatives with bridge N-atom have been found to be potent drug in medicinal science and possess wide range of biological activities like Anti inflammatory, Antifungal, Antitumor, Analgesic, Cytotoxic Anticancer, Antibacterial, Antipsychotic, Tranquilizer, Antileishmanial, Antimalarial[30],etc.Mannich bases have gained important because of their technological applications in polymer chemistry[31].Mannich bases compounds with the general formula ($R\text{-}CH_2NR_2$) are an important class of ligands in coordination chemistry and have been studied intensively , mainly because of their application in organic synthesis , pharmaceutical, industrial and polymer chemistry [32,33].Mannich bases also act as important

pharmacophores or bioactive leads which are further used for synthesis of various potential agents of high medicinal value which possess amino alkyl chain. The examples of clinically useful Mannich bases which consist of amino alkyl chain are cocaine, fluoxetine, atropine, ethacrynic acid, trihexyphenidyl, procyclidine, ranitidine, biperiden [34-36]. Mannich base complexes have remained an important and popular area of research due to their simple synthesis, adaptability, and diverse range of applications. From the survey of existing literature, it appears that metal complexes of Mannich bases played a vital role in the development of coordination chemistry[37].The most important applications of Mannich bases are in the field of pharmaceutical products[38,39]. Studies have revealed that Mannich bases show good anticancer[40], anti mycobacterial[41], remarkable anti-HIV and anti tubercular activities[42]. The presence of the basic Mannich side-chain has shown marked antimalarial[43], anti-inflammatory, analgesic[44,45], and antimicrobial activities[46]. Imidazole nucleus is also a major component of a variety of drugs such as angiotensin II receptor antagonists, oral anti-inflammatory agents, protein kinase inhibitors and fungicides[47] It is, frequently, found as a part of a large number of biologically and medicinally, significant substances[47,48].

1.7. Mechanism of Mannich reaction:

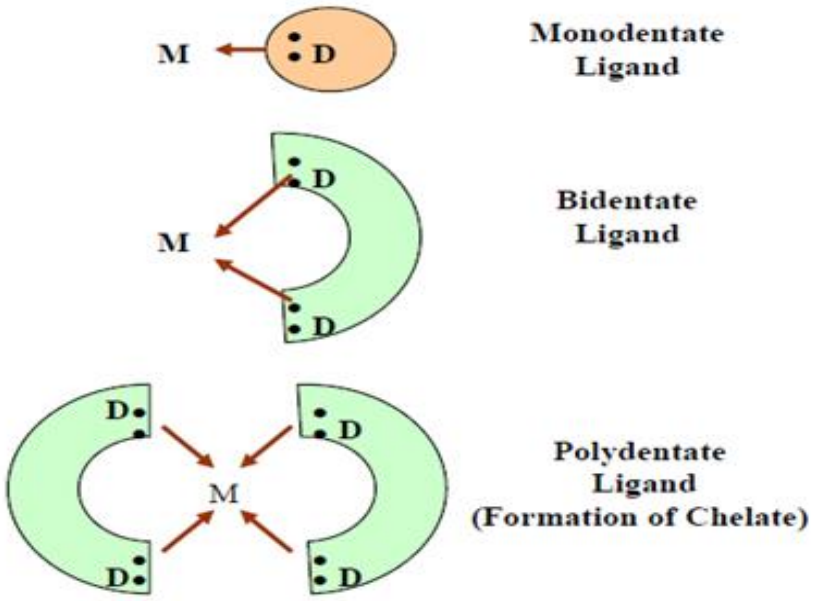


Scheme 1. 2. Mechanism of Mannich reaction

1.8.Mannich base as chelation agent:

Organic chelating agents containing amide moiety as a functional group have a strong ability to form metal complexes and exhibit a variety of biological activities such as antibacterial, antifungal, anti T.B activity, anti HIV activity, antiviral, antiulcer, anti-hypertensive[49-55]. The number of studies have been done in the various Mannich base complexes formed by the condensation of secondary amines with different aldehydes and amides[56-59].Although the concept of chelation is based on simple coordination chemistry, evolution of an ideal chelator and chelation therapy that ,completely, removes specific toxic metal from desired site in the body involves an integrated drug design approach. Chelating agents are organic or inorganic compounds capable of binding metal ions to form complex ring-like structure called 'chelates'. Chelating agents possess "ligand" binding atoms that form either two covalent linkages or one covalent and one co-ordinate or two co-ordinate linkages in the case of bidentate chelates. Mainly atoms like S, N and O function as ligand atoms in the form of chemical groups like –SH, –S-S, –NH2, =NH, –OH, –OPO3H, or >C=O. Bidenate or multidentate ligands form ring structures that include the metal ion and the two-ligand atoms attached to the metal(Scheme1.3)[60]. Many donors act as bidentate ligands. Five-membered chelate rings are ,specially, stable and they are often formed by ligands with YCCY skeletons such as Y-CH2-CH2-Y, Y-CO-CH2-Y *etc.* where Y is OR, NR2, O, S, NR, *etc.* There are, also, examples of inorganic chelate ligands which form five-membered ring with metal ions. Other types of chelating ligands are possible, like EDTA4−, which is a hexadentate ligand. In the simplest case a proton (H+) that can absorb the lone pair of electrons of ligand-binding atom(s) of the chelator may be involved in the coordination complex formation. However, the

positive charge on proton remains since there is no loss or gain of electrons in the process



Scheme 1.3.Formation of metal ligand complexes using mono, bi,and polydentate ligands

The latter may also be known as the 'net ionic charge' of the complex, which plays a crucial role in governing the pharmacokinetic fate and, ultimately, the toxicological behavior of such complexes *in vivo.* In the biological environment metal cations eg:Na+, Mg+, Cu+, Cu2+, and Zn2+ and specially the transition metals Mn, Fe and Co may be involved in such complex formation. Although the stability of such complexes varies, the deciding factors are based on the properties of both the chelating agent and the chelated metal. The stability constant of a complex can be, quantitatively, expressed in equilibrium equation values, which depend on the atomic structure of the chelated metals.

Further, pH is also an important factor influencing complex formation and stability. Most chelating agents are unstable at low pH, whereas at high pH metals tend to form insoluble hydroxides which are less accessible to chelating agents. This feature becomes significant in pathological conditions leading to acidosis or alkalosis[61].

Optimally, effective chelation can be achieved by virtue of some combination of the basic properties of both metal ions, chelating agents and the resulting metal complex. A chelating agent that will occupy more of the coordination positions of a metal ion will, generally (but not always) give a complex of greater stability than otherwise. Similarly, whereas the net ionic charge of the chelator defines its absorption, distribution and ability to reach the metal ion for binding; the net ionic charge of the complex decides its elimination from the specific site and excretion from the body. Thus, it is important that a chelator satisfy criteria that allow it to:

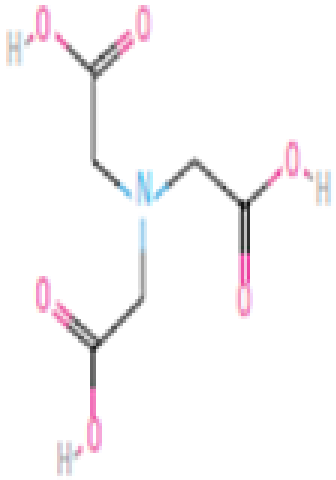
1- transport across physiological barriers into compartments where a toxic metal ion is concentrated.

2-form a stable complex with the metal after removing it from the biological chelator, if required at the site.

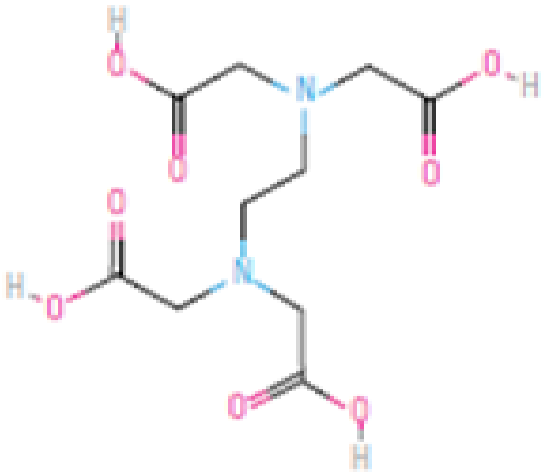
3-form a chelation complex whose properties render it non-toxic and facilitate its excretion, not only from the site of deposition, but also from the body [61].

Aminopolycarboxylate chelating agents are used ,extensively, in many domestic products and industrial processes, with the most important applications in cleaning compounds, pulp and paper manufacturing, and agriculture[62-66]. Chelating agents form stable water- soluble complexes with alkali and transition metal ions, thus increasing metal solubility and preventing metal catalyzed reactions. Therefore, chelating agents prevent

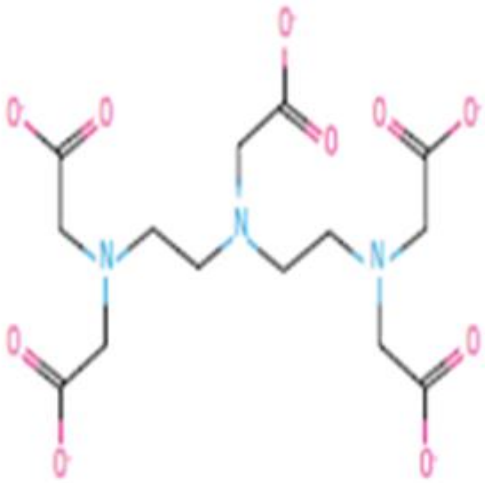
metals from interfering with the detergent's ability to remove soils and stains from clothing, from degrading oxidizing and bleaching agents in paper and textile manufacturing, and from precipitating in fertilizers. Chelating agents are also used in soil remediation to remove heavy metal contamination[67]. Because of their broad application range, chelating agents are ,typically, produced and used in large quantities. In 2004, the global consumption of the most common amino poly carboxylic acids, such as ethylene di amine tetra acetic acid (EDTA),nitrile tri acetic acid(NTA),di ethylene tri amine penta acetic acid (DTPA).



NTA



EDTA



DTPA

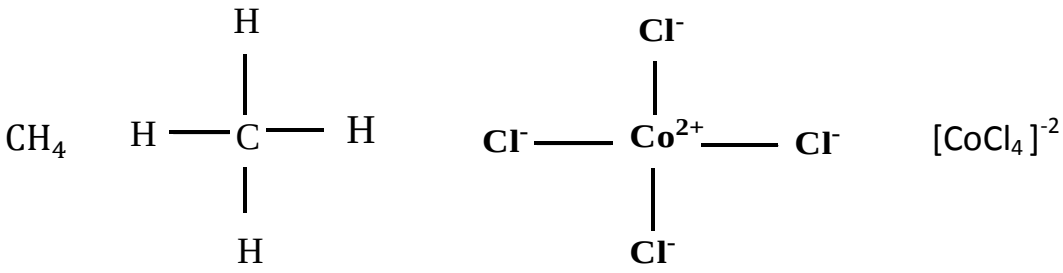
Scheme1. 4.example of some chelating agents

averaged over 200,000 tons per year[68]. Chelating agents that form low or moderately high stability constants, such as NTA, are ,readily, biodegradable However, chelating agents that form stronger metal complexes, such as EDTA and DTPA, degrade slowly and therefore are persistent in the environment[63,64-66,68]. Although these chelating agents do not concentrate in the food chain, up to 800 μg/L of EDTA has been found in some U.S. industrial and municipal wastewater treatment plants and up to 12 mg/Lin European bodies of water[64,66,67].In wastewater treatment plants, chelating agents can interfere with metal removal processes, allowing toxic metals to pass through untreated and contaminate the environment[68,69].

1.9.Complexes of Transition Elements:

A completely satisfactory definition of a complex compound is difficult to formulate, it is attempted below, complex compounds are compounds which contain a central atom or ion closely surrounded by a cluster of other ions or molecules called ligands are usually bonded to nuclear atom thus no perfect definition exists: it is a matter of judgement what are, classically, described as coordinate bonds, and complexes or complex compounds are often referred to as coordination" compounds ".The number of nearest neighbors (ligands) to the nuclear atom is referred to as the "coordination number" of the central atom and these neighbors constitute what is known as the first coordination sphere Complex ions tend to retain their identity even in solution, partial dissociation may occur. Another distinguishing characteristic is that both the nuclear atom and ligands are, usually, capable of independent existence as stable chemical species, as usual, cases occur in which it is not clear whether the compounds should be considered as complexes or not. As always with definition. It is usefulness that matters. The critical question is whether it is useful to consider a particular compound as a complex compound, such as $ALFr_6^{3-}$, $Ti(H_2O)_6^{3+}$and $CoCLr_4^{3+}$ are usefully considered as complexes: CH_4, CIO_4^- (has not independent existence), an intermediate type is that formed by ligands being added to molecules, as opposed to atoms or ions e.g.:

$SiF_4 + 2F^- \rightarrow SiF_6^{2-}$ these are normally considered as complexes, a sub-group called adducts is formed by the reaction of two neutral molecules, e.g.: $BF_3 + NH_3 \rightarrow BF_3 + NH_3$.



No complex Complex

Using the above model of complexes it is expected that the most stable coordination compound would be formed by the interaction of highly polarizing cations with stable ligands, e.g.; NH_3 H_2O, CN^-, Cl^- and NO_2 ,this is roughly correct, but the situation is ,much, more complicated. Transition Elements have great ability to form complex compounds and this is due to availability of incomplete d-orbitals, which allow it to accept electrons from donor ligands. The followings are some examples of complexes of different transition metals with different ligands to show the ability of these elements towards complex formation[70].

$[CuCL_4]^{2-}$ $[Cu(NH_3)_6]^{2+}$ $[Cu(H_2O)_6]^{2+}$

Square-Planar Octahedral Octahedral

Monodentate ligand

$[Ni(en)_6]^{2+}$ $[Ni(DMG)_2]$

Nickel (II) ethylenediamine Nickel dimethyl glyoxime

1.10. Color of transition metal complexes:

Transition metal complexes ,often, have spectacular colors caused by electronic transitions by the absorption of light. For this reason, they are often applied as pigments. Most transitions that are related to colored metal complexes are either d–d transitions or charge transfer bands. In a d–d transition, an electron in a d orbital on the metal is excited by a photon to another d orbital of higher energy. A charge transfer band entails promotion of an electron from a metal-based orbital into an empty ligand-based orbital (Metal-to-Ligand Charge Transfer or MLCT). The converse also occurs: excitation of an electron in a ligand-based orbital into an empty metal-based orbital (Ligand to Metal Charge Transfer or LMCT). These phenomena can be observed with the aid of electronic spectroscopy; also known as UV-Vis[71].

1.11. Effect of Metal Ions:

Ions of the transition elements have a tendency towards the formation of complexes containing coordinate bonds, and these complexes are apparently more stable than those formed by electrostatic forces. The tendency to form coordinate compounds is indeed, one of the most fundamental inorganic properties of both organic and inorganic molecules. The radii of the transition metal cations are less than the radii of cations which are is electronic with inert gases. This may account, in port for the greater stability of the transition ion complexes. According to Pauling the inner 3d orbitals of transition elements have about the same energy as the 4s and 4p orbitals of the valence shell, and if they are not ,completely, occupied by unshared electron pairs, they play a very important part in bond formation. The formation of complex ions by coordinate bonds appears to follow two

general rules:

1- The central ion tend to accept electrons to fill incomplete stable orbitals.

2- The central ion tends to accept sufficient coordinated molecules or ions to produce a symmetrical structure of molecules packed round the central ions[72].

1.12. Effect of Ligand:

The nature of coordinating group varies considerably from inorganic to organic species. The hydroxide ion has strong coordinating tendency, partly because it has three pairs of unshared electrons, but chiefly because it is of negative charge. Many organic anions form stable coordination compounds, formate and acetate ions from strong bonds but monocarboxilic acids with longer chains show ,rapidly, decreasing ability to coordinate. The aliphatic monoamines coordinate less readily, than does ammonia, the secondary amines coordinate less readily than the primary, and tertiary amines are almost devoid of ability to coordinate with metal ions. This is probably due to steric factors. Tertiary amines coordinate firmly with the hydrogen ion, that is they are strong bases [16].

1.13. Stability of Complexes:

In recent years a number of attempts have been made[73], to correlate the stability constants of metal chelates with various properties of either the metal ion or ligand in order to evaluate the factors affecting metal chelate stability. One of the most extensive is Pearson's classification into hard and soft ligand and metal ion. The metal ions are classified as hard or soft acids, and the ligand as hard or soft bases; the generalization about stabilities is then that soft ligands form stable complexes with soft metal ions; hard-

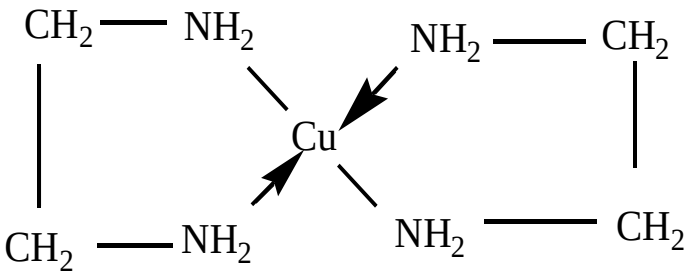
ligand hard-ion complexes are also stable. Mixtures of hard-ion soft-ligand or soft-ion hard-ligand are less stable.For metal complexes with multidentate ligands, the stability of the metal chelate is in part governed by the chelate structure The type of ligand has a distinct influence on the stabilities of complexes, in an extended form of the series, the stabilities of complexes by a particular chelating molecule with a series of metal atoms was first discovered by Mellor and Mally (1948), for the bivalent metals,which is in the order as, Cu > Ni > Co > Zn > Cd. [72].

1.14. The Coordination Chemistry of Metal Used:

1.14.1. The Coordination Chemistry of Copper (II):

The dipositive state is the most important one for copper; most copper (I) compounds are fairly ,readily, oxidized to copper (II) compounds, but further oxidation to copper (III) is difficult. The copper (II) having one unpaired electron and its compounds are paramagnetic. Most copper (II) salts ,readily, dissolve in water and give the aqua ion, $[Cu(H_2O)_6]^{2+}$.Addition of ligands to such aqueous solutions leads to form complexes by successive displacement of water molecules, with NH_3, for example, the species $[Cu(NH_3)(H_2O)_5]^{2+}$.. $[Cu\ (NH_3)_4(H_2O)_2]^{2+}$, but the addition of the fifth and sixth molecules of NH_3 is difficult. Similarly it is found that with (en), $[Cu\ en\ (H_2O)_4]^{2+}$ and $[Cu\ (en)_2(H_2O)_2]^{2+}$ form readily, but $[Cu(en)_3]^{2+}$ form's only at extremely high concentrations of ethylenediamine. Multidentate ligands that coordinate through oxygen or nitrogen (Scheme 1.5), such as amino acids from copper (II) complexes often of considerable complexity; for example, copper (II) ion reacts with glycine (Scheme1.6) to produce copper glycine in which each glycine

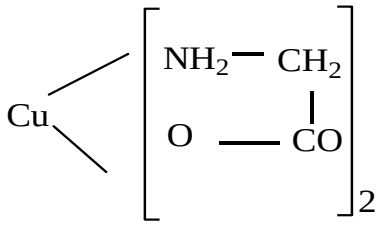
molecule is attached to the copper atom by one covalent bond and one coordinate bond [15].



Scheme1. 5. Ethylene di amine copper (II)

It has also been established that five-membered rings are more stable than comparable six-membered rings.This decreasing stability with increasing ring size continues so that there are a few complexes known with seven membered rings and none with larger rings[16]. Copper (II) reacts with glycine to give a colour complex

Glycine coordinates to copper (II) ion as a bidentate ligand, copper-glycine is an inner complex. The deep blue colour of the compound indicates copper nitrogen linkage and the possibility of the of the formula $Cu(NH3COO)_2$ is eliminated by the fact that N-Diethyl glycine gives an analogous compound[74].



Scheme1. 6. Glycine copper (II) complex

1.14.2. The Coordination Chemistry of Cobalt(II):

In its ordinary aqueous chemistry, cobalt has two important oxidation states, II and III, in a queous solution containing no complexing agents, oxidation to cobalt (II) is very unfavourable:

$[Co\ (H_2O)_6]^{3+} + e = [Co\ (H_2O)_6]^{2+}$ $E° = 1.84v$

Although in the presence of complexing agents, such as NH_3,which form .stable complexes with cobalt(II) the stability of trivalent cobalt is greatly improved: $[Co\ (NH_3)_6]^{3+} + e = [Co\ (NH_3)_6]^{2+} E° = 0.1\ v$

The trend towards decreased stability of the very high oxidation states and increased stability of oxidation state (II) compound which has been noted through the first row of transition metals Ti, V, Cr, Mn, and Fe and cobalt (II)[18].Indeed, the former trend culminates in the Cobalt (II) which forms numerous complexes, mostly octahedral or tetrahedral, but there are a fair number of square planar as well as some which are five coordinate[75,76]. There are more tetrahedral complexes of cobalt (II) than for any other transition metal ion. This is in accord with the fact that for a d^7 ion, ligand field stabilization energies disfavour the tetrahedral configuration relative to the octahedral one to a smaller extent than for any other d^nConfiguration[77]. Because of the small stability difference between octahedral and tetrahedral cobalt (II) complexes, there are several cases in which the two types may be in equilibrium [78]. mostly octahedral or Tetrahedral complexes are ,generally, formed with monodentate anionic ligands such as Cl^-, Br^-, I^-, SCN^-, NT_3 and OH^-. With a combination of two such ligands two neutral ones, tetrahedral complexes of the types CoL_2X_2 are formed in some cases. Several neutral bidentate ligands give planar complexes although it is known that the accompanying anions are coordinated to some degree so that these complexes could also be considered

as very distorted octahedral ones[79,80].An important feature of the chemistry of cobalt (II) is the very readily oxidation by molecular oxygen in the presence of a variety of complexing ligands especially nitrogen donors. As mentioned already, cobalt (II) occurs in a great variety of structural environments, because of this, the electronic structures, hence the spectral properties of the ion, are extremely varied[81].

1.14.3.Coordination chemistry of zinc(II):

Zinc is a member of the group 12 of the Periodic Table. The oxidation state of most compounds of this group is the oxidation state of +2.Zinc may be classified as a post –transtion main group element with Zinc(II)[82-85].

No compound of zinc in oxidation states other than+1 or +2 are known[86]. calculations indicate that a zinc compound with the oxidation state of+4 is unlikely to exist[87].As a metal, Zinc has ,relatively, low melting (419 .5℃) and boiling points(907℃). the melting point is the lowest of all the d-block metals except for Mercury and Cadmium; for this, among other reasons, ,Zinc ,Cadmium and Mercury are often not considered to be transition metals like the rest of the d-block metals are[88].

The chemistry of Zinc is dominated by the +2 oxidation state. when compound in this oxidation state are formed, the outer shell s electrons are lost,yielding a bare Zinc ion with the electronic configuration[Ar]$3d^{10}$[89].

Zinc chemistry is similar to the chemistry of the late first –row transition metals,Nickel and copper, though it has a filled d shell and diamagnetic compounds are, generally, colorless.Zinc tends to form bonds with a greater degree of covalency and much more stable complexes with N – and S-donors [90].

The most common structure of zinc complexes is tetrahedral which is due to the fact that the octet rule is obeyed in these cases. Never the less, octahedral complexes comparable to those of the transition elements are not rare. $Zn^{+2}$is a class acceptor in the classification of ahrl and, chatt and davies [91],and so forms stronger complexes with the first row donor atoms oxygen or nitrogen than with second row sulfur or phosphorus. In aqueous solution an octahedral complex,$[Zn(H_2O)_6]^{+2}$ I is the predominant species[92].The nitrate $Zn(NO_3)_2$, Chlorate $Zn(ClO_3)_2$, Sulphate $ZnSO_4$, Phosphate $Zn_3(PO_4)_2$,Cyanide $Zn(CN)_2$and the chromate $nCrO_4$(one of the few colored zinc compounds) are a few examples of other common inorganic compounds of zinc[93,94].

1.15. Antimicrobial activity:

Antimicrobial drugs or chemicals are the substances used to kill or slow down the growth of microorganisms. They include antibiotics; antiviral, antifungal and anti-parasitic agents[95]. Antimicrobial chemotherapy has been used from last six decades against infectious diseases caused by a variety of pathogens. Since then, many antimicrobial drugs were discovered, hundreds of drugs are in use new a days. Anti-microbial drugs are most commonly available today[96]. Since the introduction of penicillin as antibiotics in the control of infectious diseases, frequent use of antimicrobial drugs cause variety of problems, such as drug resistance, allergic reactions, nutritional loss, toxicity and much more. Almost all of the major categories of antibiotics in the clinical application showed resistance to microorganism specially β- lactam, macrolides, vancomycin and quinolones derived bacterial drug's resistance is a source of concern for healthcare officials. The effective treatment against microbial

agents is limiting day by day[97,98].Many other antimicrobial drugs are toxic too. So, there is a real need to discover new compounds with high efficiency towards pathogens and less toxicity, which may be different from available resistant drugs. This provides a great opportunity to synthetic chemists for the synthesis of such new compounds having lower cytotoxicity and better antimicrobial properties. The biological activity of compounds depends on structure of molecule[99]. It has been shown that heterocyclic compounds are more, biological active as compared to others[100]. Heterocyclic compounds particularly five and six member heterocyclic have attracted the attention of pharmaceutical community over the years due to their therapeutic value[101]. Poly functionalized heterocyclic compounds containing Nitrogen, sulphur, oxygen as hetero atoms play an important roles in the drug discovery process[102]. Benzimidazole is one such compound which attract attention of synthetic chemists for the synthesis of antimicrobial drugs[103].

1.16. Effect of complication on biological activity :

The metallo elements which are present in trace and ultra-trace quantities play vital roles at the molecular level in a living system. In a healthy body, of an adult, trace and ultra-trace elements weigh less than 10 grams in total but life depends upon these elements for more than this figure[104]. The Transition metal ions are responsible for the proper functioning of different enzymes. If their concentration exceeds a certain level, then their toxic effects are evident. It has been found that the activity of the biometals is attained through the formation of complexes and the thermodynamic and kinetic properties of the complexes govern the mode of biological action. Sometimes, the permeability, ie., lipophilicity of drugs increased through the

formation of chelates in vivo and the drug action is ,significantly, increased due to much more effective penetration of the drug into the site of action. The knowledge of drug action in vivo is extremely important in designing more potential drugs. Interaction of various metal ions with antibiotics may enhance or suppress their antimicrobial activity but ,usually, in many cases the pharmacological activity of antibiotics after complexation with metals is enhanced as compared to that of the free ligands[105]. Generally, it has been observed that transition metal complexes have greater activity and less toxic effects. The preparation and study of inorganic compounds containing ,biologically, important ligands is made easier because certain metal ions are active in many biological processes. The fact that Copper, together with magnesium, calcium, iron, Zinc, Cobalt, Chromium, Vanadium and Manganese are essential metallic elements and exhibit great biological activity when associated with certain metal-protein complexes, participating in oxygen transport, electronic transfer reactions or the storage of ions[106].has created enormous interest in the study of systems containing these metals[107].

N-[morpholinobenzyl] benzamide and it is Cu(II),Co(II),Ni(II) and Zn(II)complexes have been synthesized. their probable structure have been determined on the basis of their microanalytical .IR, UV-Vis, HNMR, CNMR, mass spectral data .the biological activities of the ligand and it is metal chelates against some type of bacteria .The Complexes have proved to higher activity than that of the free Mannich bases [108].some complexes of Cu (II), Co(II), Ni (II) and Zn(II)with a new Mannich base N(morpholinosalicylyl)acetamide (MSA)The structure of each complex was characterized by spectroscopic methods (IR, UV-Visible, ^{1}H NMR), conduct metric, magnetic data, and elemental analysis. Antibacterial activity of the

ligand and its complexes was tested against some selected bacteria. The ligand and all the complexes showed antimicrobial activity [109].

Mannich base and its metal [Co(II), Cu(II), Mn(II)] complexes, were characterized using Analytical methods such as TLC, solubility test, melting point and spectral studies [UV, ^{1}H NMR, and ^{13}C NMR]. Both the ligand and its metal complexes were tested against some microorganisms for their antimicrobial activity[110].The Mannich base –N[Morpholinobenzyol acetamide] and its transition metal complexes with Ti (III), V (III), Mn (III), Fe (III), Co (III), MoO(V), Ru (III), Ru (II), MoO2 (VI) and UO2 (VI) have been synthesized. The ligand and its metal complexes have been characterized by M.P., elemental analyses and spectral studies. The ligand and the corresponding metal complexes were screened for their antibacterial activities[111].

A new Mannich base, N[Morpholinosalicylylbenzohydrazide] (MSB), formed by the condensation of morpholine, benzohydrazide and salicylaldehyde and its Co(II), Ni(II) Cu(II) and Zn(II) complexes have been synthesised. Their structures have been elucidated on the basis of analytical, magnetic, electrical conductivity and spectral methods. On the basis of colour,magnetic moments and spectral data, the geometries of Co(II),Ni(II), Cu(II) and Zn(II) complexes have been assigned. The electrochemical property of the ligand and its complexes in acetonitrile solution was studied by cyclic voltammetry. The X-band ESR spectra of the Cu(II) complex in DMSO at 300 and 77 K were recorded and their salient features are reported. Antibacterial activities of the ligand and its complexes were tested against some selected bacteria. The ligand and all the complexes showed antimicrobial activities[112].

1.17.The objectives of the study :

The objectives of this study are:

To prepare Mannich compounds by Mannich reaction .

To use these compounds as ligands with some metal to form complexes .

To characterize these complexes by IR and Uv/Vis spectrums .

To evaluate suitable conditions and biological activities of these reactions .

CHAPTER TWO

Materials and Methods

Chapter Two

Materials and Methods

2.1. Materials

2.1.1.Chemicals

-Ethanol (CH_3CH_2OH)

-Ammonia (NH_3)

-Benzoyl chloride (C_6H_5COCl)

-Benzaldehyde(C_6H_5CHO)

-Morpholine(C_4H_9NO)

-Salicylaldehyde ($C_7H_6O_2$)

-Acetamide (C_2H_5NO)

-Copper (II) chloride Dihydrate ($CuCl_2.2H_2O$)

-Cobalt (II) chloridehexa hydrate ($CoCl_2.6H_2O$)

-Zinc (II) chloride ($Zncl_2$)

All chemicals used in this research were purified grade.

2.1.2. Instruments and Equipment:

- Infra-Red Spectroscopy (IR): ThermoNicolet,300 IR,U.S.A.

- Ultra Violet-Visible Spectroscopy (UV-VIS): JENWAY, UV-VIS Spectrophotometer, Model**:** 6505, Serial No.2270.

- Water Bath: ANALOG Water Bath,Volts:220V50Hz ,watts 1.4KW/7A,Model:LWB-222 A, Serial No.DLCCCD1556C.

- Sensitive Balance: Made in Germany,ModelPFB200-3,SerialNO.WF131341

-PH Paper:

UNIVERSAL PH (1-14),LABSTAR.

2.1.3. Glass wares:

- All glass ware were Pyrex type

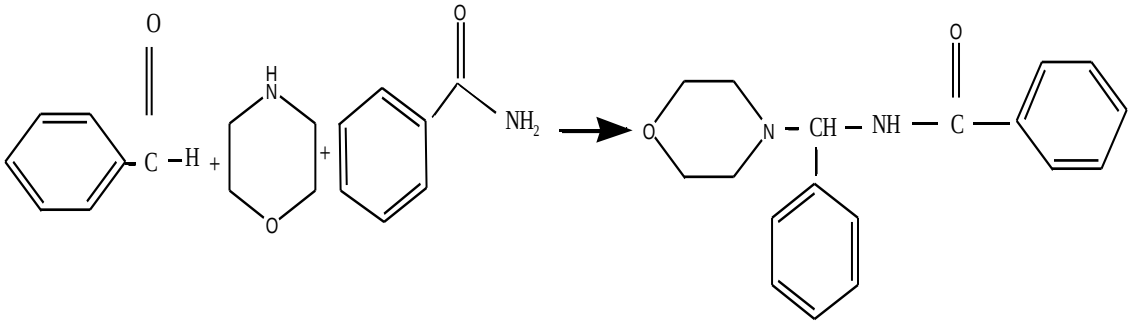
2.2. Methods:

2.2.1 Synthesis of Benzamide:

To 1 mL of benzoyl chloride, 2 mL of ammonium hydroxide (30%) was added. This mixture was allowed to stand for 2 minutes and then 4 mL distilled water was added to it. The crude product was recrystallized with abs ethanol .

2.2.2 Synthesis of Morpholinobenzoylbenzamide(MBB)

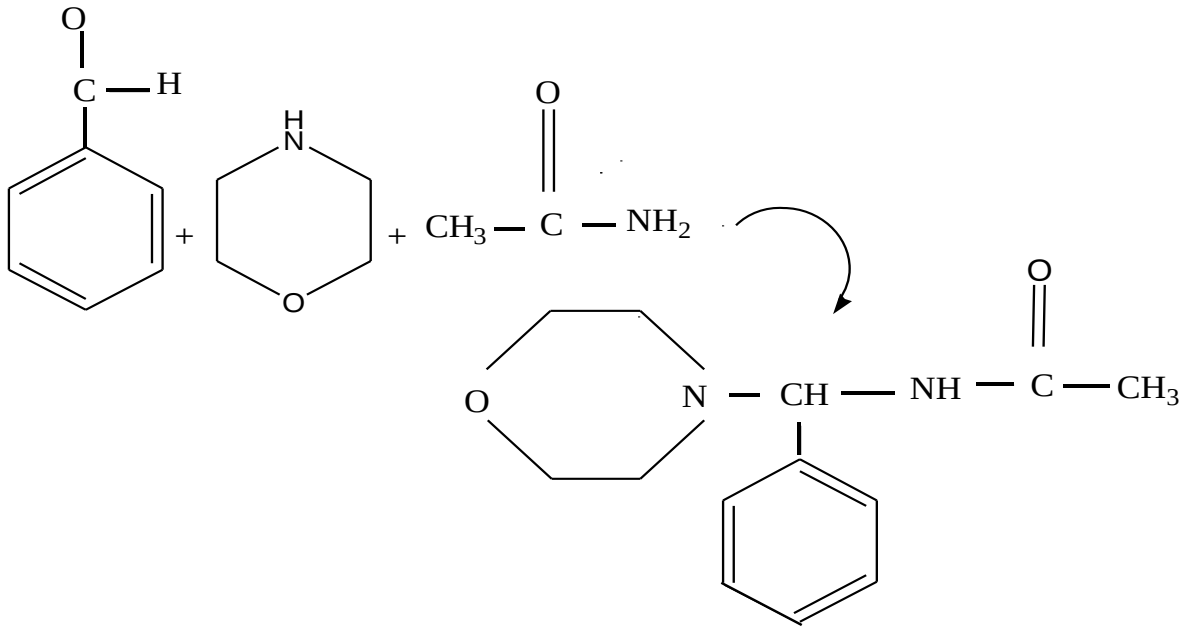
Benzamide(1.21g) in 20ml of ethanol was mixed with morpholine (0.8ml,10mmol)with stirring to go aclear solution under ice cold condition. To the contents, benzaldehyde (1ml,10 mmol) was added drop wise using dropper with stirring for 20 min. the reaction mixture was then kept at room temperature for 5days. The colour less solid ,obtained ,Scheme 2.1 was filtered and recrystallized with ethanol.



Scheme 2.1. Preparation of MBB

2.2.3.Preparation of Morpholinobenzoylacetamide(MBA)

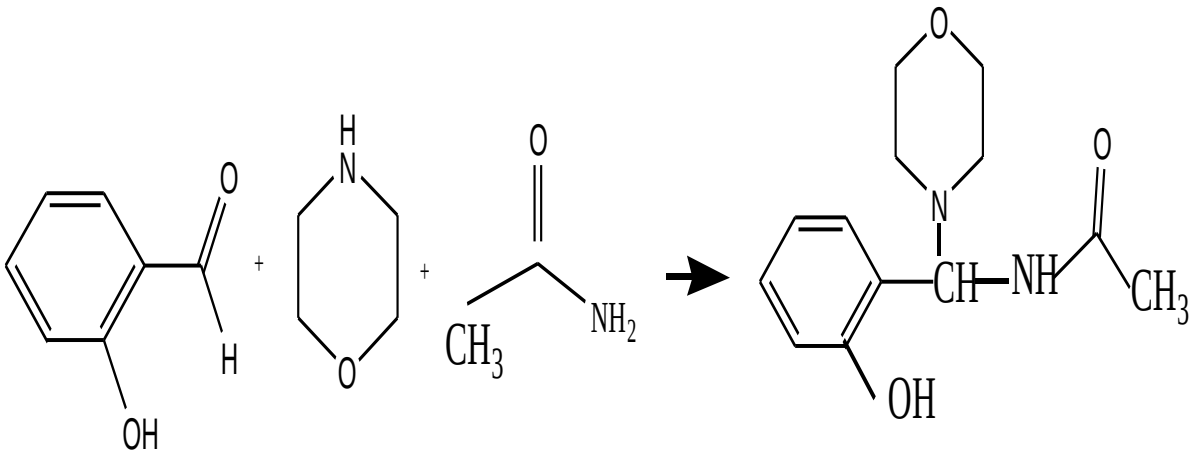
Acetamide (0.59g) in ethanol was mixed with morpholine (0.8ml,10mmol) and the mixture was treated with benzaldehyde (1ml,10mmol) in the ratio of 1:1:1. The reaction mixture was then kept at room temperature for 5 days. The solid obtained(Scheme2.2) was filtered and recrystalised from ethanol.



Scheme 2.2.Preparation of MBA

2.2.4.Synthesis of Morpholinosalicylacetamide(MSA)

an ethanolic solutionof salicylaldehyde, morpholine and acetamide were taken in 1:1:1 mole ratio. Morpholine 0.79 mL ,10 mM), acetamide(0.59 g, 10 mM) and(1.047 mL,10mmol) of salicylaldehyde were mixed under ice-cold condition. The product obtained(Scheme 2.3) was a yellow solid and it was recrystallised with methanol.



Scheme 2.3.Preparation of MSA

2.2.5 Synthesis of metal complexes

The Mannich base (dissolved in $CHCl_3$) and the metal chlorides in ethanol were mixed in 1:1 molar ratio. The reaction mixture was, gently, warmed on a water-bath for one hour. The resulting solid complex were filtered washed with distilled water and recrystallised with ethanol and dried .

2.2.6.Synthesis of metal complexes in PH=8

A solution of MCl_2 .nH_2O (M = Cu,Co,Zn) (2.04×10^{-3}mol) in ethanol (5 mL) was added drop wise to the solution of ligand (2.04×10^{-3}mol) in ethanol (30 mL) with stirring at room temperature. The pH of the reaction mixture was adjusted by addition of 0.1 M aqueous NaOH solution in the range of 7.0 to 8.0. After addition of base, the solid complex formed, filtered, washed with distiled water, and air dried.

2.2.7. Test of anti bacterial activity:

the suspension of bacteria were made in sterile normal saline. Compared bacterial suspension with 0.5 MC Far land standard. By swab dip in bacterial suspension and spread all over the media (M.H).were made9 bore in media by using glass borer (size 7mm). using automatic pipette dispensed 50 M of

chemical complexes in each bore according to complex type Leaved for 5 min ,and incubate these plate in incubator for 24h in 37℃ and the clear zone around the pore was readed which indicate bacterial sensitivity to the complex by using ruler(read in mm).

CHAPTER THREE

Results and discussions

Chapter Three

3. Results and Discussion

Products were identified and characterized using infra-red spectra and ultra-violet visible spectrophotometry.

Table 3.1shows the analytical data of the compounds prepared, UV-Visible, shows Characteristic absorption spectra at spectroscopy wavelength. yield % and colour of complexes are characteristic of the metal used.

Table 3.1: Analytical data of the prepared Compounds.

Compounds	yield %	Colour	M.W	M.F	λ_{max}
MB*A*	76.9	Yellow	234	$C_{13}H_{18}O_2N_2$	-
MSA	72	Yellow	250	$C_{13}H_{18}O_3N_2$	-
MBB	64.1	White	296	$C_{18}H_{20}O_2N_2$	-
Cu+MB*A*	48.6	Green	403.54	$[Cu(C_{13}H_{18}O_2N_2)Cl_2 2H_2O]$	235
Co+MBA	43.1	Green	398.9	$[Co(C_{13}H_{18}O_2N_2)Cl_2]\ 2H_2O$	205
Zn+MBA	31.5	White	405.38	$[Zn(C_{13}H_{18}O_2N_2)Cl_2]2H_2O$	215
Cu+MSA	44.4	Green	419.54	$[Cu(C_{13}H_{18}O_3N_2)Cl_2 2H_2O]$	240
Co+MSA	31.9	Green	414.9	$[Co(C_{13}H_{18}O_3N_2)Cl_2]2H_2O$	280
Zn+MSA	20.5	PaleYellow	421.38	$[Zn(C_{13}H_{18}O_3N_2)Cl_2]2H_2O$	215
Cu+MBB	62.1	Green	463.54	$[Cu(C_{18}H_{20}O_2N_2)Cl_2\ 2H_2O]$	420
Co+MBB	32.6	Pink	458.9	$[Co(C_{18}H_{20}O_2N_2)Cl_2]2H_2O$	215
Zn+MBB	25.2	White	465.38	$[Zn(C_{18}H_{20}O_2N_2)Cl_2]2H_2O$	225
Cu+MBAatPH=8	45	Green	403.54	$[Cu(C_{13}H_{18}O_2N_2)Cl_2 2H_2O]$	415
Co+MBAatPH=8	35.7	Violt	398.9	$[Co(C_{13}H_{18}O_2N_2)Cl_2]2H_2O$	660
Zn+MBAatPH=8	33.9	White	405.38	$[Zn(C_{13}H_{18}O_2N_2)Cl_2]2H_2O$	420
Cu+MSA atPH=8	58.5	Green	419.54	$[Cu(C_{13}H_{18}O_3N_2)Cl_2 2H_2O]$	415
Co+ MSAatPH=8	57.9	Pale Green	414.9	$[Co(C_{13}H_{18}O_3N_2)Cl_2]2H_2O$	405
Zn+ MSAat PH=8	47.9	Pale Yellow	421.38	$[Zn(C_{13}H_{18}O_3N_2)Cl_2]2H_2O$	405
Cu+MBB at PH=8	69.5	Green	463.54	$[Cu(C_{18}H_{18}O_2N_2)Cl_2\ 2H_2O]$	405
Co+MBB at PH=8	77.7	Green	458.9	$[Co(C_{18}H_{18}O_2N_2)Cl_2]2H_2O$	405
Zn+MBB at PH=8	98.6	White	465.38	$[Zn(C_{18}H_{18}O_2N_2)Cl_2]2H_2O$	425

The complexes prepared were coloured microcrystalline powders accept some zinc complexes are colorless The reason behind this is because zinc d orbitals are completely filled up with electrons, meaning that it is not possible for any electron to transition as they are all filled up. All the complexes are stable at room temperature. They are in insoluble in water and sparingly soluble in common organic solvents but soluble in DMSO. The percentage of yield varies from 20.5% to 98.6%. The λ_{max} was calculated by using double beam UV-Visible JENWAY spectrophotometer, ranging from 205to66o nm, is characteristic for the electronic transitions. the PH was effect the preparation of some ligand metal complexes as shown in Table (3.1) it was increased the yield in some product and decrease it in the other this can be explained by at this PH the ligands are free to coordinate with the central metal atom because no presence of hydrogen ion which prevent coordinated ligand with The metal to form complexes.

3.2.Infrared Spectral:

Table3.2 and 3.3 show the IR spectra of the ligands and their complexes

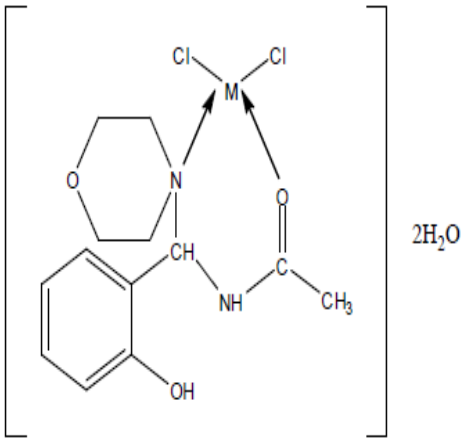
Table 3.2 absorption bands of ligands and its complexes

Compounds	Vibration frequency of various functional groups(in cm^{-1})				
	N-H	C-N-C	C=O	M-O	M-N
MBB	3290	1113	1639	-	-
MSA	3299	1118	1653	-	-
MBA	3296	1112	1646	-	-
MBB-Cu	3359	1111	1635	517	410
MBB-Co	3367	1109	1635	529	411
MBB-Zn	3290	1112	1637	578	459
MSA-Cu	3211	1115	1608	561	430
MSA-Co	3253	1109	1651	552	423
MSA-Zn	3496	1103	1623	584	449
MBA-Cu	3350	1111	1645	592	465
MBA-Co	3476	1107	1617	506	416
MBA-Zn	3152	1101	1625	641	499

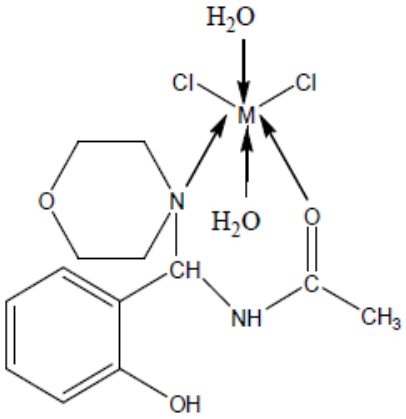
Table 3.3 IR Spectral of Complexes in PH=8

Compounds	Vibration frequency of various functional groups(in cm^{-1})				
	N-H	C-N-C	C=O	M-O	M-N
MBB-Cu	3297	1112	1638	470	417
MBB-Co	3382	1113	1637	581	438
MBB-Zn	3369	1111	1638	568	417
MSA-Cu	3346	1113	1624	597	469
MSA-Co	3536	1105	1628	731	423
MSA-Zn	3501	1106	1652	553	463
MBA-Cu	3434	1104	1628	517	425
MBA-Co	3554	1103	1625	727	408
MBA-Zn	3152	1103	1552	643	465

The IR spectrum of the free ligand was compared with those of the metal complexes to determine the coordination sites involved in coordination. In the ligands (MBB,MSA,,MB*A*) the infrared bands of **ν**N-H observed at3290 ,3299,3296 cm^{-1} respectively, **ν**C=O of amide observed at1639,1653,1646cm^{-1}respectively and **ν**C-N-C of morpholine observed at1113,1118,1112cm^{-1} respectively. In IR spectra of all the complexes, the **ν**N-H band remained at the same position as in the free ligands, indicating that the secondary nitrogen is not coordinated. A band of *ν*C=O of amide and νC−N−C stretching vibration of the morpholine ring This bands shifted to lower frequencies in the metal complexes, indicating coordination through oxygen atom of amide moiety and nitrogen of morpholine entity present in the ligands. suggesting the involvement of the nitrogen atom from the morpholine ring to the central metal ion. The oxygen atom from the amide to be involved in coordination of the metal ion. The new bands at 470-731 and 408-499 cm^{-1} in the spectra of the metal complexes were assigned to νM−O and νM−N stretching vibrations. The presence of coordinated water molecules in Cu (II) complex is determined by the appearance of bands at 3443-3571cm^{-1} and a peak at 863 cm^{-1} is assignable to the OH stretching and rocking mode of coordinated water molecules. The rocking vibration of water is not observed in the IR spectra of Co (II) and Zn (II) complexes. This is confirmed that water molecule is not coordinated in these complexes.



M=Co,Zn



M=Cu

Scheme 3.1. Proposed structure of metal complexes

3.3.Antibacterial activity of the ligand and their complexes (zone inhibition in mm):

Table 3.4 the solvent

Compounds	Gram Negative			Gram Positive		
	Pseudomonas aeruginosa	*Salmonella typhi*	*E.Coli*	*S.Aureus*	*E.fecalis*	*Bacillus cereus*
DMSO	NI	NI	NI	NI	NI	NI

NI: no inhibition

Table 3.5 MBB and their complexes

Compounds	Gram Negative			Gram Positive		
	Pseudomonas aeruginosa	*Salmonella typhi*	*E.coli*	*S.Aureus*	*E.fecalis*	*Bacillus*
MBB	10	7	7	7	7	13
Cu(II)complex	7	12	11	13	11	9
Co(II)complex	7	13	10	10	8	9
Zn(II)complex	7	8	8	9	8	7

Table 3.6 MBB complexes at PH=8

Compounds	Gram Negative			Gram Positive		
	Pseudomonas aeruginosa	*Salmonella typhi*	*E.coli*	*S.Aureus*	*E.fecalis*	*Bacillus*
Cu(II)complex	7	11	11	14	11	9
Co(II)complex	7	12	8	9	7	7
Zn(II)complex	7	10	9	10	7	14

Table 3.7 MSA and their Complexes

Compounds	Gram Negative			Gram Positive		
	Pseudomonas aeruginosa	*Salmonella typhi*	*E.coli*	*S.Aureus*	*E.fecalis*	*Bacillus*
MSA	10	10	16	10	10	12
Cu(II)complex	10	10	14	21	19	22
Co(II)complex	12	20	16	16	14	18
Zn(II)complex	12	13	12	13	9	17

Table 3.8 MSA Complxes at PH=8

Compounds	Gram Negative			Gram Positive		
	Pseudomonas aeruginosa	*Salmonella typhi*	*E.coli*	*S.Aureus*	*E.fecalis*	*Bacillus*
Cu(II)complex	9	14	13	19	14	16
Co(II)complex	16	21	16	18	17	15
Zn(II)complex	11	15	14	14	7	15

Table 3.9 MBA and their complexes

Compounds	Gram Negative			Gram Positive		
	Pseudomons aeruginosa	*Salmonella typhi*	*E.Coli*	*S.Aureus*	*E.fecalis*	*Bacillus*
MBA	7	7	10	7	7	7
Cu(II)Complex	11	7	10	13	7	10
Co(II)Complex	13	20	14	14	13	11
Zn(II)Complex	10	14	15	12	12	10

Table 3.10 MBA Complexes at PH=8

Compounds	Gram Negative			Gram Positive		
	Pseudomonas aeruginosa	*Salmonella typhi*	*E.coli*	*S.aureus*	*E.fecalis*	*Bacillus*
Cu(II)Complex	11	7	9	12	7	10
Co(II)Complex	15	20	13	15	15	12
Zn(II)Complex	10	7	10	9	9	9

The antimicrobial activity of the ligands and its Cu (II), Co (II) and Zn (II) complexes were conducted against various microbes like the Gram Positive bacteria species *Staphlococcus aureus, Enterococcus fecalis,Bacillus cerus* and Gram negative bacteria *Escherichia coil,Salmonella typhi* ,and *Pseudomonas aeruginosa* effect of the investigated compounds have been tested by the disc diffusion method.. No inhibitory effect was observed for DMSO used as control. A comparative study of inhibition values of the Mannich base ligands and their complexes indicated that the biological activity for(MBB) alone against *Pseudomonas* was higher than the complexes form.and *Bacillus cerus* lower than the complexes form. this ligand have no activity *against Staphlococcus aureus, Enterococcus fecalis*, *Escherichia coli and Salomnella typhi* , the (MSA)against *Salmonella typhi* showed lower activity than their complexes and similar the Cu complex ,and *Pseudomonas aeruginosa* showed higher activity than copper complexes at PH=8 and similar Cu complex .*E,coli* showed higher activity than the Cu and Zn complexes and similar the cobalt complex. *Staphlococcus aureus, Bacillus cerus* lower activity than their complexes, *Enterococcus fecalis* showed higher activity than the Zn complexes. (MBA)this ligand no activity against *Pseudomomnasaeruginosa , Salmonellatyphi, Staphylococcusaureus, Entrococcus fecalis,Bacilluscerus*.this ligand against *Escherichia coli* showed higher activity than the Cu complex at PH =8,Cu complex at PH=8 no activity against *Salmonella typhi* and *Entrococcus fecalis*, Zn complex at PH=8 showed no activity against *Salmonella typhi*.

3.4.Conclusion

Ligands Morpholinobenzoylbenzamide ,Morpholinobenzoylacetamide and Morphosalisylacetamide were prepared and complexes of Copper (II), cobalt(II) and Zinc(II) were prepared and was reacted with the metal chloride using dimethylsulphoxide and ethanol as a solvents. these ligands and their complexese was prepared at PH=8.

These ligands and their complexes are characterized and identified using infra-red ,ultra-violet spectra and yield and color determination. These complexes are stable at room tempreture. These complexes use to reduce the biological activity of certain microbes.

3.5. Recommendation:

- Conduct and develope studies about Morphlinobenzylbenzamide(MBB), Morpholinobenzylacetamide(MBA),andMorpholinosalicylacetamide(MSA).

- Further studies should be carried out using other ligands and metals.

- More advance analytical techniques should be investige to the prepared compounds such as XRD, SEM, NMR.

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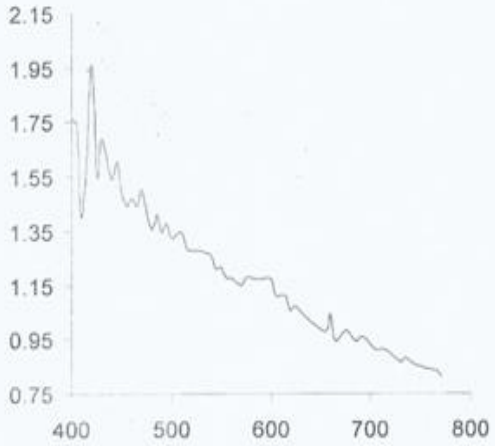
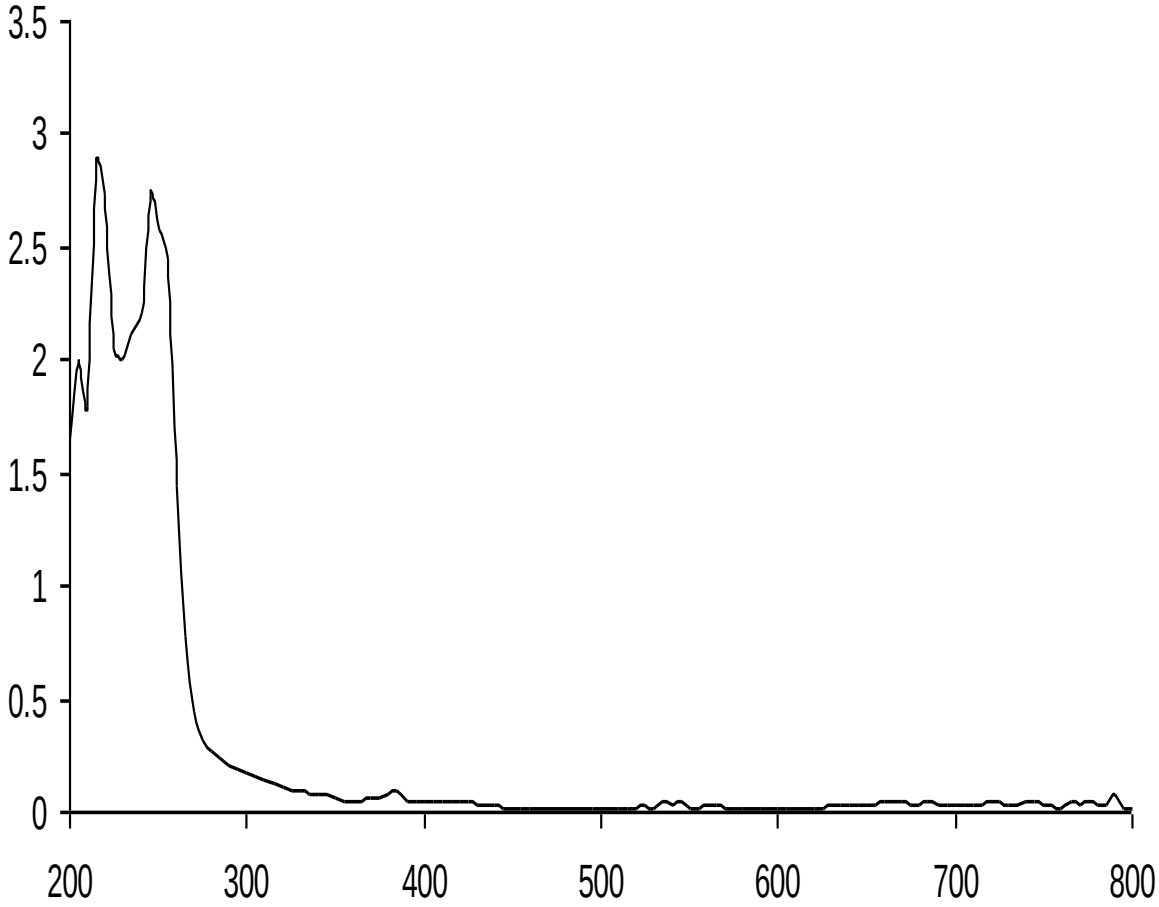
Appendixes

Uv-Vis of MBB+Cu



nm	abs
420	1.963

Uv-Vis of MBB+Co

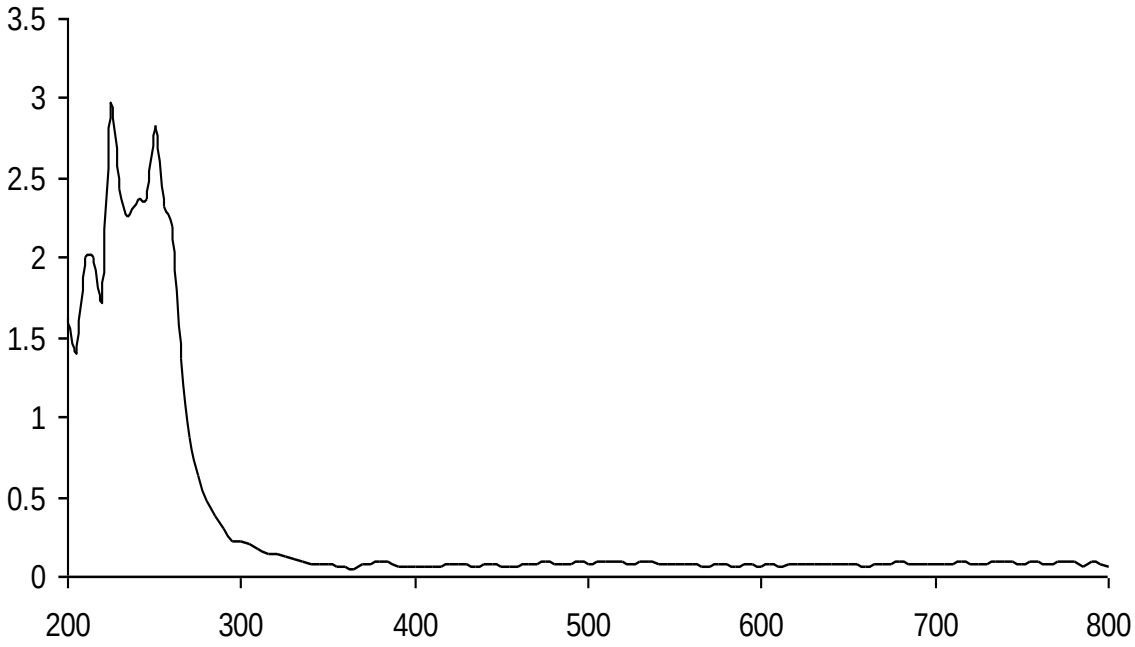


Abs:nm

2.880:215

Uv-Vis of MBB +Zn

abs

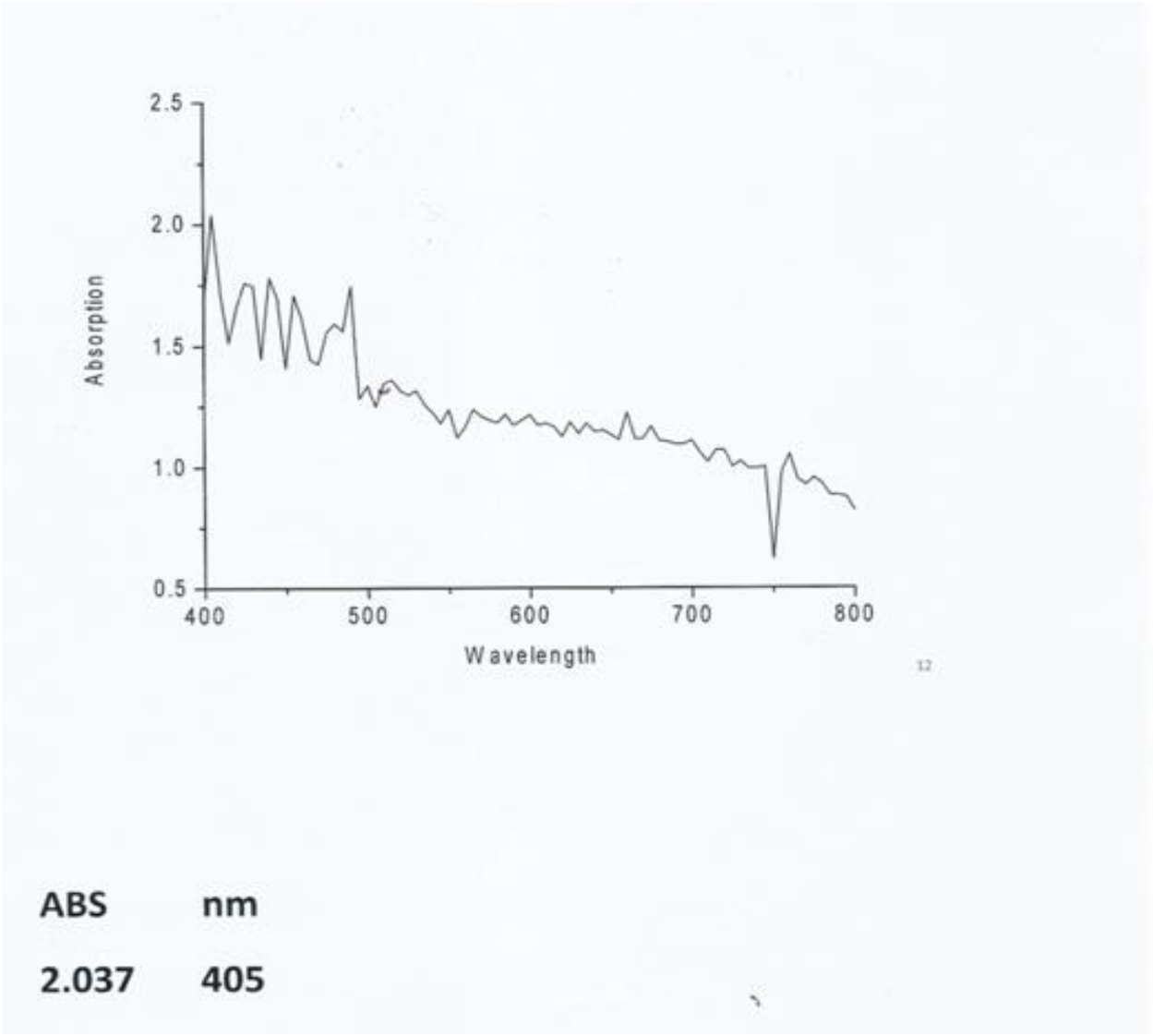


nm

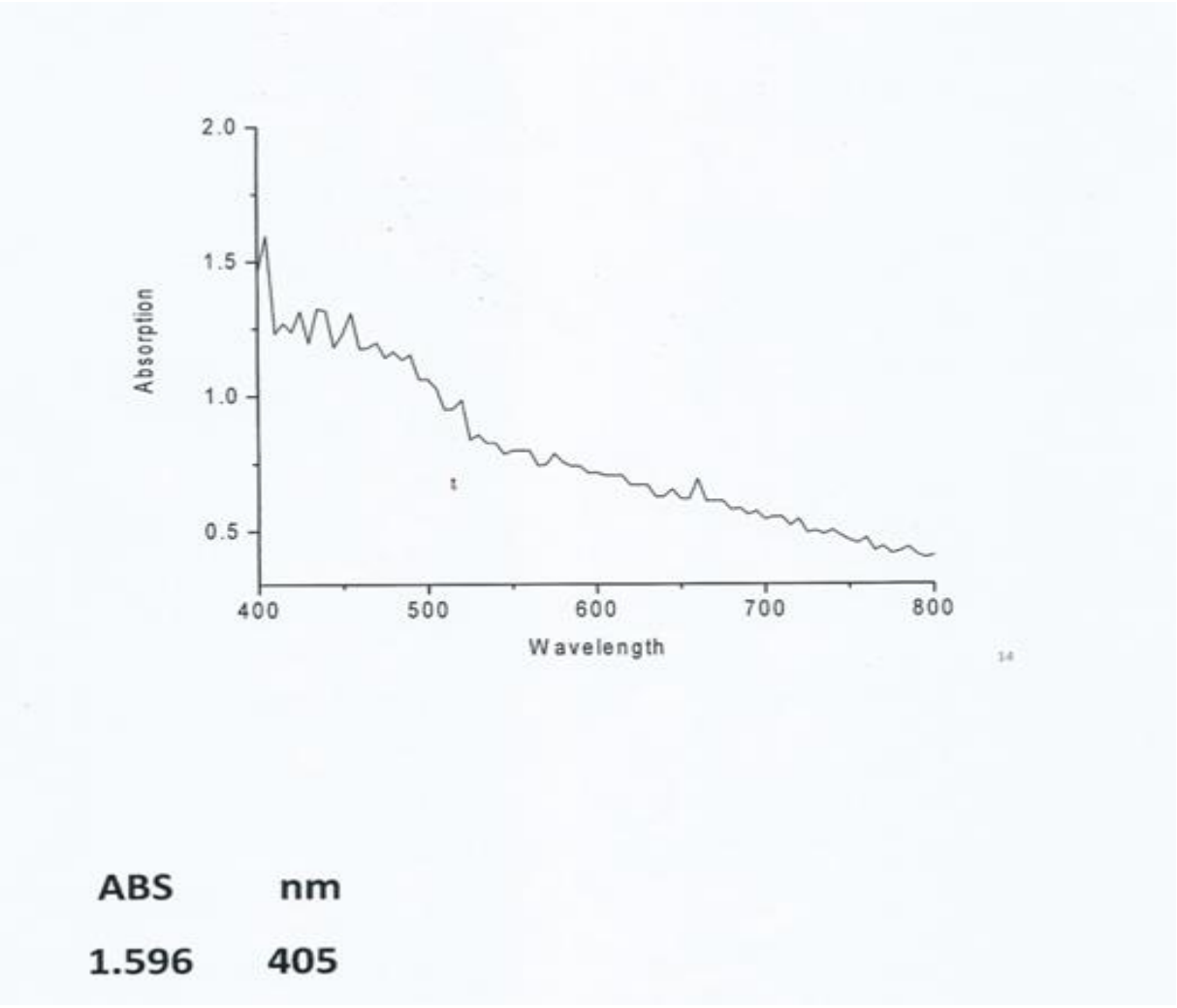
Abs:nm

2.955:225

Uv-Vis of MBB+Cu(PH=8)



Uv-Vis of MBB +Co(PH=8)



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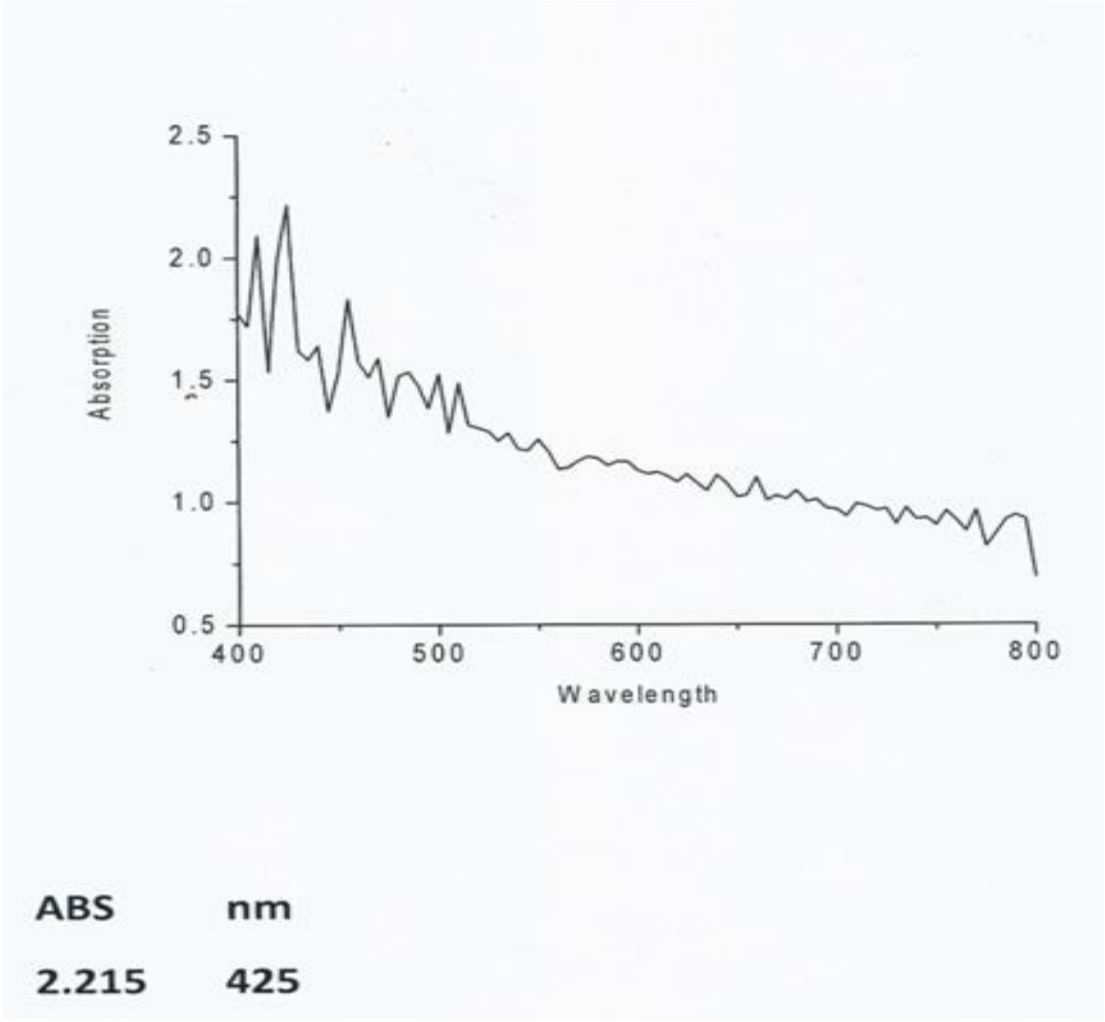
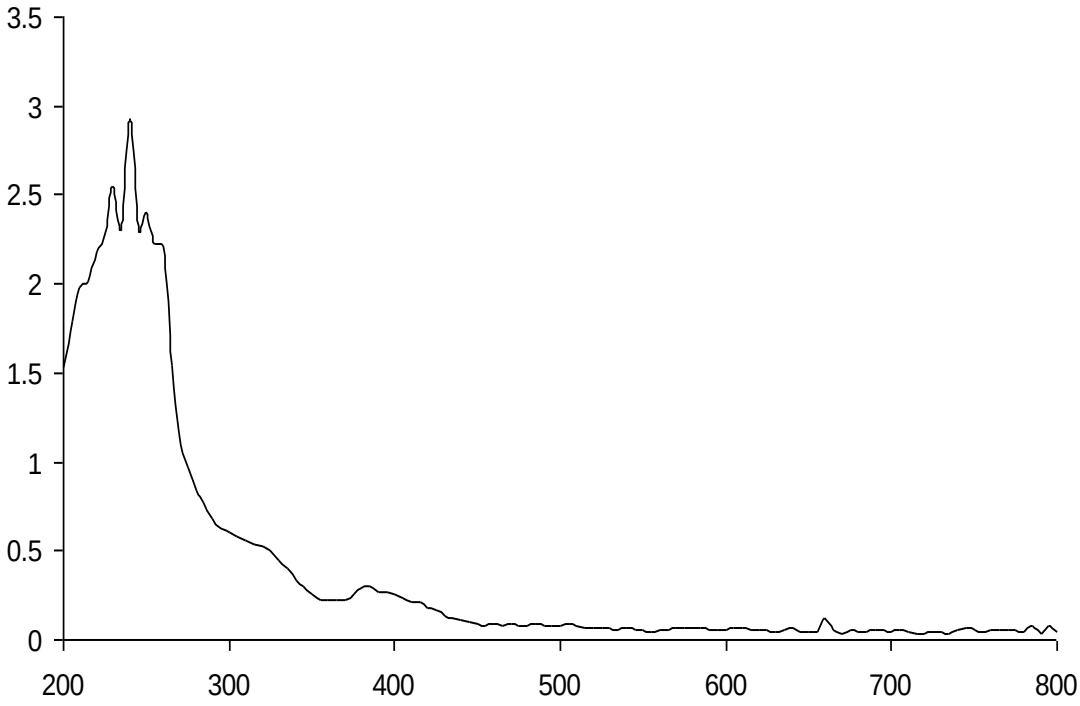


Uv-Vis of MSA+Cu

abs



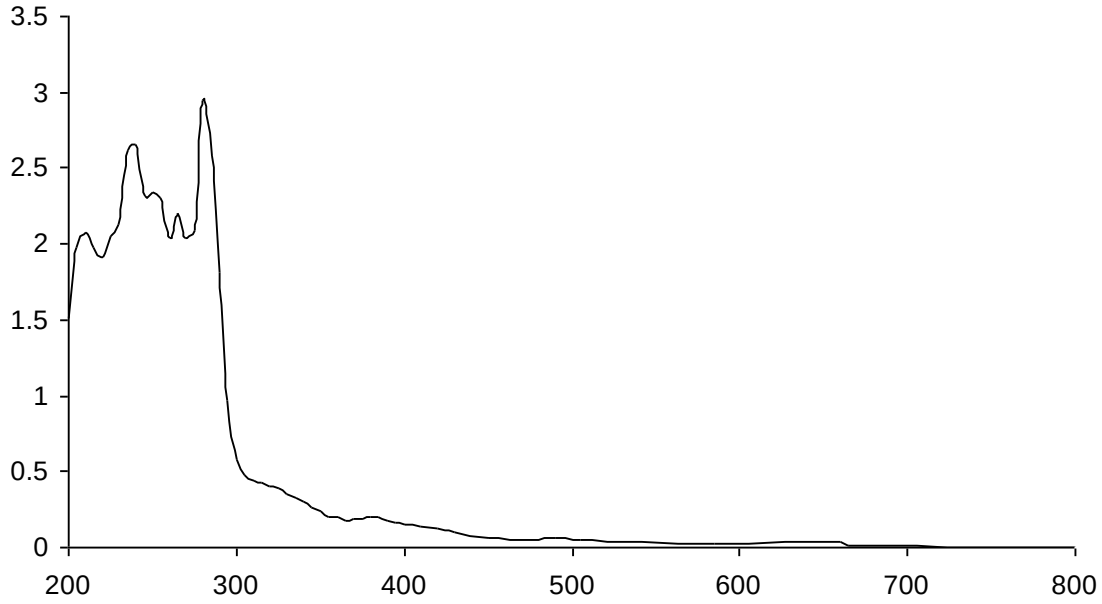
nm

Abs:nm

2.929:240

Uv-Vis of MSA+Co

abs



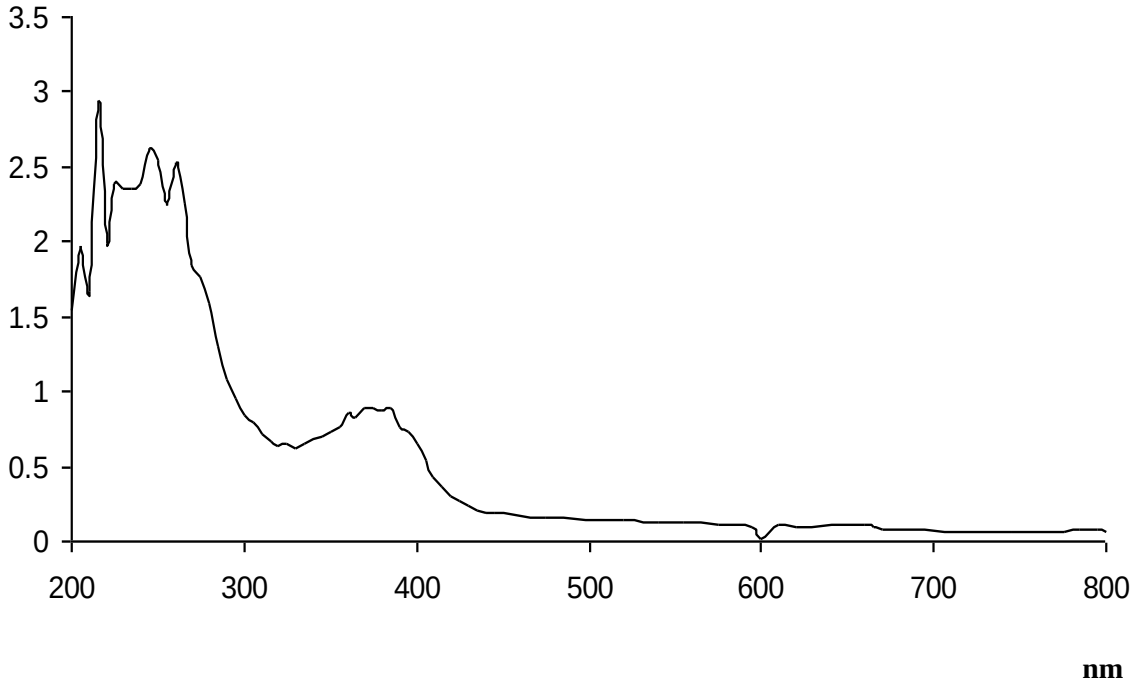
nm

Abs:nm

2.940:280

Uv-Vis of MSA+Zn

abs



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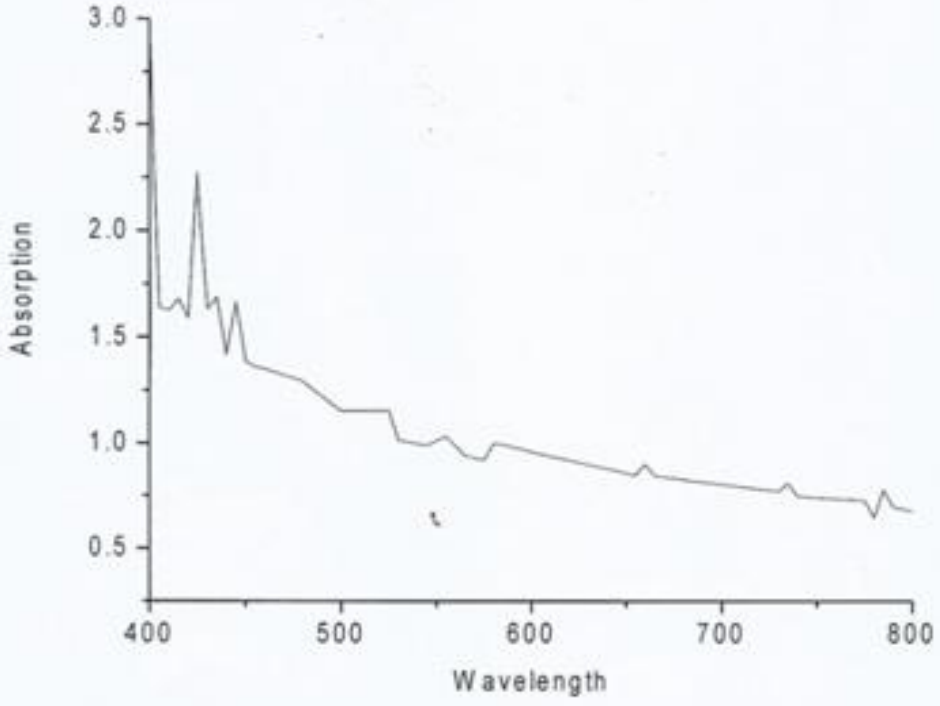
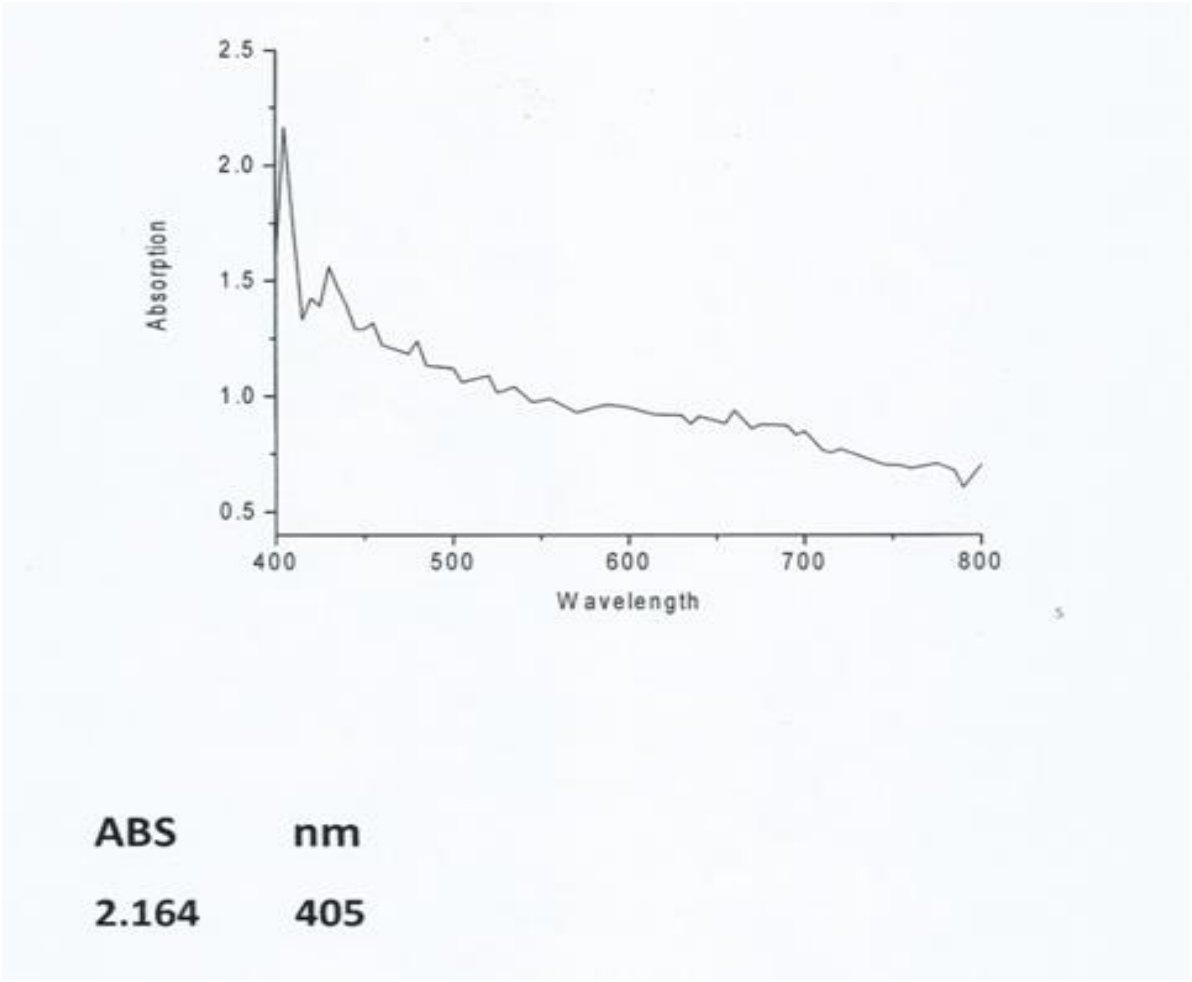


ABS	nm
1.679	415

Uv-Vis of MSA +Co(PH=8)



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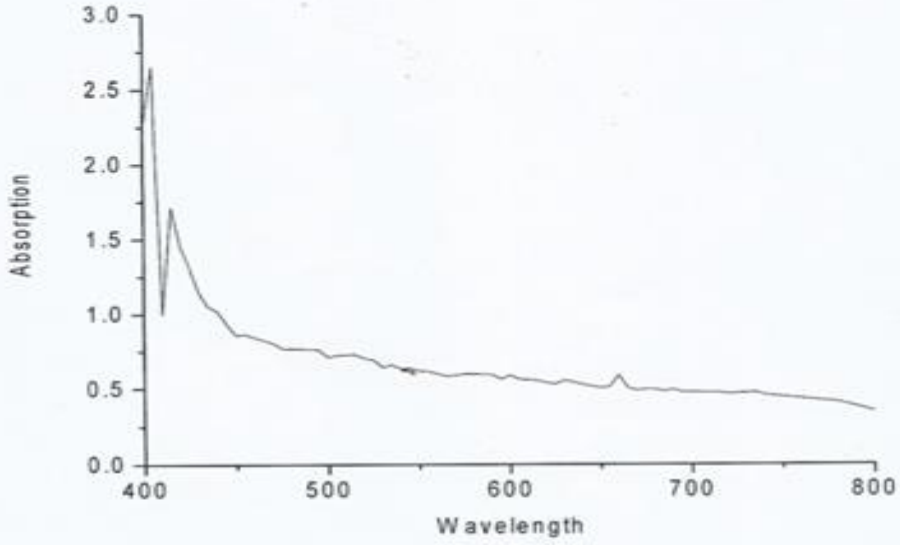
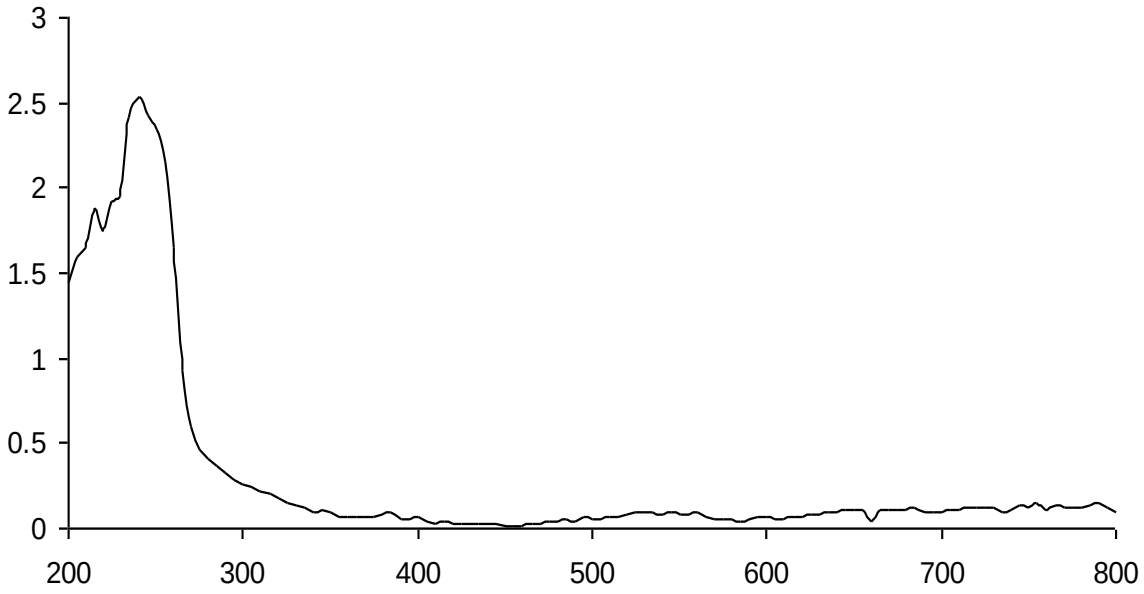


ABS	nm
2.651	405

Uv-Vis of MBA +Cu

abs



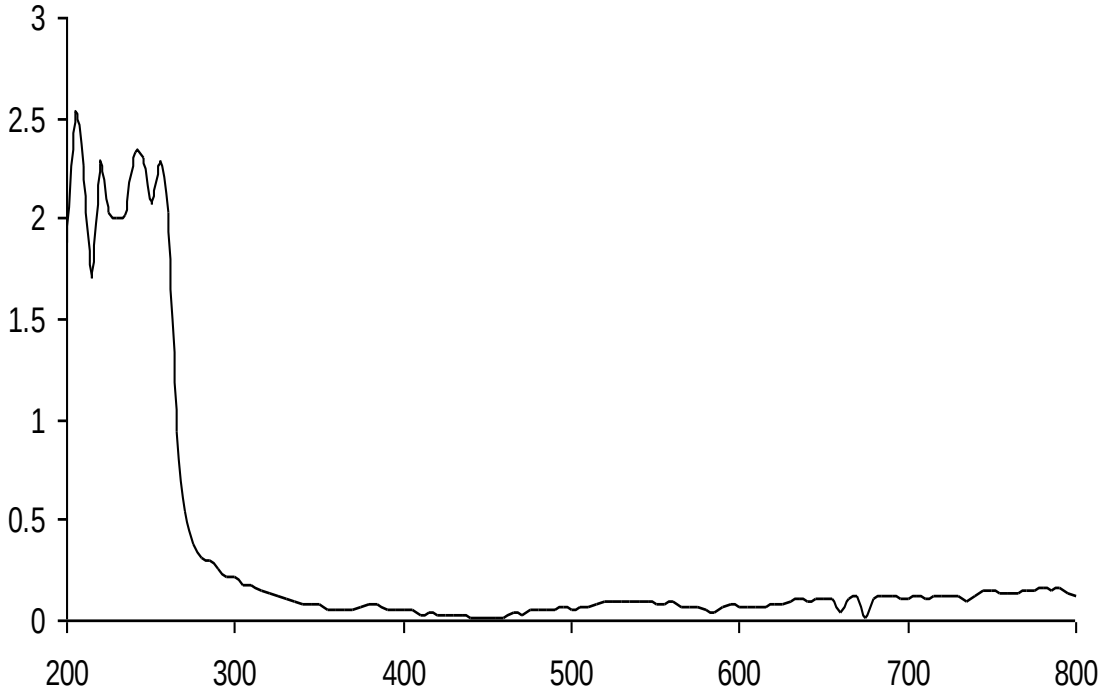
nm

Abs:nm

2.411:235

Uv-Vis of MBA +Co

abs

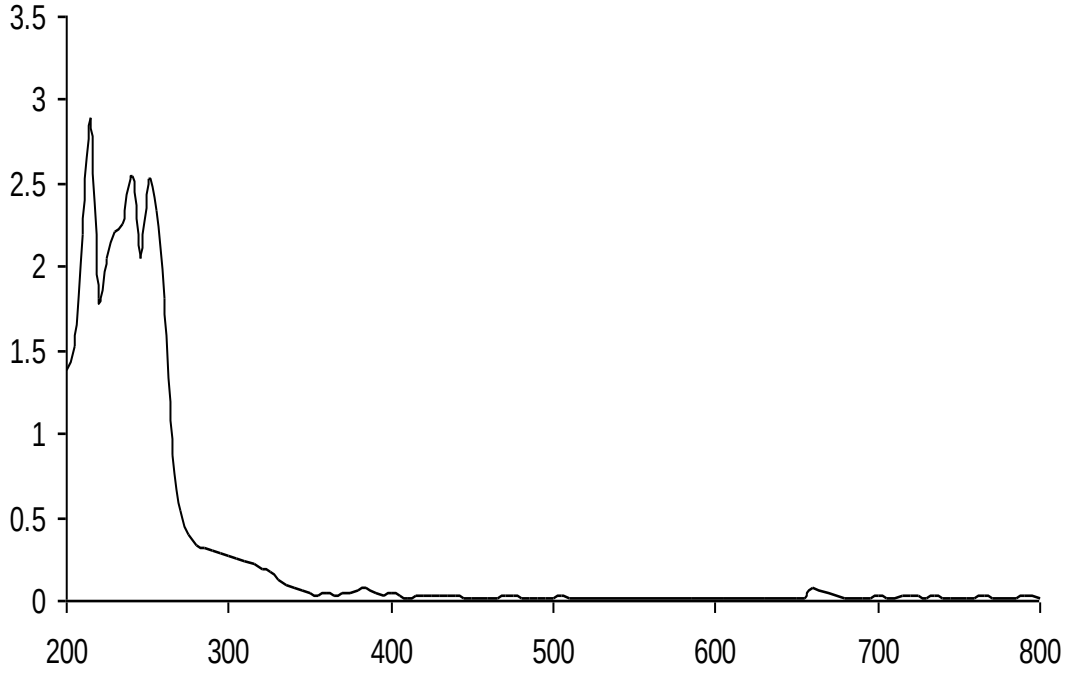


nm

Abs:nm

2.516:205

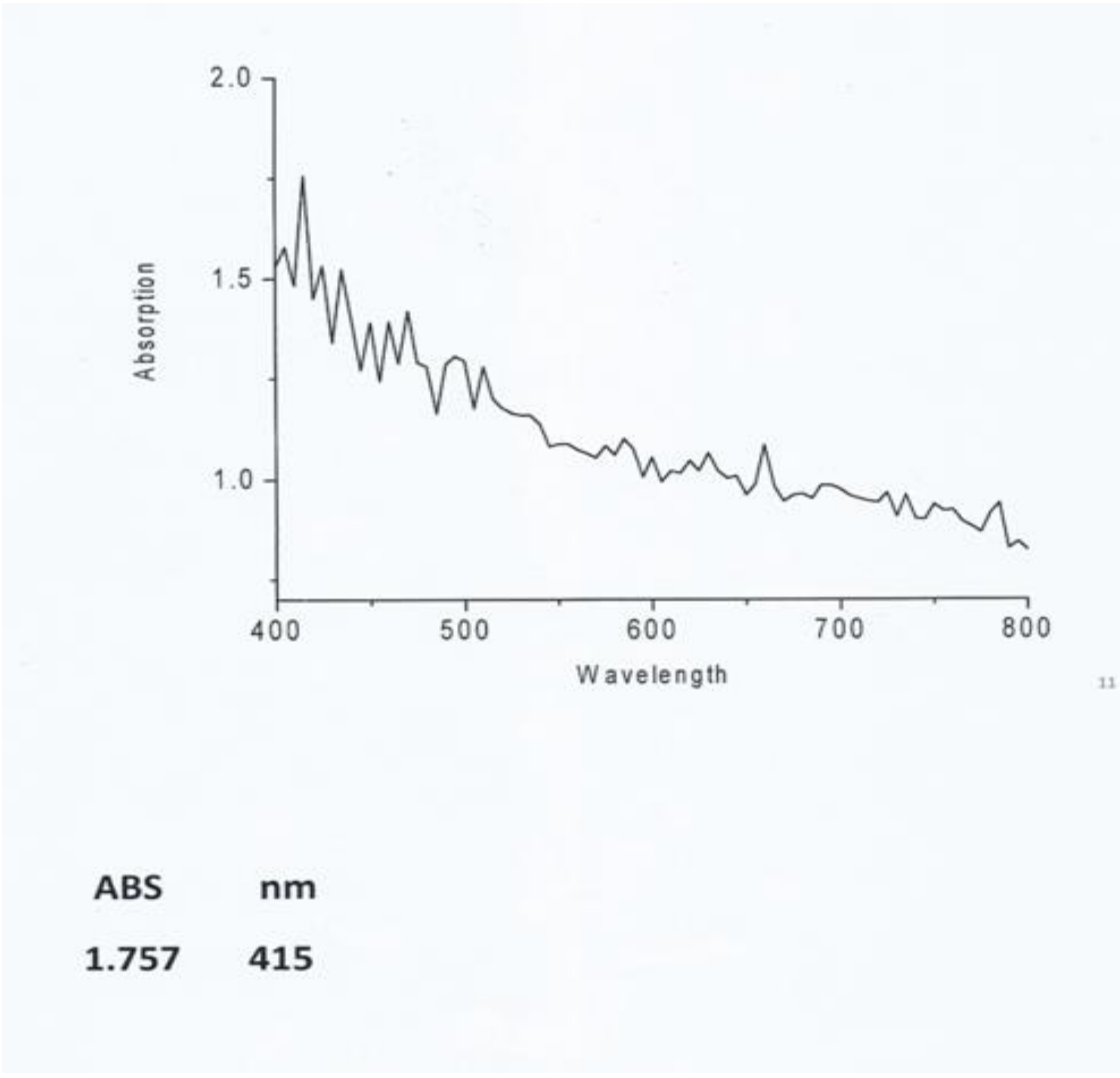
Uv-Vis of MBA+Zn



abs:nm

2.903:215

Uv-Vis of MBA+Cu (PH=8)



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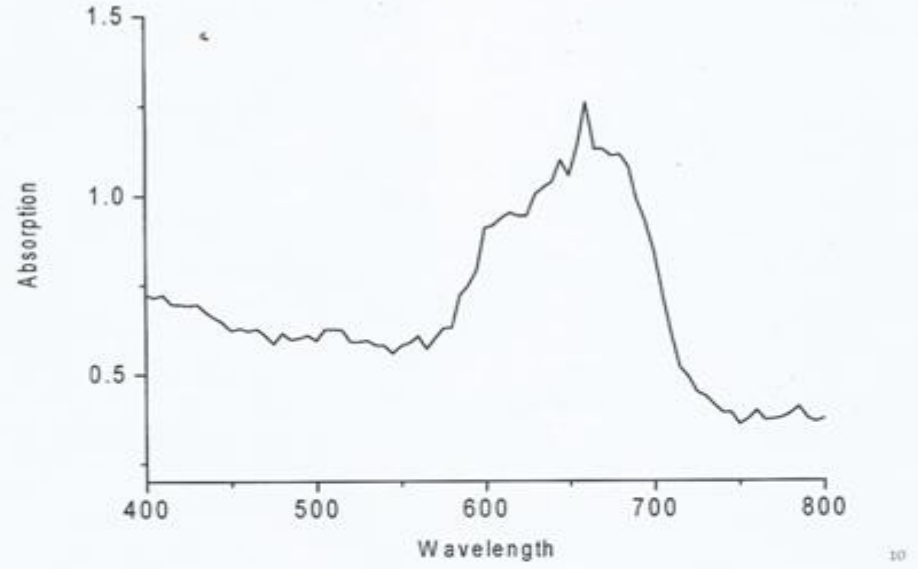
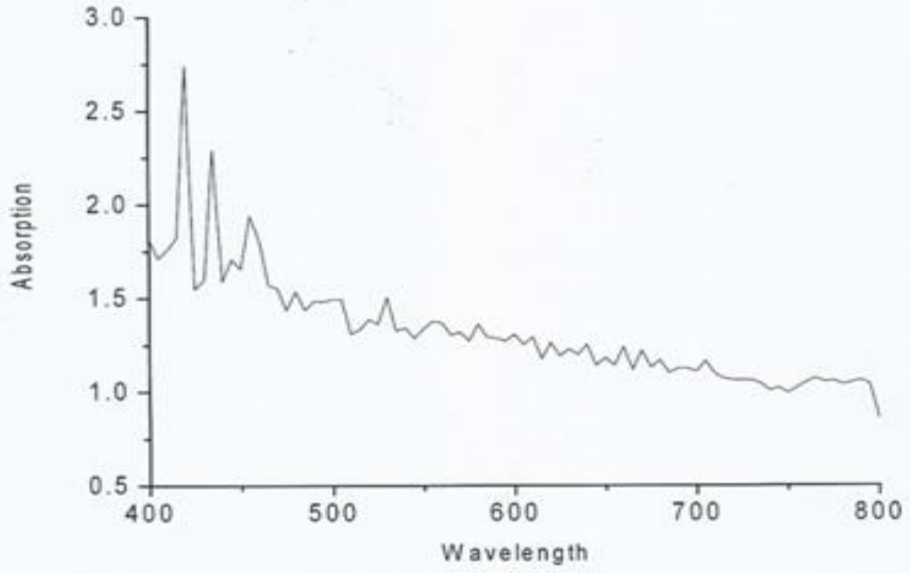


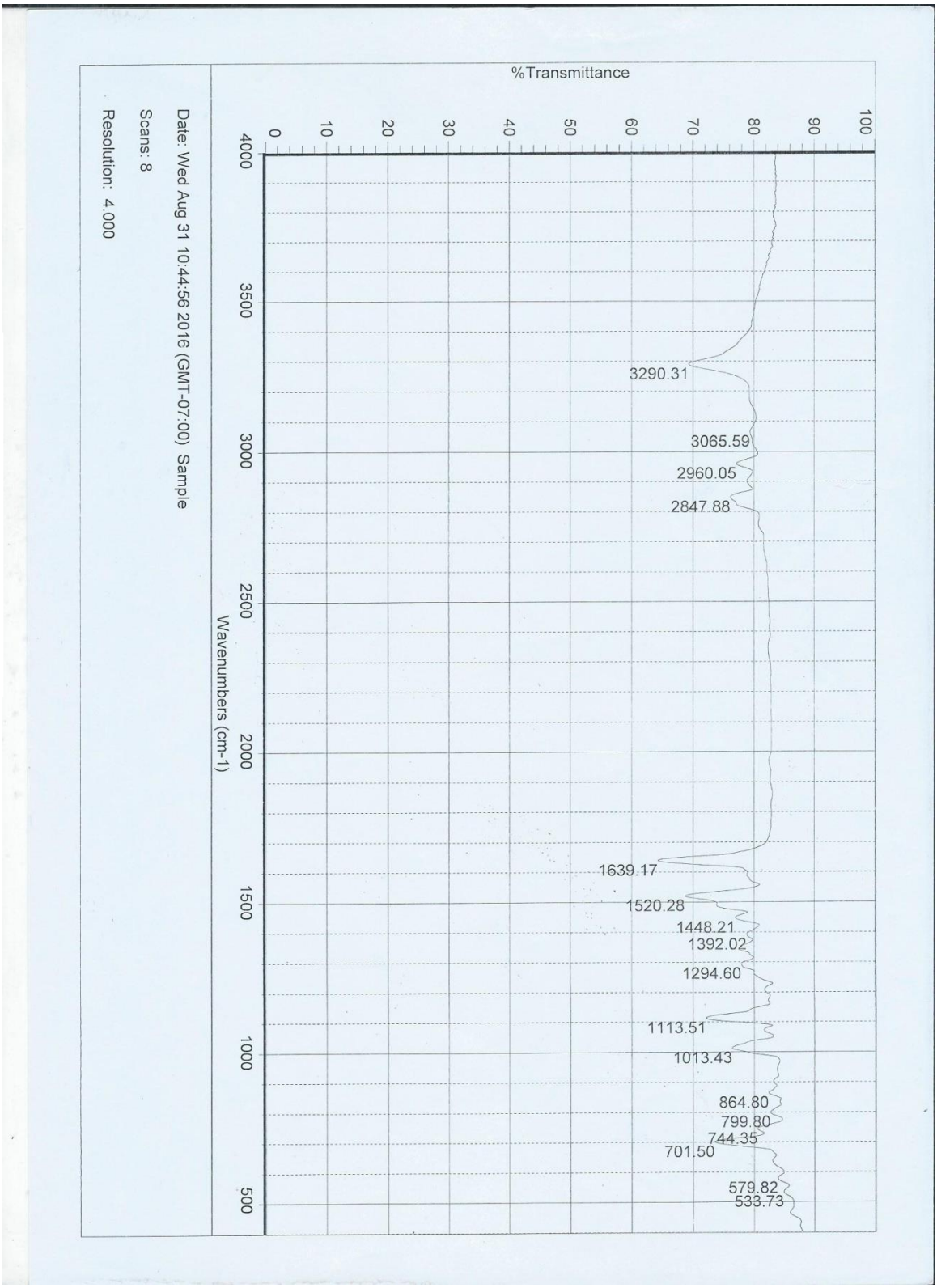
ABS	nm
1.259	660

Uv-Vis ofMBA +Zn(PH=8)



ABS	nm
2.742	420

IR Spectral of MBB



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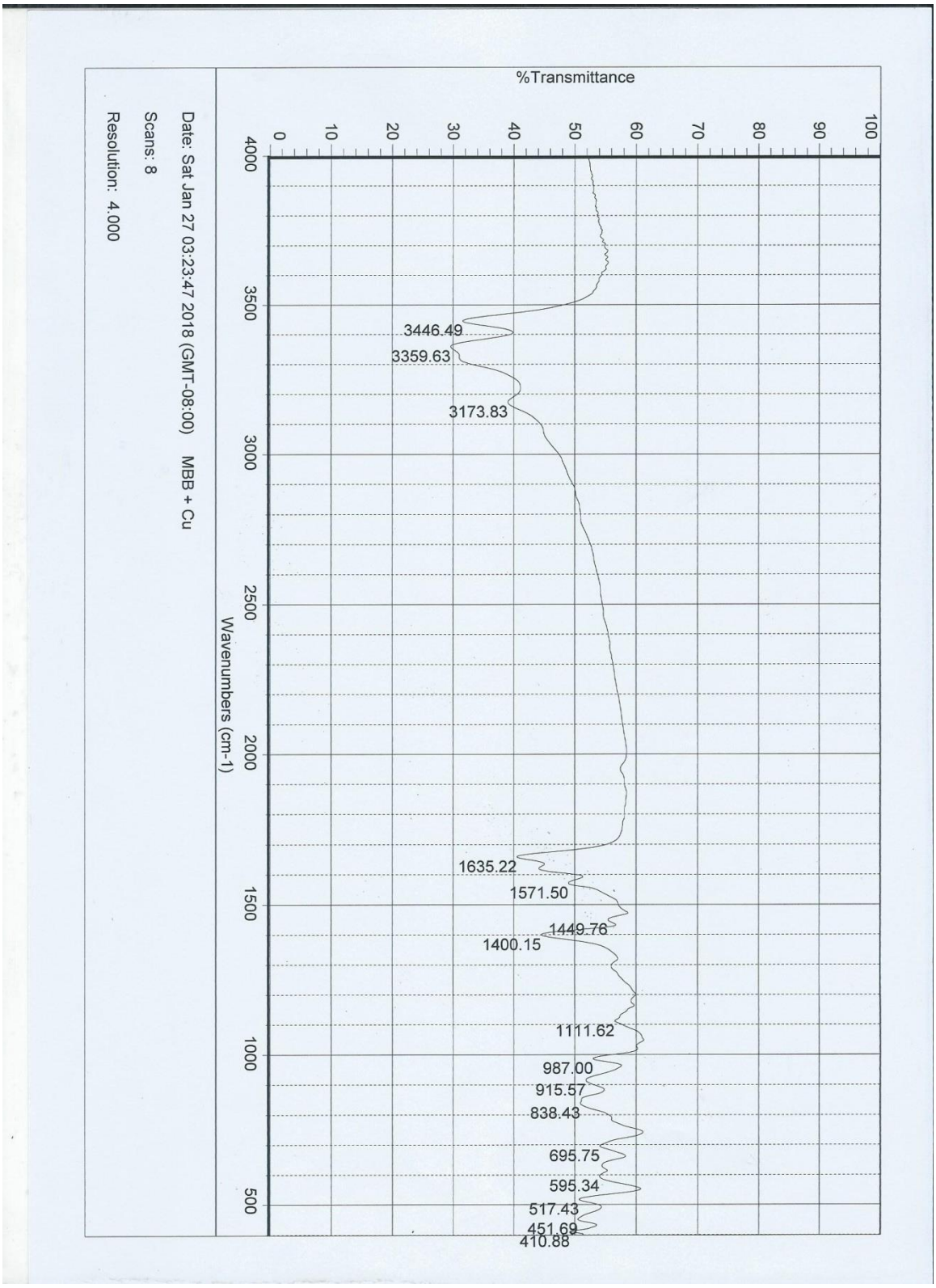

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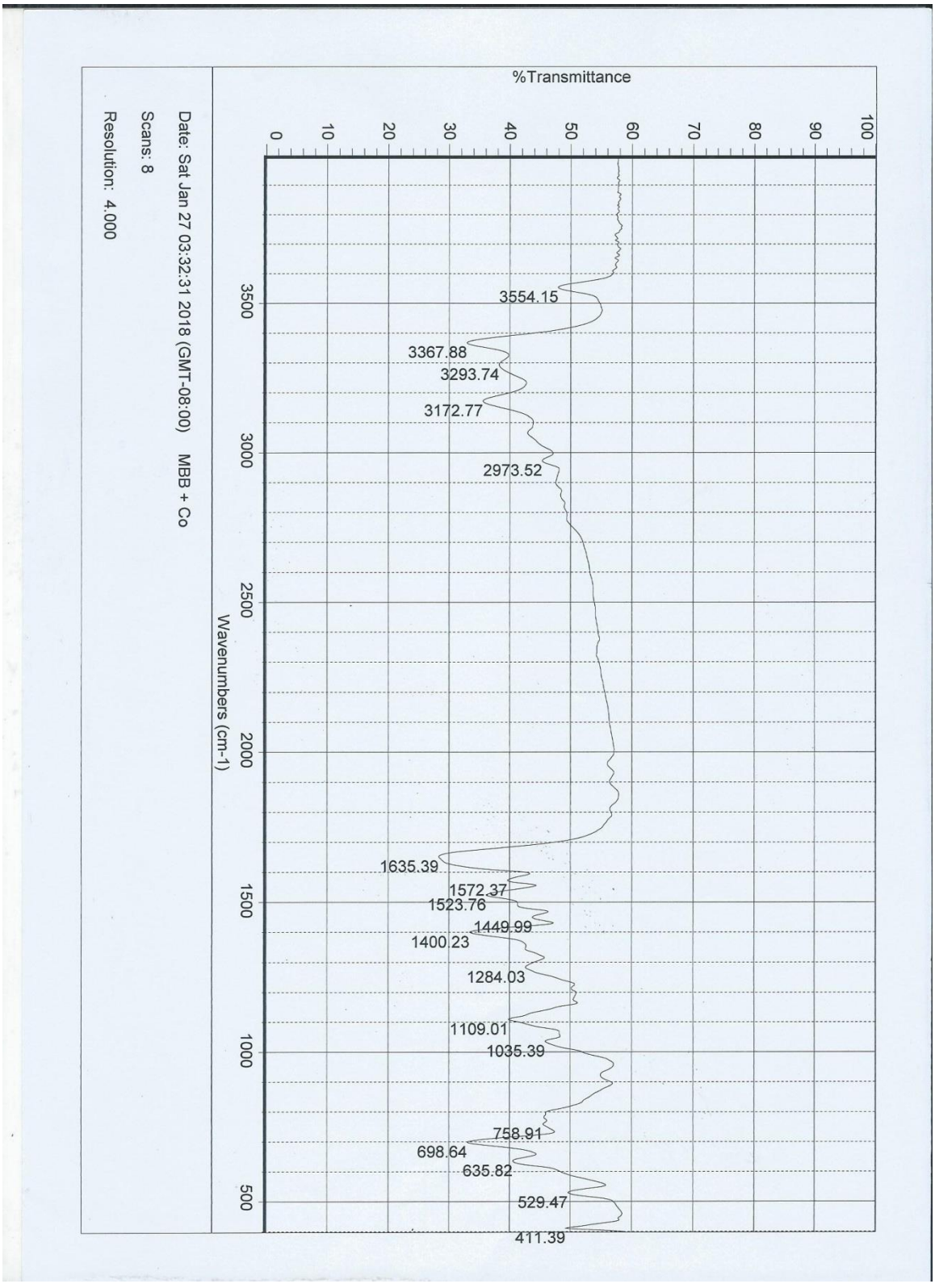

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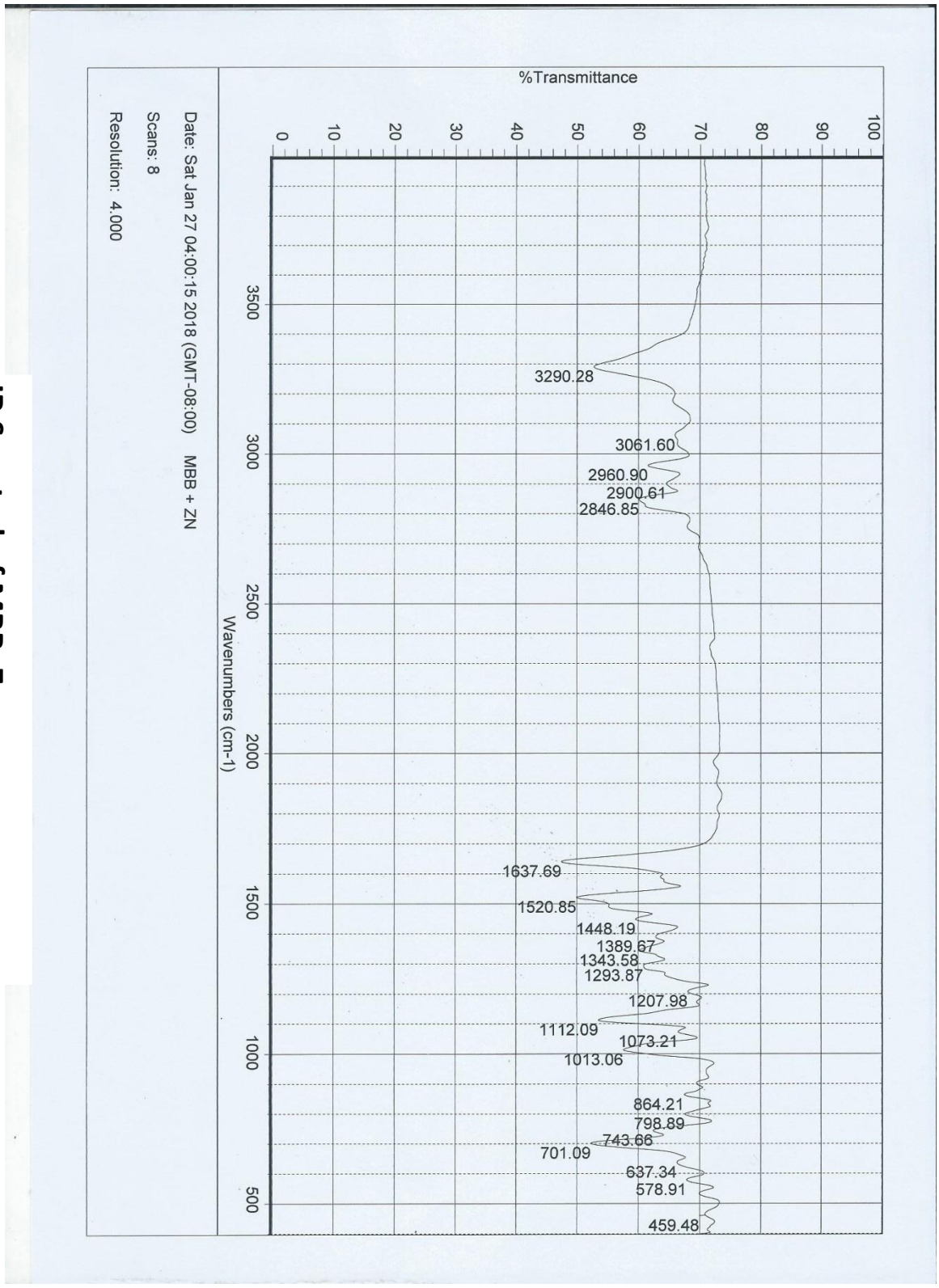
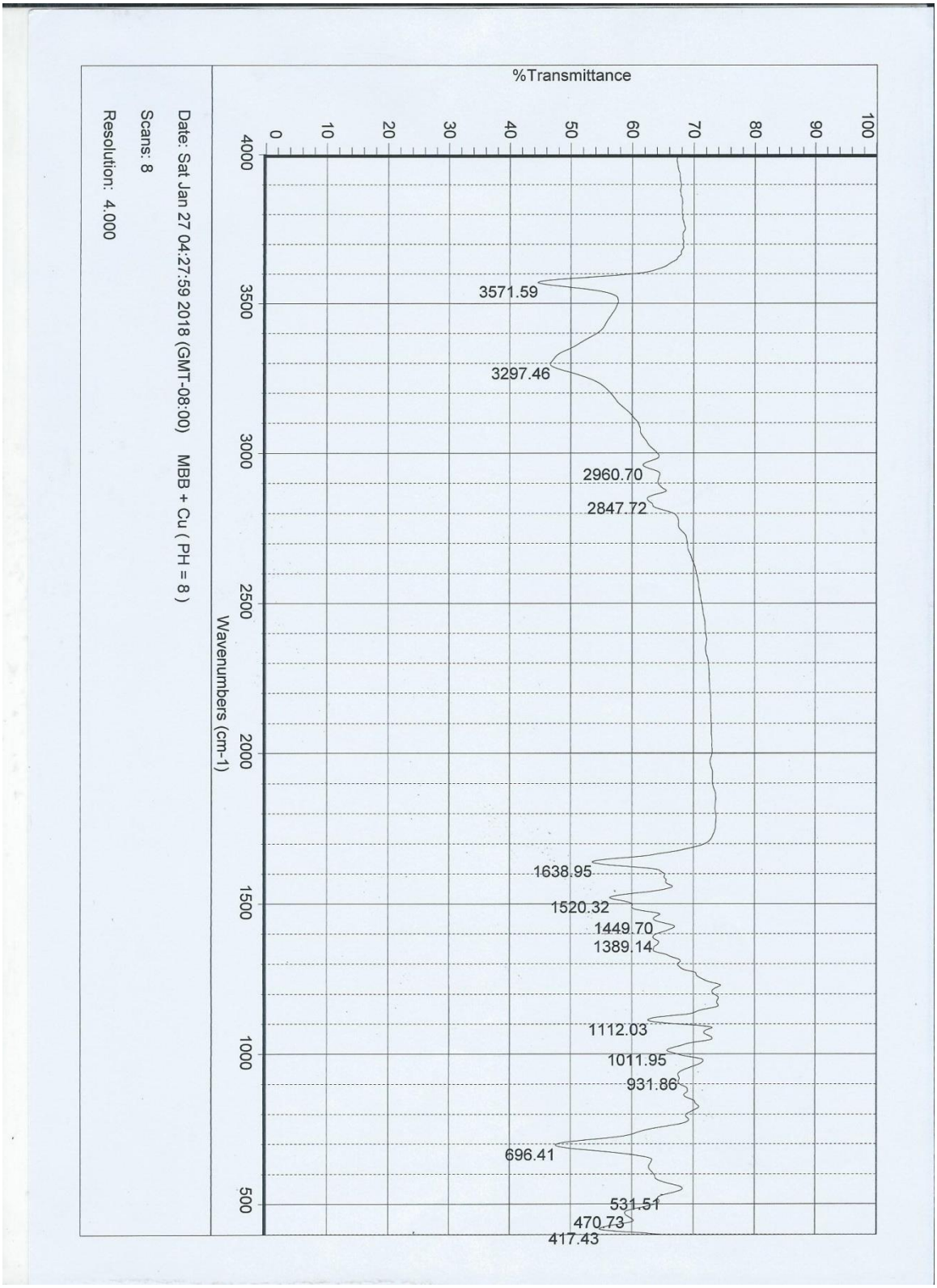
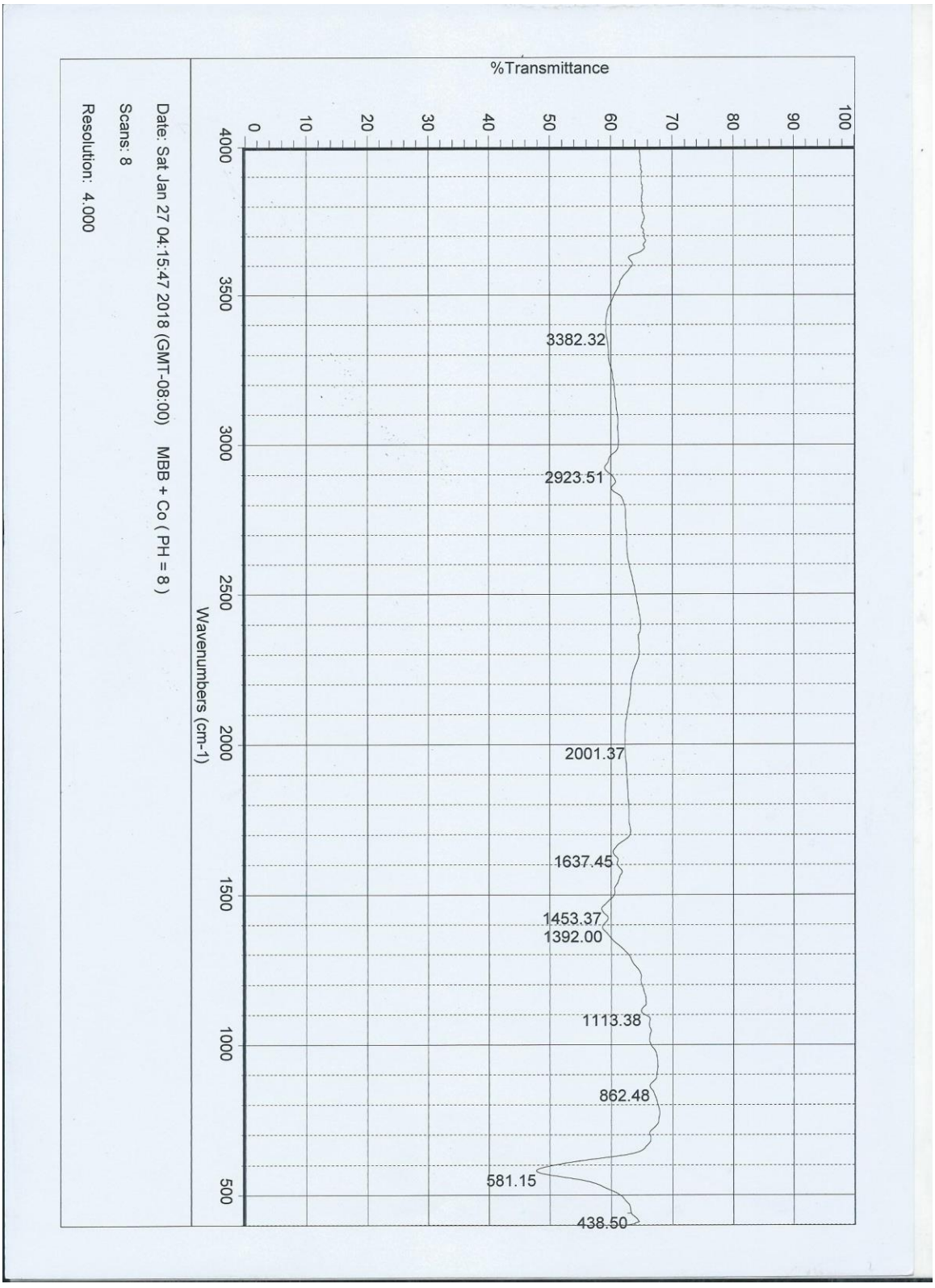


IR Spectral of MBB+Cu (PH=8)



IR Spectral of MBB+Co(PH=8)



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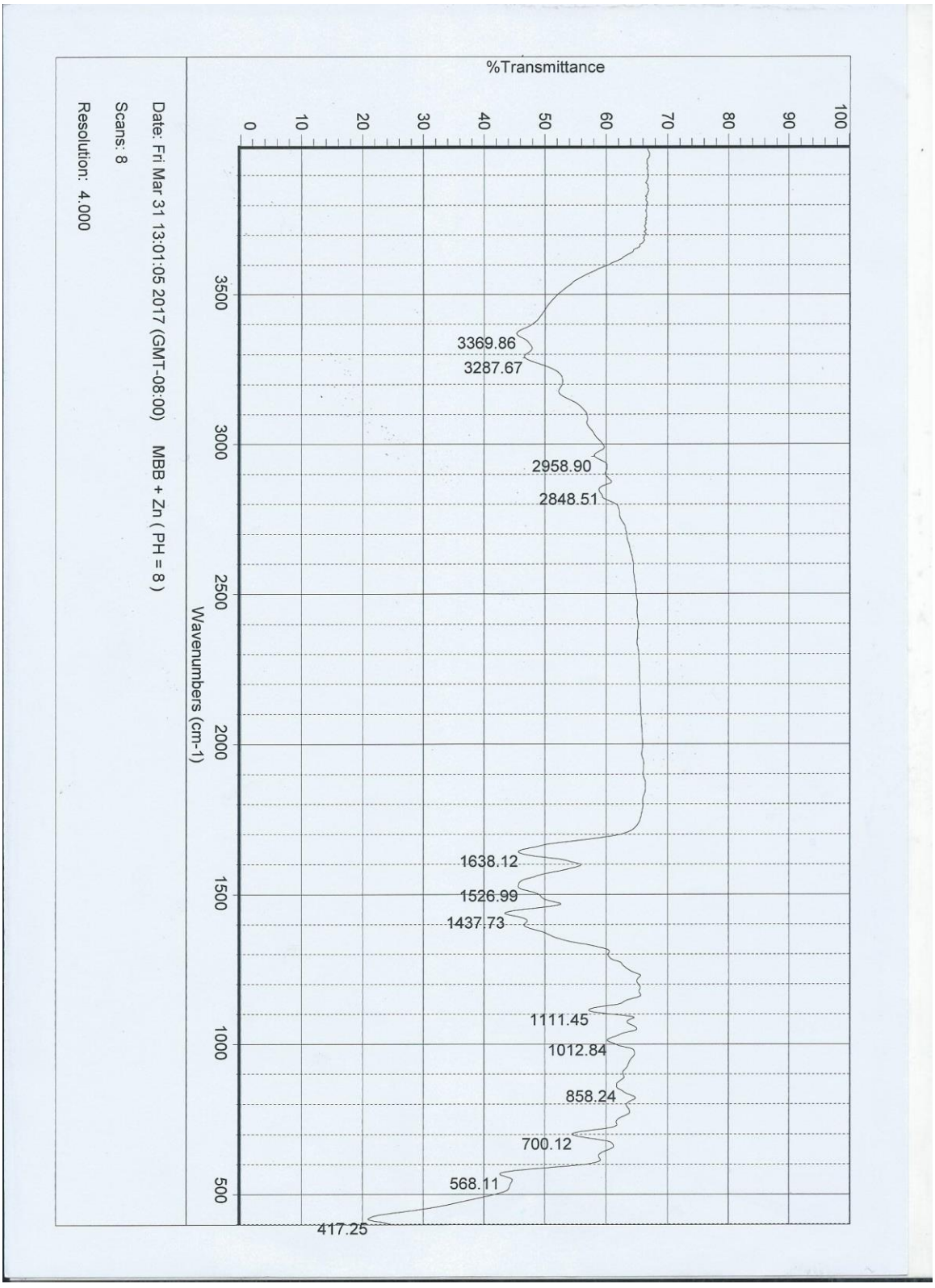
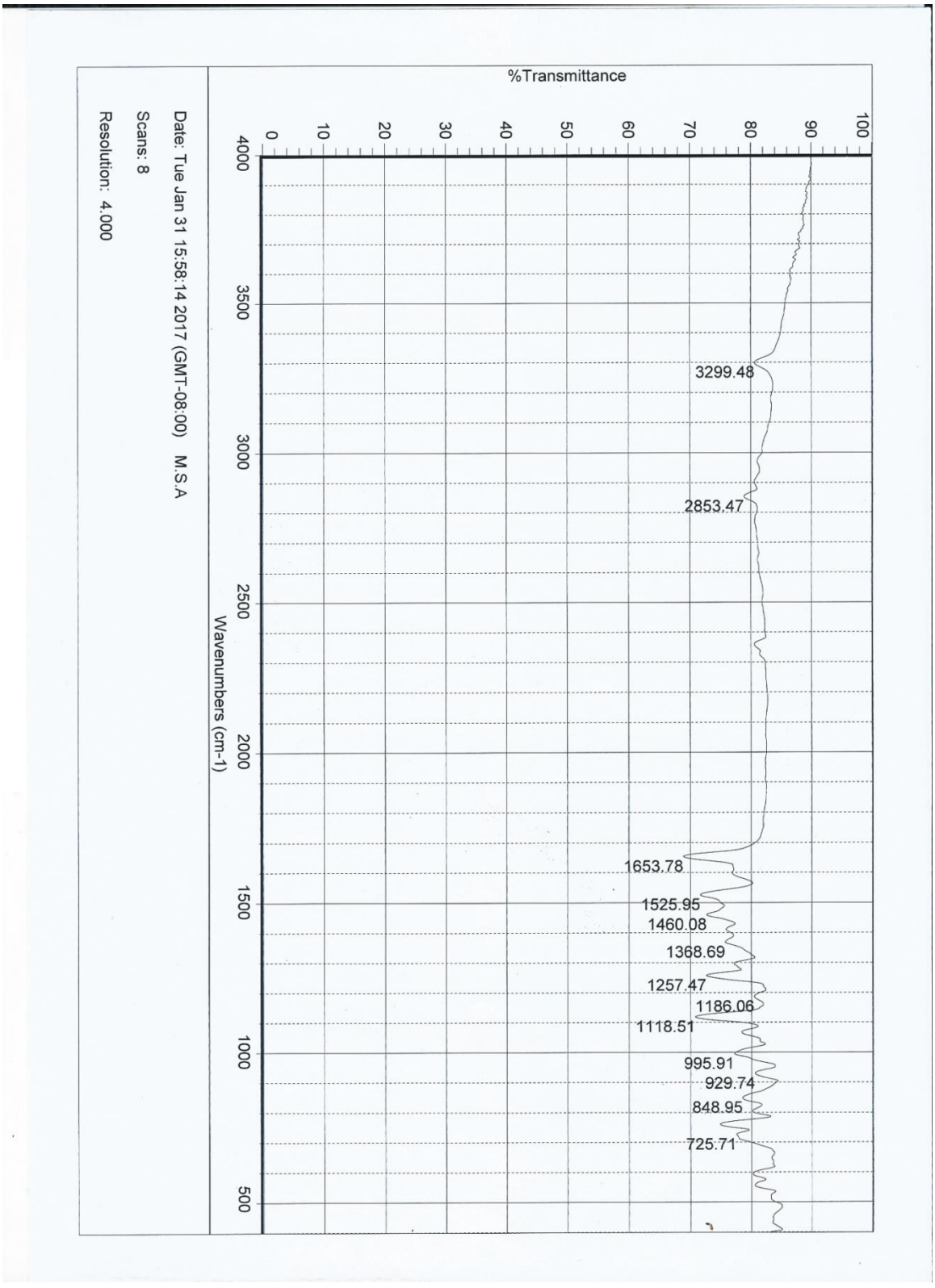


IR Spectral of MSA



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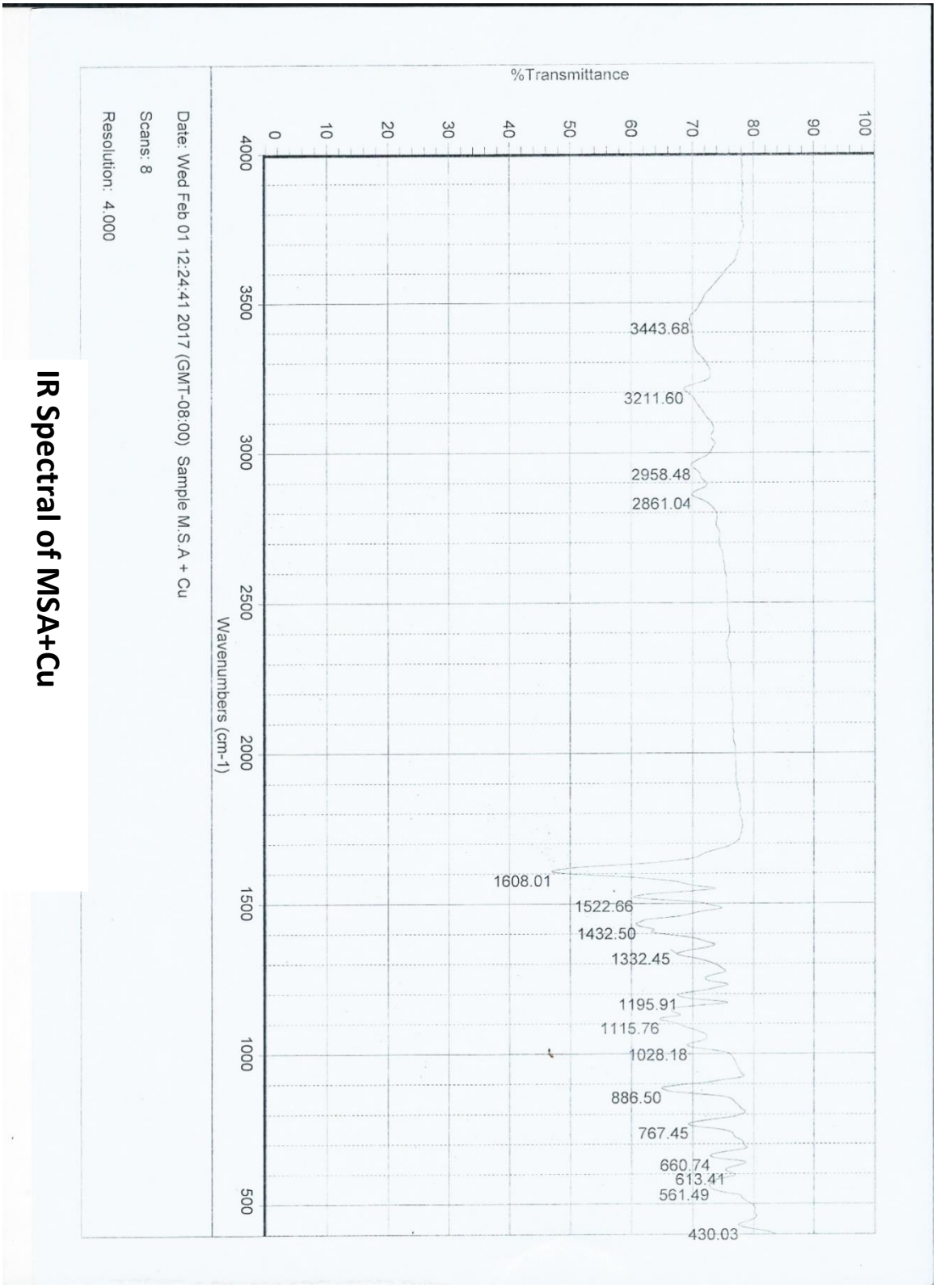

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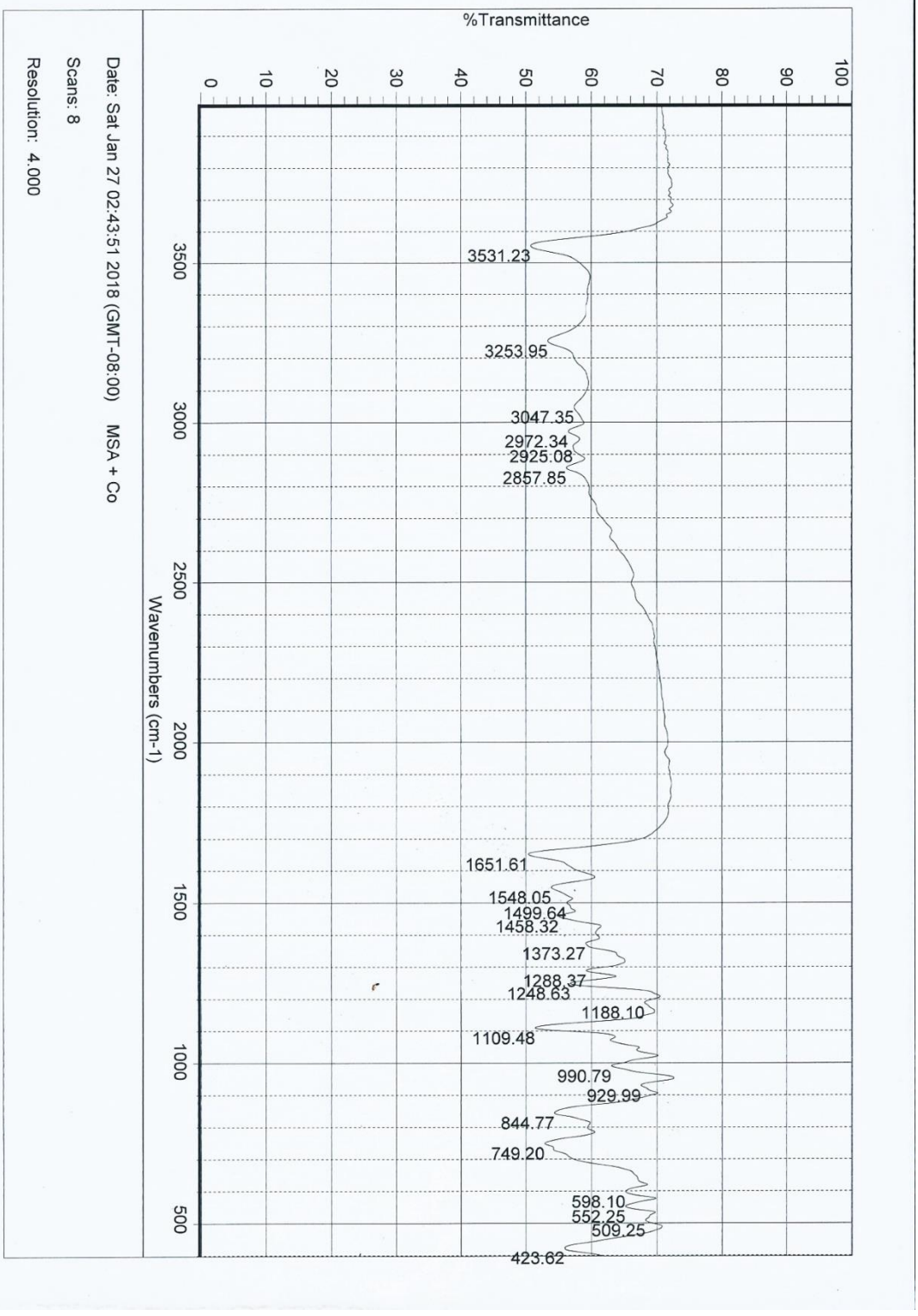
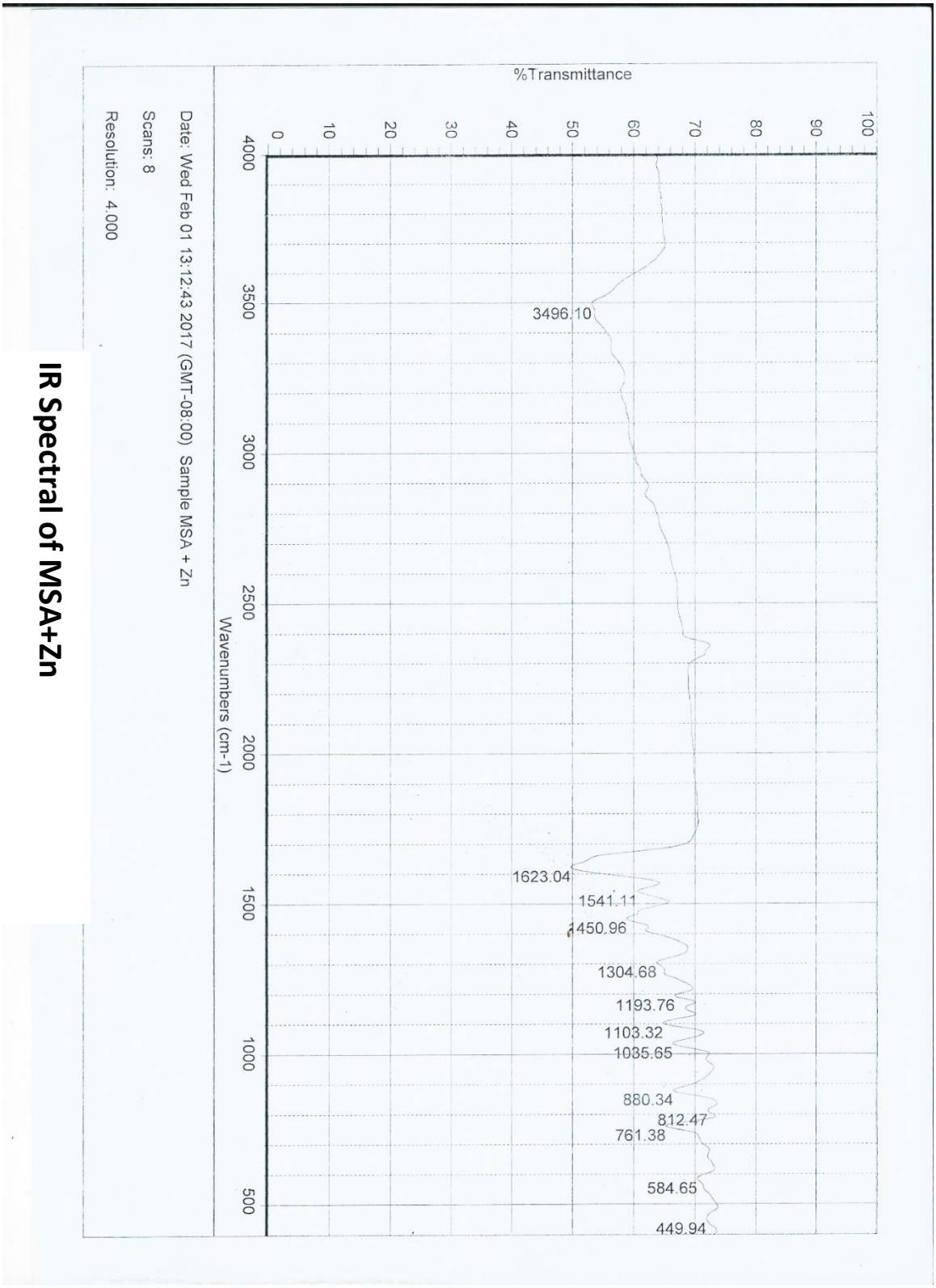
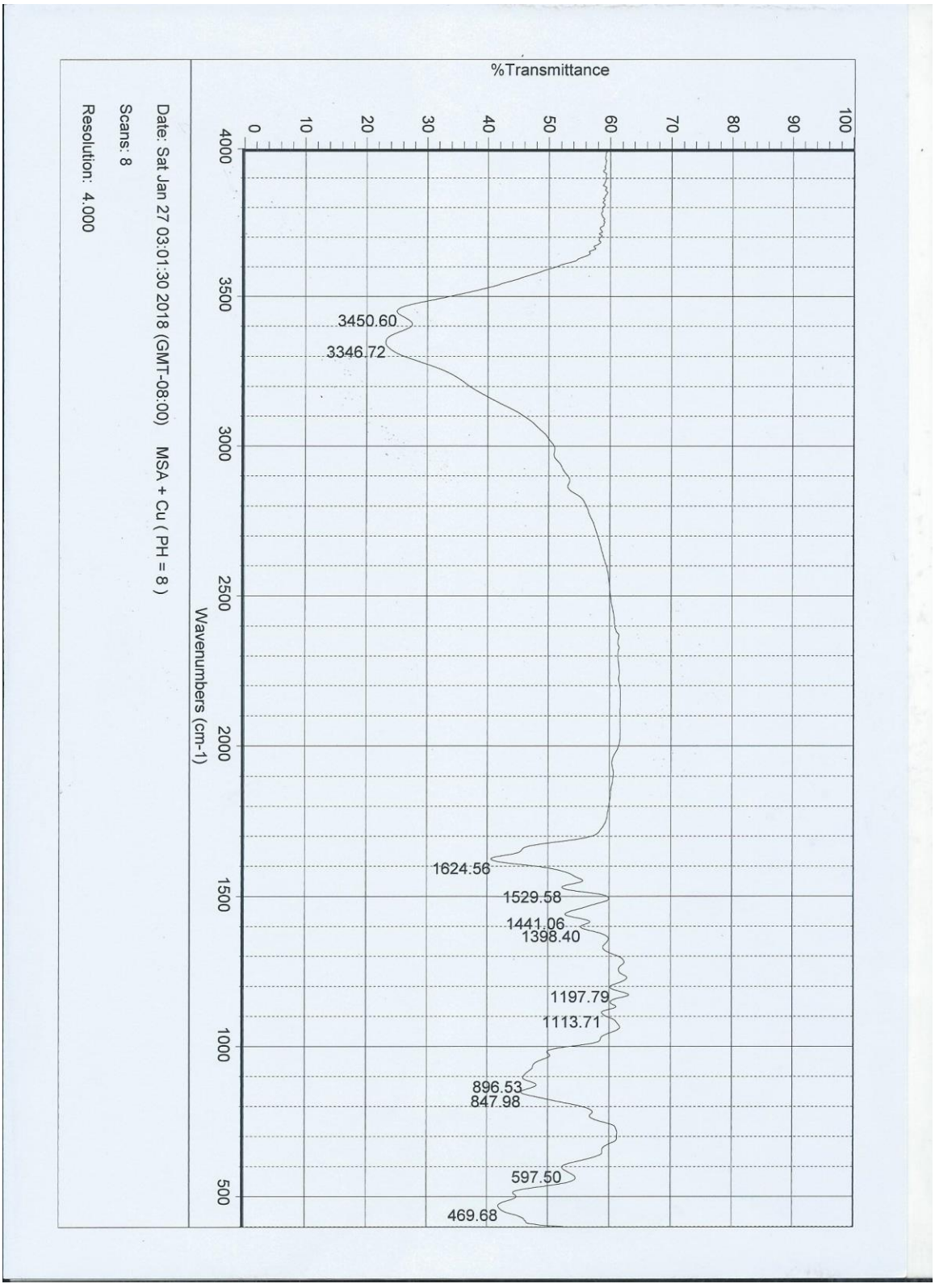




IR Spectral of MSA+Zn

IR Spectral of MSA +Cu(PH=8)



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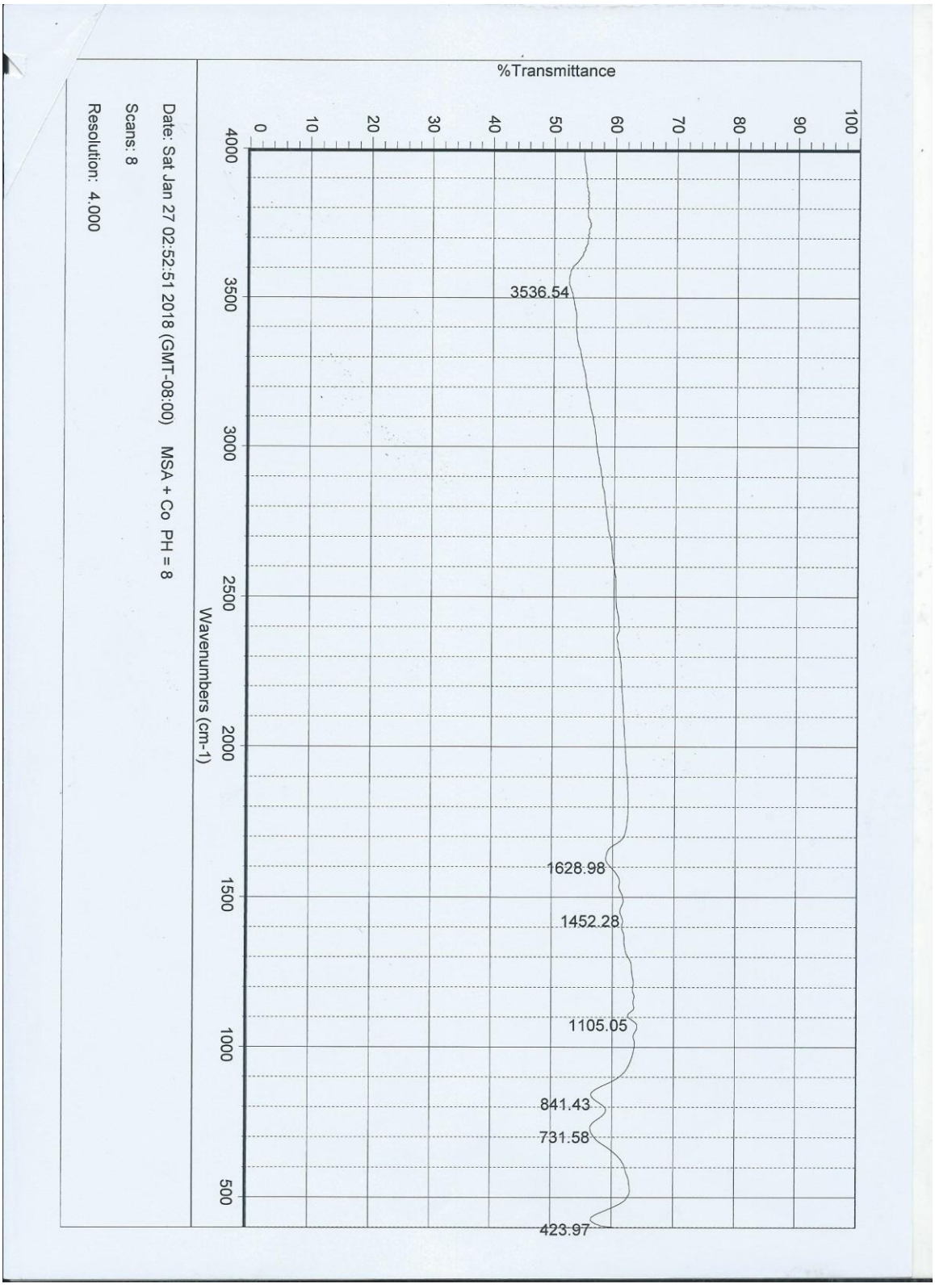
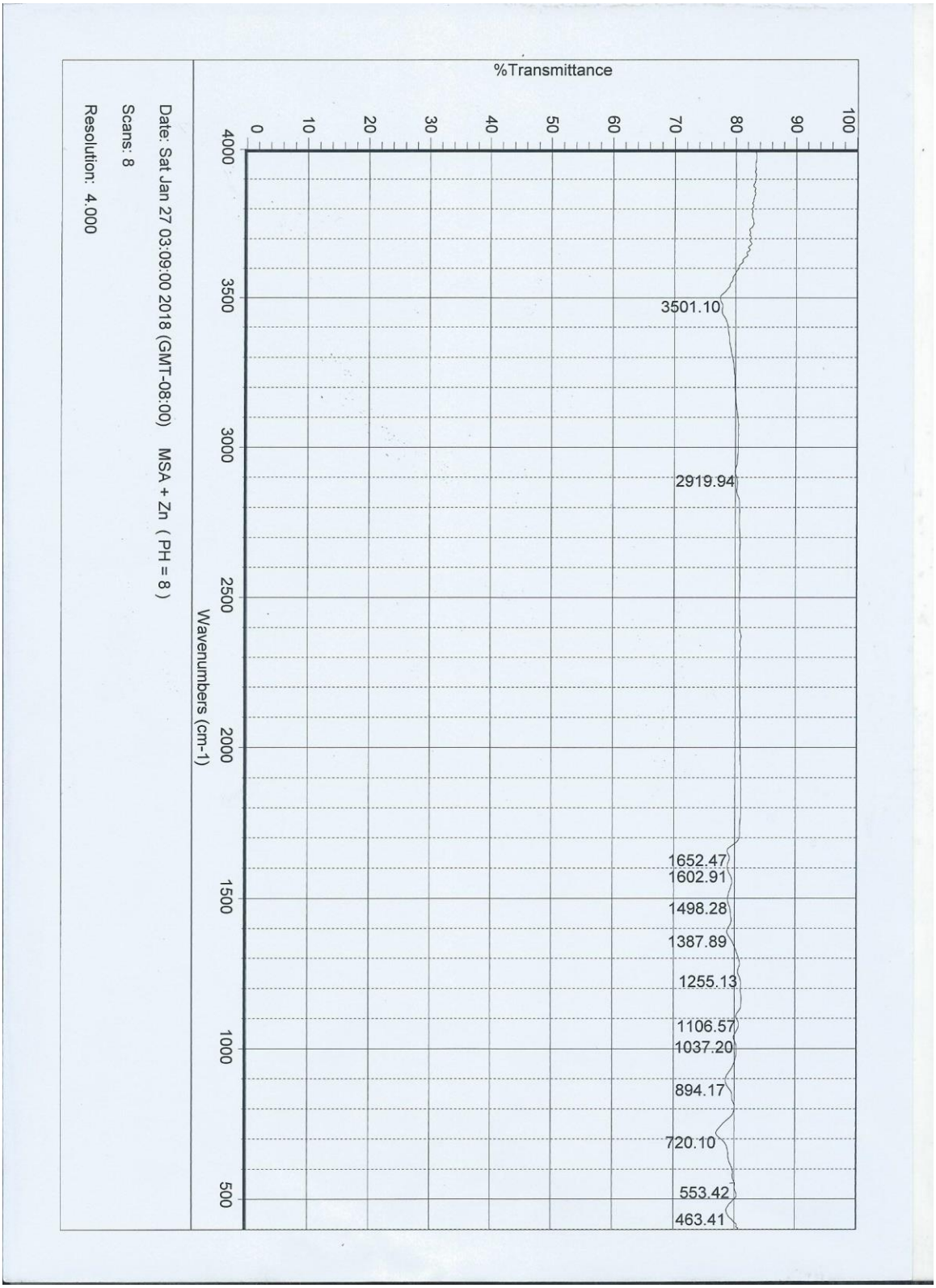
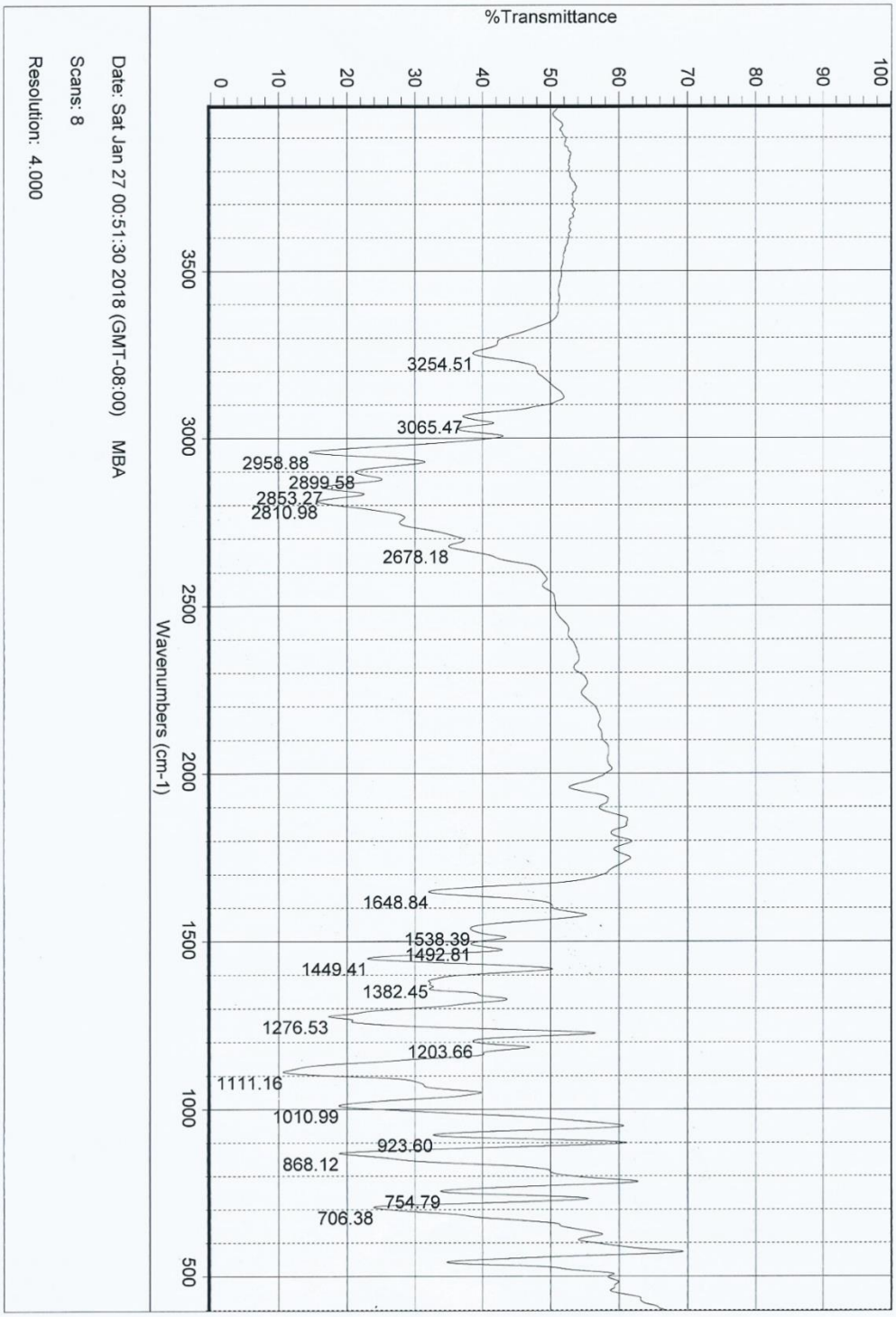


IR Spectral of MSA +Zn(PH=8)



IR Spectral of MBA



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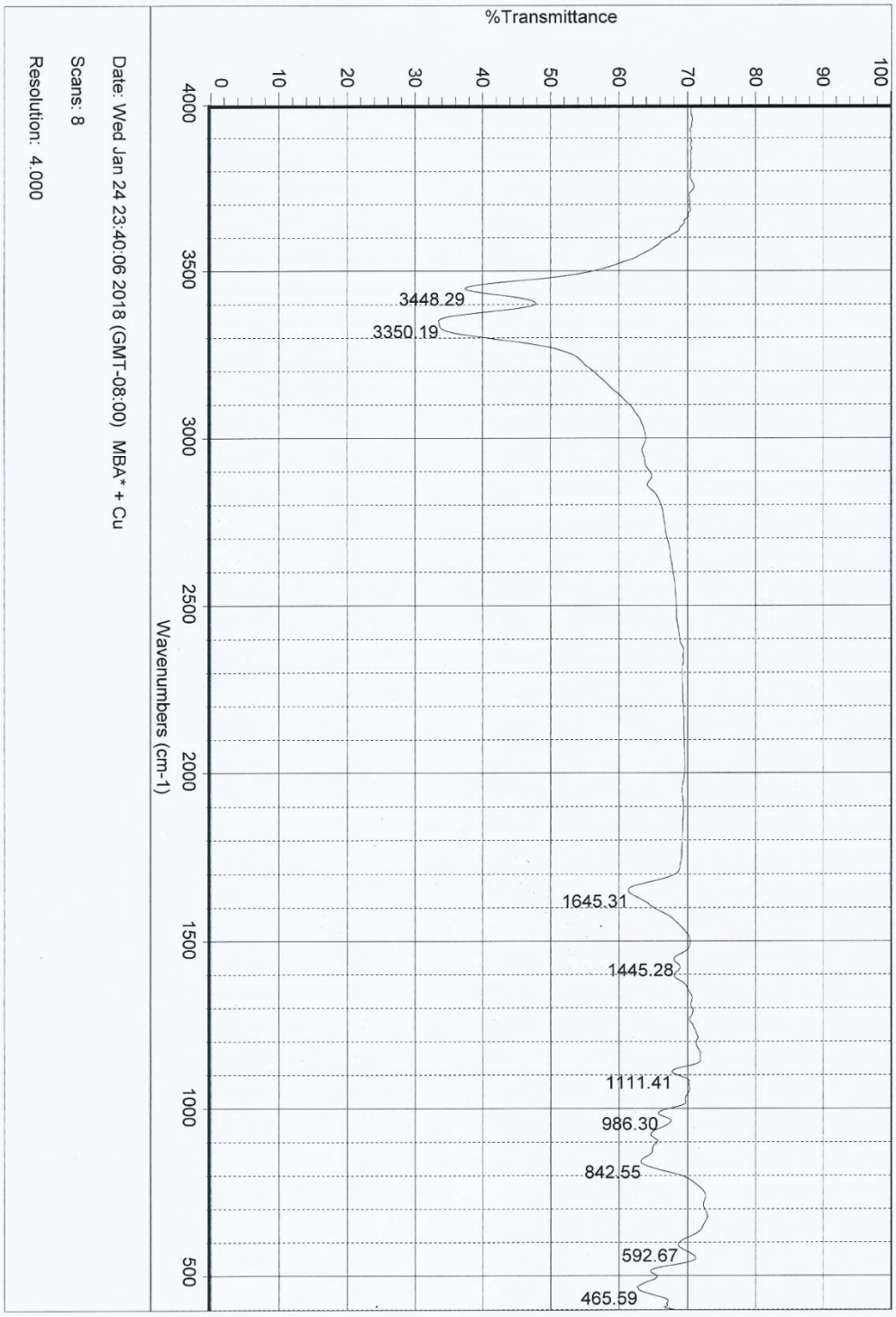

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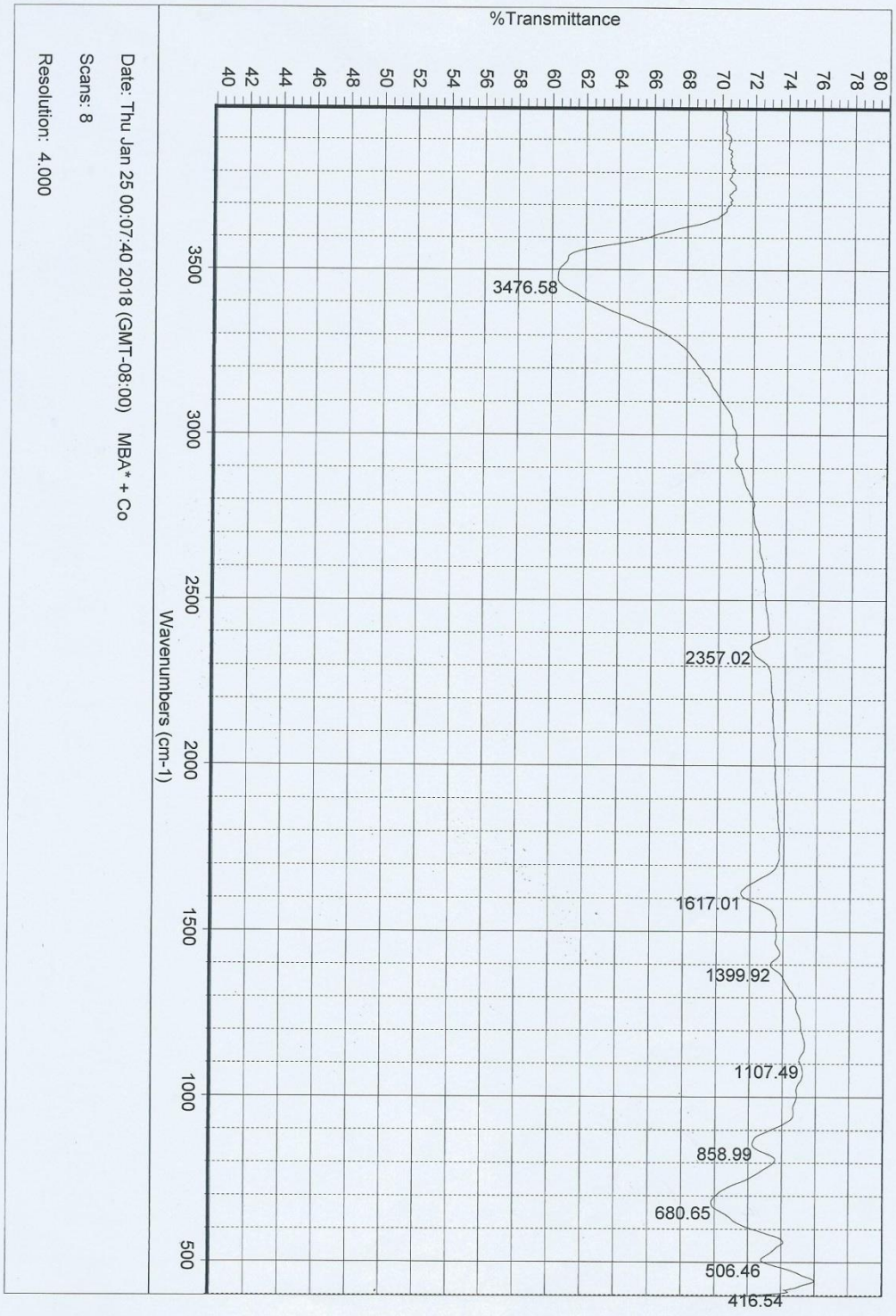

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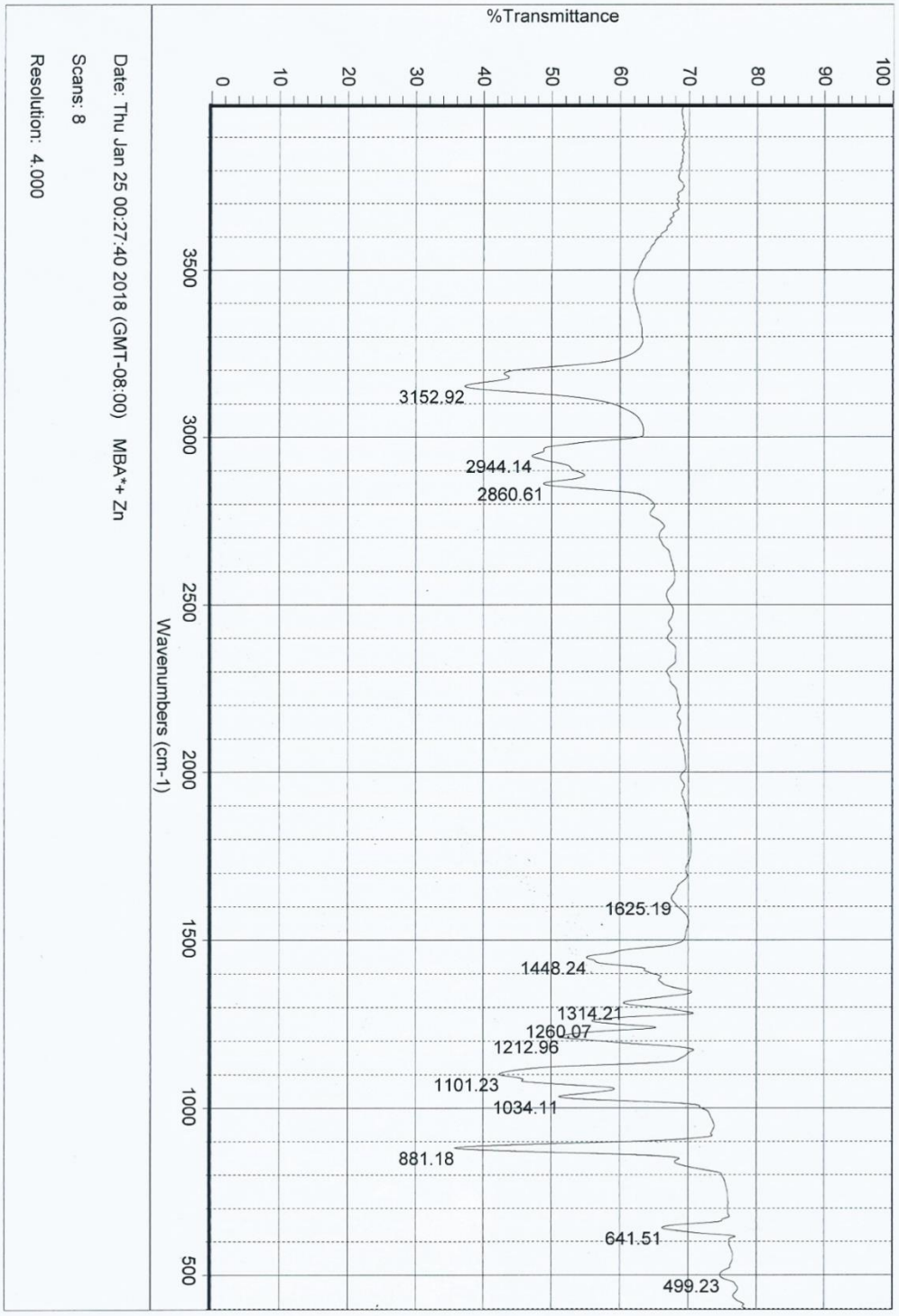
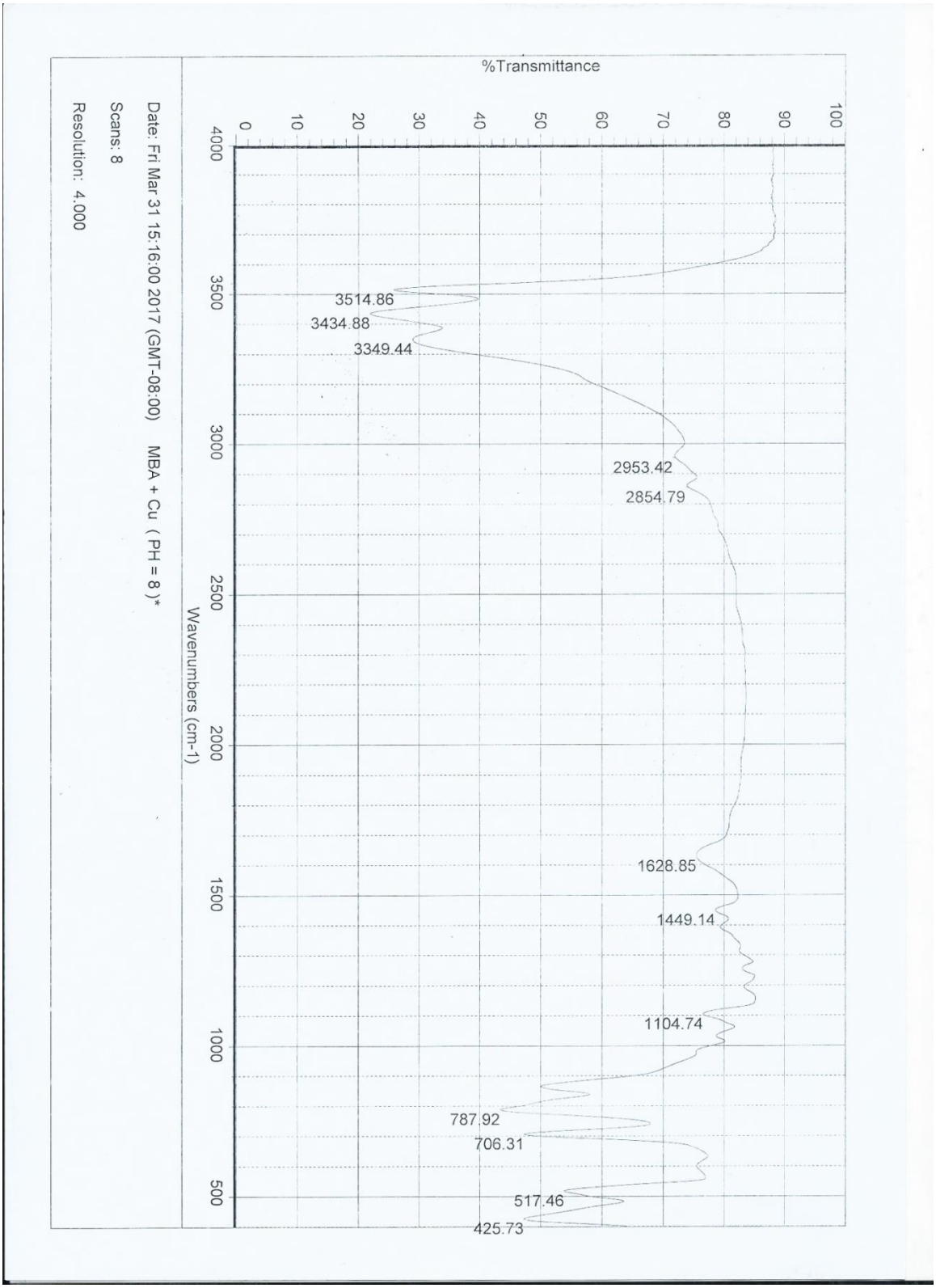
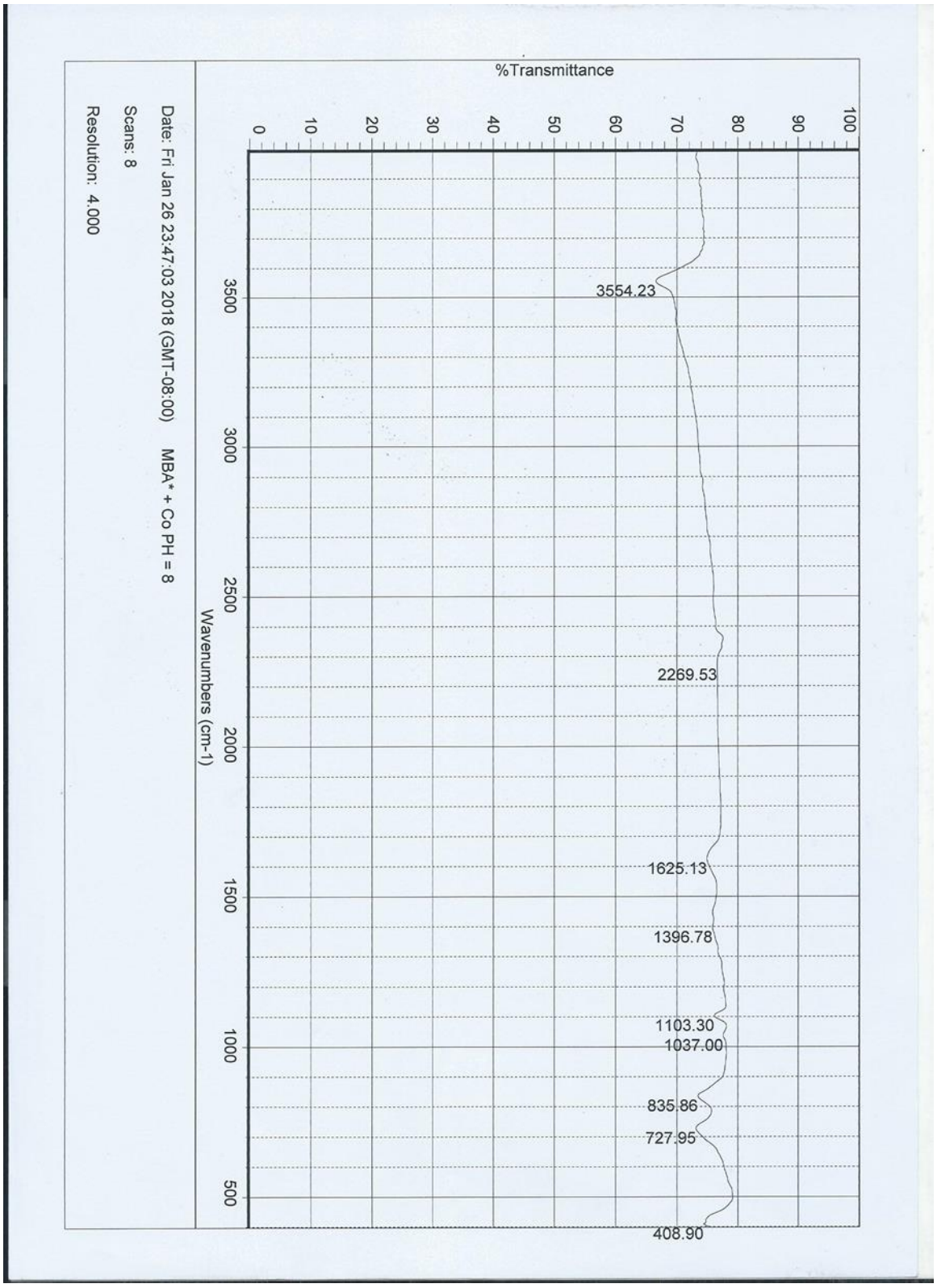


IR Spectral of MBA +Cu (PH=8)



IR Snectral of MBA+Co (PH=8)



IR Spectral of MBA+Zn (PH=8)