COORDINATION CHEMISTRY OF IBUPROFEN WITH SELECTED TRANSITION METALS: SYNTHESIS AND CHARACTERIZATION.

A PROJECT REPORT SUBMITTED

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CERTIFICATION

This is to certify that this project work was carried out by AYORINDE RUTH AYO MIDE, under the supervision of

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DEDICATION

My sincere heart of thanks goes to Almighty God for protection and mercy as well as the wisdom granted unto me throughout the National Diploma program

I dedicate this project to my loving and caring parents Elder and Mrs. Ayorinde and to my siblings Bukola, David and john

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My sincere heart of gratitude goes to the almighty God, the all in all and most high for the knowledge given to me for the successful completion of my national diploma program.

This project would not have been possible without the cooperation of a very number of people. My debt in this regard, however, is to my supervisor in person of Mr Ogunyemi O.J whose patience, criticisms and comments extends to fully in time as they did in details. I am extremely grateful and I hope that the final result will not be a disappointment to him.

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I also appreciate my siblings and my friends Yusuf, Bukola, Temitope.Thank you all and God bless you all.

ABSTRACT

Some Ibuprofen complexes of Ni[ii], Cu[ii] and Iron[ii] were prepared from the reaction of ibuprofen and metal salts.

The complexes were characterized using physical properties like melting point and solubility test.

LIST OF ABBREVIATONS

Ni	Nickel
Zn	
Fe	
S	
Ns	
Ss	
Uv	
IR	
G/mol	

TABLE OF CONTENT

CHAPTER ONE

1.1 INTRODUCTION

Ibuprofen was the first member of Propionic acid derivatives introduced in 1969. It is a popular domestic and over the counter analgesic and antipyretic for adults and children. Ibuprofen has been rated as the safest conventional NSAID by spontaneous adverse drug reaction reporting systems in the UK. This project summarizes the main pharmacological effects, therapeutical applications and adverse drug reactions, drug-drug interactions and food drug interactions of ibuprofen that have been reported especially during the last 10 years. Ibuprofen is (2RS)-1[4-(2-methyl propyl) phenyl] propionic indomethacin, are still the most common side effects.1 acid (BP. 2004). Ibuprofen was the first member of propionic acid derivatives to be introduced in 1969 as a better alternative

to Aspirin. Gastric discomfort, nausea and vomiting, though less than aspirin or Ibuprofen is the most commonly used and most frequently prescribed NSAID[2][3] It is a non-selective inhibitor of cyclooxygenase-1 (COX-1) and Cyclooxygenase-2 (COX-2).[4]. Although its anti inflammatory properties may be weaker than those of some other NSAIDs, it has a prominent analgesic and antipyretic role. Its effects are due to the

inhibitory actions on cyclo-oxygenases, which are involved in the synthesis of prostaglandins. Prostaglandins have

an important role in the production of pain, inflammation and fever.[5]

1.2 CLINICAL PHARMACOLOGY OF IBUPROFEN

Ibuprofen is supplied as tablets with a potency of 200 to 800 mg.[6] The usual dose is 400 to 800 mg three times a day.[7] It is almost insoluble in water having pKa of 5.3.[8] It is well absorbed orally; peak serum concentrations are attained in 1 to 2 hours after oral administration. It is rapidly bio-transformed with a serum half life

of 1.8 to 2 hours. The drug is completely eliminated in 24 hours after the last dose and eliminated through metabolism.[9][10]. The drug is more than 99% protein bound, extensively metabolized in the liver and little is excreted unchanged.[11]

Although highly bound to plasma proteins (90-99%),displacement interactions are not clinically significant, hence the dose of oral anti-cogulants and oral hypoglycemic needs not be altered.1 More than 90% of an ingested dose is excreted in the urine as metabolites or their conjugates, the major metabolites are

hydroxylated and carboxylated compounds.[6][12]. Old age has no

significant effects on the elimination of ibuprofen.[13]. Renal impairment also has no effect on the kinetics of the drugs, rapid elimination still occur as a consequence of metabolism.[14]. The administration of ibuprofen tablets either under fasting conditions or immediately before meals yield quiet similar serum concentrations-time profile. When it is administered immediately after a meal, there is a reduction in t0he rate of absorption but no appreciable decrease in the extent of absorption.[15]

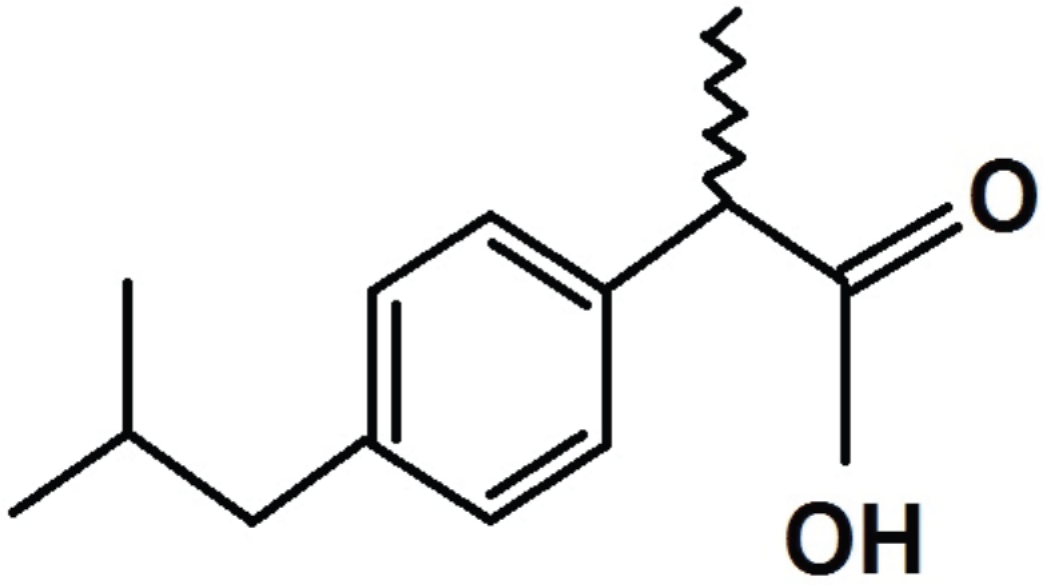

Figure 1. Structural formula of Ibuprofen

1.3 Therapeutic Application of Ibuprofen

A low dose ibuprofen is as effective as aspirin and paracetamol for the

indications normally treated with over the counter medications.[16]. It is widely used as an analgesic, an anti inflammatory and an antipyretic agent.[17-19]. Recemic ibuprofen and S(+) enantiomer are mainly used in the treatment of mild to moderate pain related to dysmenorrhea, headache, migraine, postoperative dental pain, management of spondylitis, osteoarthritis, rheumatoid arthritis and soft tissue disorder.[20]. A number of other actions of NSAIDs can also be attributed to the inhibition of prostaglandins (PGs) or thromboxane synthesis, including alteration in platelet function. (PGI2 and Thromboxane), prolongation of gestation and labor

(PGE2, PGF2A), gastrointestinal mucosal damage (PGI2 and PGE2), fluid and electrolyte imbalance (renal PGs), premature closure of ductus arteriosus (PGE2) and bronchial asthma (PGs).[21]. The main therapeutic applications of ibuprofen are as follows:

1.3.1 Patent Ductus arterosus (PDA)

This is a frequent complication in premature infants. So far, intravenous indomethacin is the standard mode of medical therapy.[22]. However, because of adverse effects of indomethacin, other PG inhibitors such as ibuprofen have been studied for the closure of ductus arteriosus, and results indicated that ibuprofen is

as effective as indomethacin.[23]

1.3.2 Rheumatoid and osteo-arthritis (RA and OA)

Ibuprofen is widely used in the management of numerous inflammatory, musculoskeletal and rheumatic disorders, because they are highly effective having minimal toxicities.[24],[25]. Ibuprofen 2400 mg per day resulted in rapid improvement and complete resolution of gouty arthritis within 72 hours.26 In doses of approximately 2400 mg daily, it is equivalent to 4g of aspirin in

terms od anti inflammatory effects.[27] Higher doses, 1200 to 1600

mg per day have been compared with a number of NSAIDs and it

has been found to be as effective and well tolerated.[28]. Osteoarthritis

is very common and treatment involves NSAIDs, particularly ibuprofen.[29],[30] For control of joint symptoms, diclofenac, ibuprofen, tolmetin and naproxen are equally effective.[31]. Roughly 1% of rheumatoid arthritis (RA) patients receiving NSAIDs are prone to develop major GI bleeds.[32]. With ibuprofen, gastric toxicity has been observed in 10 - 32% of patients.[33].

Table 1: Doses of Ibuprofen in adult & Children (34)

Patient	Ibuprofen	Doses
Adult	Analgesia	200-400mg. Every 4-6hrs

Children	Anti- inflammatory Antipyretic Anti-inflamatory	300 mg, Every 6-8 hrs or 400-800 mg 3-4 times daily. 5-10 mg/kg. Every 6 hrs (max. 40 mg/kg per day). 20-40 mg/kg/day in 3-4 divided dose.

1.3.3 Cystic fibrosis (CF)

High dose ibuprofen therapy has also been shown to be effective in decreasing inflammation, probably by decreasing polymorphonuclear cell influx into the lungs.[34]. The risk of developing GI side effects from high dose ibuprofen therapy is low in patients with CF.[35],[36]

1.3.4 Orthostatic hypotension

Ibuprofen is useful in the treatment of severe orthostatic hypotension as with other NSAIDs.[37]. Toxic effects are unlikely at doses below 100

mg/kg but can be life-threatening or severe above 400 mg/kg.[38].However, large doses do not indicate that the clinical course is likely to be lethal.[39]

1.3.5 Dental pain

Ibuprofen is one of the most effective and widely used NSAID in treatment of dental pain.[40]. Dental practitioners have relied on ibuprofen and other NSAIDs to manage acute and chronic orofacial pain.[41] A dose of 400 mg of ibuprofen provides effective analgesic for the control of postoperative pain after third molar surgery.[42]. A liquid gel preparation of ibuprofen 400mg provides faster relief and superior overall efficacy in post surgical dental pain.[27]

1.3.6 Dysmenorrhea, fever and headache

Non-prescription ibuprofen is useful for managing minor aches and pains, reducing fever and relieving symptoms of dysmenorrhea.[43-45].Dysmenorrhea is the most common menstrual complain.[46].Ibuprofen was superior to placebo for pain relief and menstrual fluid PGF2 alpha suppression.[47]. Cycloxygenase inhibitors reduce

the amount of menstrual prostanoids release, with concomitant reduction

in uterine hyper contractility.[48]. Over-the-counter (OTC) ibuprofen preparations are mainly used for acute indications, such as fever or headaches, especially tension type headache.[49-51.It has been reported that the combined use of paracetamol

and ibuprofen reduce fever very rapidly.[52]. Fever almost invariably accompanies uncomplicated falciparum malaria. In a randomized double-'blind' study, a single dose of ibuprofen was compared with paracetamol for the treatment of fever >38·5 °C due to uncomplicated falciparum malaria. Ibuprofen was significantly more

effective than paracetamol in lowering temperatures throughout the first 4-5 hrs after dosing and thus should be considered as an antipyretic agent in the management of uncomplicated falciparum infections, providing there is no contraindication to its use.[53]. Evers *et al*. in 2006, conducted a double blind study to investigate the efficacy of zolmitriptan and ibuprofen in the treatment of migraine in children and adolescents. Pain relief rates after two hours were

28% for placebo, 62% for zolmitriptan and 69% for ibuprofen.[54]

1.3.7 Prophylaxis of Alzheimers disease

The administration of NSAIDs, particularly ibuprofen markedly reduced neurodegeneration.[55],[56]. In some studies, ibuprofen showed superior

results compared to placebo in the prophylaxis of Alzheimer's disease, when given in low doses over a long time. Further studies are needed to confirm the results before ibuprofen can be recommended for this indication.[57]

1.3.8 Parkinson's disease (PD)

Inflammation and oxidative stress have been implicated as pathogenic mechanisms in PD.[58] Epidemiologic evidence showed that regular use of NSAIDs, particularly non aspirin COX inhibitors such as ibuprofen lower the risk of PD.[59],[60]. It induced apoptosis significantly in early and late stages, suggesting that these anti-inflammatory agents might inhibit microbial proliferation.61

1.3.9 Breast cancer

Harris et al. in 1999 conducted a study for utilization of NSAIDs in breast cancer. Breast cancer rate was decreased by approximately 50% with regular ibuprofen intake and 40% with regular aspirin intake. Results suggested that specific NSAIDs may be effective chemo preventive agents against breast cancer.[62]

1.4 Adverse Reactions

NSAIDs are widely used, frequently taken inappropriately and potentially dangerously.[63]. Nevertheless, ibuprofen exhibits few adverse effects.[64] The major adverse reactions include the affects on the gastrointestinal tract (GIT), the kidney and the coagulation system.[65]. Based on clinical trial data, serious GIT reactions prompting withdrawal of treatment because of hematemesis, peptic

ulcer,[66] and severe gastric pain or vomiting showed an incidence of 1.5% with ibuprofen compared to 1% with placebo and 12.5% with aspirin.[67]. Ibuprofen was a potential cause of GI bleeding,68],[69] increasing the risk of gastric ulcers and damage, renal failure, epistaxis,[70-73] apoptosis,[74] heart failure, hyperkalaemia,[75] confusion and bronchospasm.[76]. It has been estimated that 1 in 5 chronic users(lasting over a long period of time) of NSAIDs will develop gastric damage which can be silent.[77]. Other adverse effects of ibuprofen have been reported less frequently. They include thrombocytopenia, rashes, headache,

dizziness, blurred vision and in few cases toxic amblyopia, fluid retention and

ibuprofen.[78] Effects on kidney (as with all NSAIDs) include acute renal failure, interstitial nephritis, and nephritic syndrome, but these very rarely

occur.[27]

1.5 LIGAND AND COMPLEX FORMATION

A ligand is an ion or molecule that donates two or more lone pairs of electrons to a metal ion to form coordination or dative bond.

According to Lewis Theory, ligand is a lewis base due to the electrons they donate to empty orbital. They are either anion or polar molecues. Ligands can be classified based on electron pair they donate according to ligand theory. These includes

i. MONODENTATE LIGAND: they donate one lone pair of electron to neutral metal e.g $pt(Cl)_4$.

ii. Bidentate LIGAND: they donate two lone pair of electron to neutral matal e.g CH_3NH_3

iii. POLYDENTATE LIGAND: they donate more than two lone pairs of electron i.e the binding site is beyond one e.g tetraethylenediammine.

1.6 WHY DRUG-METAL COMPLEX

New development in chemotherapy includes the synthesis and characterization of new drug involving metals. Selective novel metal chelators for the treatment of diseases that involves metal or mineral inbalance. Promising research involves some complexes with different metal ions including those of cobalt, copper, titanium, iron, platinum , gold, molybdenum, tin and manganese. Drug metal complexes are used in treatment of metal deficiency diseases.

1.7 CHEMISTRY OF TRANSISTION METALS USED

1.7.1 NICKEL

Nickel compounds are chemical compounds containing the element nickel which is a member of the group 10 of the periodic table. Most compounds in the group have an oxidation state of +2. Nickel is classified as a transition metal with nickel(II) having much chemical behavior in common with iron(II) and cobalt(II). Many salts of nickel (II) are isomorphous with salts of magnesium due to the ionic radii of the

cations being almost the same. Nickel forms many coordination complexes. Nickel tetracarbonyl was the first pure metal carbonyl produced, and is unusual in its volatility. Metalloproteins containing nickel are found in biological systems. Nickel forms simple binary compounds with non metals including halogens, chalcogenides, and pnictides. Nickel ions can act as a cation in salts with many acids, including common oxoacids. Salts of the hexaaqua ion ($Ni \cdot 6\ H_2O^{2+}$) are especially well known. Many double salts containing nickel with another cation are known. There are organic acid salts. Nickel can be part of a negatively charged ion (anion) making what is called a nickellate. Numerous quaternary compounds (with four elements) of nickel have been studied for superconductivity properties, as nickel is adjacent to copper and iron in the periodic table can form compounds with the same structure as the high-temperature superconductors that are known.

1.7.1.1 Colour

Most of the common salts of nickel are green due to the presence of hexaaquanickel(II) ion, $Ni(H_2O)_6^{2+}$.

1.7.1.2 Geometry

Nickel atoms can connect to surrounding atoms or ligands in a variety of

ways. Six coordinated nickel is the most common and is octahedral, but this can be distorted if ligands are not equivalent. For four coordinate nickel arrangements can be square planar, or tetrahedral. Five coordinated nickel is rare.

1.7.1.3 Complexes

Simple complexes of nickel include hexaquonickel(II),yellow tetracyanonickelate $[Ni(CN)_4]^{2-}$, red pentacyanonickelate $[Ni(CN)_5]^{3-}$ only found in solution, $[Ni(SCN)_4]^{2-}$ and $[Ni(SCN)_6]^{4-}$. Halo- complexes include $[NiCl_4]^{2-}$, $[NiF_4]^{2-}$, $[NiF_6]^{4-}$, $[NiCl_2(H_2O)_4]$ $[Ni(NH_3)_4(H_2O)_2]^{2+}$, $[Ni(NH_3)_6]^{2+}$, $[Ni(en)_3)]^{2+}$.[78] Some complexes have fivefold coordination. (tris(N,N-dimethyl-2-aminoethyl)amine); P(o-$C_6H_4SMe)_3$; $P(CH_2CH_2CH_2AsMe_2)_3$[78] Other ligands for octahedral coordination include PPh_3, PPh_2Me and thiourea.

Nickel tetrahedral complexes are often bright blue and 20 times or more intensely coloured than the octahedral complexes.[78].The ligands can include selections of neutral amines, arsines, arsine oxides, phosphines or phosphine oxides and halogens. Several nickel atoms can cluster together in a compound with other elements to produce nickel cluster complexes. One example where nickel atoms form a square

pyramid is a nickel hydride cluster complexed by triphenyl phosphine ligands and bonding a hydrogen atom on each edge. Another example has a square planar Ni_4H_4 shape in its core.[79] .Nickel bis(dimethylglyoximate), an insoluble red solid is important for gravimetric analysis.

1.7.2 COPPER

Copper along with silver and gold belong to group 1B in the periodic table. These three metals are often referred to as coinage metals. Copper has the electronic configuration of $1S^2 2S^2 2P^6 3S^2 3P^6 3d^{10} 4S^{1.}$ Copper is a tough, malleable, ductile metal which resist chemical attack. It has an atomic number of 29, atomic mass of 63.54 and belongs to period 4 and sub-group1B on the periodic table; it has two natural isotopes with atomic masses between 58 and 68. Copper has a melting point of 1083^0C, boiling point of 259^0C and a density of $8.93 g/cm^{3.}$

1.7.2.1 Deficiency

Because of its role in facilitating iron uptake, copper deficiency can produce anemia-like symptoms, neutropenia, bone abnormalities, hypopigmentation, impaired growth, increased incidence of infections,

osteoporosis, hyperthyroidism, and abnormalities in glucose and cholesterol metabolism. Conversely, Wilson's disease causes an accumulation of copper in body tissues.

Severe deficiency can be found by testing for low plasma or serum copper levels, low ceruloplasmin, and low red blood cell superoxide dismutase levels; these are not sensitive to marginal copper status. The "cytochrome c oxidase activity of leucocytes and platelets" has been stated as another factor in deficiency, but the results have not been confirmed by replication.[80]

1.7.2.2 TOXICITY

Gram quantities of various copper salts have been taken in suicide attempts and produced acute copper toxicity in humans, possibly due to redox cycling and the generation of reactive oxygen species that damage DNA.[80][81]. Corresponding amounts of copper salts (30 mg/kg) are toxic in animals.[82] A minimum dietary value for healthy growth in rabbits has been reported to be at least 3 ppm in the diet.[83] However, higher concentrations of copper (100 ppm, 200 ppm, or 500 ppm) in the diet of rabbits may favorably influence feed conversion efficiency, growth rates, and carcass dressing percentages.[84]

Chronic copper toxicity does not normally occur in humans because of transport systems that regulate absorption and excretion. Autosomal recessive mutations in copper transport proteins can disable these systems, leading to Wilson's disease with copper accumulation and cirrhosis of the liver in persons who have inherited two defective genes.[85]

Elevated copper levels have also been linked to worsening symptoms of Alzheimer's disease.[86][87]

1.7.3 IRON

Iron shows the characteristic chemical properties of the transition metals, namely the ability to form variable oxidation states differing by steps of one and a very large coordination and organometallic chemistry: indeed, it was the discovery of an iron compound, ferrocene, that revolutionalized the latter field in the 1950s.[88]. Iron is sometimes considered as a prototype for the entire block of transition metals, due to its abundance and the immense role it has played in the technological progress of humanity.[89]. Its 26 electrons are arranged in the configuration $[Ar]3d^6 4s^2$,

of which the 3d and 4s electrons are relatively close in energy, and thus a number of electrons can be ionized.[90]

Iron forms compounds mainly in the oxidation states +2 (iron(II), "ferrous") and +3 (iron(III), "ferric"). Iron also occurs in higher oxidation states, e.g., the purple potassium ferrate (K_2FeO_4), which contains iron in its +6 oxidation state. The anion $[FeO_4]^-$ with iron in its +7 oxidation state, along with an iron(V)-peroxo isomer, has been detected by infrared spectroscopy at 4 K after cocondensation of laser-ablated Fe atoms with a mixture of O_2/Ar.[91] Iron(IV) is a common intermediate in many biochemical oxidation reactions. Numerous organoiron compounds contain formal oxidation states of +1, 0, −1, or even −2. The oxidation states and other bonding properties are often assessed using the technique of Mössbauer spectroscopy.[90] Many mixed valence compounds contain both iron(II) and iron(III) centers, such as magnetite and Prussian blue ($Fe_4(Fe[CN]_6)_3$).[89] The latter is used as the traditional "blue" in blueprints.[90]Iron is the first of the transition metals that cannot reach its group oxidation state of +8, although its heavier congeners ruthenium and osmium can, with ruthenium having more difficulty than osmium.[91]. Ruthenium exhibits an aqueous cationic chemistry in its low oxidation states similar to that of iron, but osmium does not, favoring high

oxidation states in which it forms anionic complexes.[91]. In the second half of the 3d transition series, vertical similarities down the groups compete with the horizontal similarities of iron with its neighbors in the periodic table, which are also ferromagnetic at room temperature and share similar chemistry. As such, iron, cobalt, and nickel are sometimes grouped together as the iron triad.[89]

Unlike many other metals, iron does not form amalgams with mercury. As a result, mercury is traded in standardized 76 pound flasks (34 kg) made of iron.[90]

Iron is by far the most reactive element in its group; it is pyrophoric when finely divided and dissolves easily in dilute acids, giving Fe^{2+}. However, it does not react with concentrated nitric acid and other oxidizing acids due to the formation of an impervious oxide layer, which can nevertheless react with .[91]. High-purity iron, called electrolytic iron, is considered to be resistant to rust, due to its oxide layer.

1.7.3.1 DEFICIENCY

Iron deficiency is the most common nutritional deficiency in the world.[92][93][94] When loss of iron is not adequately compensated by adequate dietary iron intake, a state of latent iron deficiency occurs, which over time leads to iron-deficiency anemia if left untreated, which is characterised by an insufficient number of red blood cells and an insufficient amount of hemoglobin.[95] Children, pre-menopausal women (women of child-bearing age), and people with poor diet are most susceptible to the disease. Most cases of iron-deficiency anemia are mild, but if not treated can cause problems like fast or irregular heartbeat, complications during pregnancy, and delayed growth in infants and children.[96]

The brain is resistant to acute iron deficiency due to the slow transport of iron through the blood brain barrier.[97] Acute fluctuations in iron status (marked by serum ferritin levels) do not reflect brain iron status, but prolonged nutritional iron deficiency is suspected to reduce brain iron concentrations over time.[98][99] In the brain, iron plays a role in oxygen

transport, myelin synthesis, mitochondrial respiration, and as a cofactor for neurotransmitter synthesis and metabolism.[100] Animal models of nutritional iron deficiency report biomolecular changes resembling those seen in Parkinson's and Huntington's disease.[100][102] However, age-related accumulation of iron in the brain has also been linked to the development of Parkinson's.[103]

1.8 AIM OF PROJECT

The aims of this research work are

(i) To synthesis novel complexes of ibuprofen

(ii) To characterize the resulting complexes using standard analytical techniques such as solubility, melting point, infrared and ultraviolet

.

CHAPTER TWO

2.1 MATERIALS AND METHODS

2.1.1 APPARATUS

The following apparatus were used in the formation of the complexes and further analytical studies were carried out.

APPARATUS	MANUFACTURER
Beakers	Pyrex scientific Ltd. England
Conical Flasks	Simax company Ltd. England
Capilary tube	Silber brand Ltd, England
Dessicator	Moncrief Scientific, England
Electrothermal melting point	Gallenkamp Ltd ,England
Round bottom flasks	Pyrex scientific Ltd, England

Hot plate with magnetic stirrer	Gallenkamp Ltd, England
Measuring cylinder	Technico scientific Ltd, England
Plastic condenser	
Reflux condenser	Moramber (Mbc) Ltd
Test tube	Pyrex scientific Ltd, England
Thermometer	Uniscope scientific Ltd, England
Infrared	Duck V Scientific 500 infrared
Ultraviolet	Jenwoy 6405 UV spectrophotometer.

2.1.2 REAGENTS

The following reagents were collected from chemistry department, Kwara State Polytechnic.

Reagent **Manufacturer**

Nickel Sulphate Hexahydrate

Molecular Formular- $NiSO_4.6H_20$ J.T Barker Chemical C.O Philliburg

Molecular mass =262.71g/mol

Copper Sulphate

Molecular formula = $CuSO_4$. Eagle Scientific England

Molecular Mass= 159.60g/mol

Iron Sulphate Heptahydrate East Aglia, Chemicals Hadheigh

Molecular Formular= $FeSO_4.7H_20$

Molecular Mass =278.02g/mol.

Ethanol East Aglia, Chemicals Hadheigh

Methanol East Aglia, Chemicals Hadheigh

Distilled water

2.1.3MATERIALS

Ibuprofen

Molecular formular= $C_{13}H_{18}O_2$

Molecular Mass=206.29g/mol

Source BIORAJ Pharmaceuticals, Ilorin.

2.2 EXPERIMENTAL PROCEDURES

All apparatus were cleaned thoroughly before use. The retort stand was set properly and a round bottom flask clamped to it. This was further positioned onto the hotplate with a magnetic stirrer. A reflux condenser was fixed into the round bottom flask containing the solution and clamped onto the retort stand. Water pipes were connected, one into the inlet and the other into the outlet with both connected to full bucket of water and an empty bucket respectively.

2.2.1 IBUPROFEN Ni (ii) COMPLEX FORMATION

3.52g of ibuprofen was weighed using a digital pocket scale and was then dissolved in 10cm3 of distilled water using a clean dried round bottom flask.

2.38g of $NiSO_4.6H_2O$ was also weighed using a digital pocket scale and was then dissolved in 10cm3 of distilled water in a beaker.

The Nickel solution was added to the ibuprofen solution and shaken vigorously for it to mix well. The magnetic stirrer was placed in the mixture and it was refluxed for 1 hour after which the solution was allowed to cool and a light blue color was observed. The resulting solution was filtered using a filter paper. The precipitate was then washed off with methanol.

The complex obtained was weighed and put in a container which was labeled IBNi(ii) complex.

The weight of the complex obtained was 1.7g of methanol.

2.2.2 IBUPROFEN Cu (ii) COMPLEX FORMATION

3.52g of ibuprofen was weighed using a digital pocket scale and was then dissolved in 10cm3 of distilled water using a clean dried round bottom flask.

1.6g of $CuSO_4$ was also weighed and was then dissolved in $10cm^3$ of distilled water in a beaker. The magnetic stirrer was placed in the mixture and it was refluxed for 1 hour after which the solution was allowed to cool and a light green color was observed. The resulting solution was filtered using a filter paper. The precipitate was then washed off with methanol. The complex obtained was weighed and put in a container which was

labeled IBCu(ii) complex. The copper solution was added to the ibuprofen solution and shaken vigorously. The weight of the complex obtained was 3.5g.

2.2.3 IBUPROFEN (Fe) FORMATION

3.52g of ibuprofen was weighed using a digital pocket scale and was then dissolved in 10cm3 of distilled water using a clean dried round bottom flask.

3.8g of $FeSO_4$ was also weighed and was then dissolved in $10cm^3$ of distilled water in a beaker. The magnetic stirrer was placed in the mixture and it was refluxed for 1 hour after which the solution was allowed to cool and a light brown color was observed. The resulting solution was filtered using a filter paper. The precipitate was then washed off with methanol. The complex obtained was weighed and put in a container which was labeled IBFe(ii) complex. The copper solution was added to the ibuprofen solution and shaken vigorously. The weight of the complex obtained was 3.2g.

2.3 CHARACTERIZATION METHODS

2.3.1 SolubilityTest.

The solubility of the complexes were determined in the following solvents. Ethanol, benzene, methanol, petroleum ether, acetone, distilled water and chloroform

2.3.2 MELTING POINT DETERMINATION

The melting point of the complexes were determined using Gallenkamp melting point apparatus, thermometer and capillary tubes

2.3.3 METHOD

One side of the capillary tubes was sealed and the samples were introduced through the open and to a depth of about 1cm of the tube. The thermometer and the capillary tubes were inserted in the hole provided in the apparatus. The apparatus was switched on and the temperature at which the sample starts to melt and ends was taken as the melting point range of the sample. The melting point temperatures were taken for both the ligand and the complexes.

CHAPTER THREE

3.1 RESULTS AND DISCUSSION

The following are the results of the analysis conducted on some of the complexes formed

3.1.1 RESULTS OF SOLUBILITY TEST

Complex	Ethanol	Benzene	Methanol	Pet. Ethe	Acetone	Distilled water	Chloroform

				r			
Ibuprofe n ligand	NS	NS	NS	NS	NS	S	NS
IBNi(ii)	SS	NS	NS	NS	NS	SS	NS
IBCu(ii)	SS	NS	NS	NS	NS	SS	NS
IBFe(ii)	SS	NS	NS	NS	NS	SS	NS

Key S= soluble, SS=slightly soluble NS= not soluble

3.1.2 INTEPRETATION OF SOLUBILITY TEST

From the results obtained from the solubility test, it was evident that all complexes and the ligand were slightly soluble in methanol. Solubility of the ligand and the complexes were poor in ethanol , benzene, petroleum ether, acetone and chloroform.

3.2 RESULTS OF MELTING POINT TEST

COMPLEX	MELTING POINT RANGE
IBUPROFEN LIGAND	190-192
IBNi(ii) COMPLEX	158-160
IBCu(ii) COMPLEX	160-162
IBFe(ii) COMPLEX	211-213

3.2.1 INTERPRETATION OF MELTING POINT RANGE

From the results obtained, it showed that the melting point of the complexes were higher than those of the ligand. This shows that there was coordination.

CHAPTER FOUR

4.1 CONCLUSION

Ibruprofen formed stable complexes with Ni (ii), Cu (ii) and Fe (ii) ions. The solubility test and melting point determination showed that coordination has taken place.

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