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A REVIEW FOR THE COORDINATION COMPOUNDS IN THE HUMAN BODY AND SOME OF ITS CLINICAL AND BIOLOGICAL ASPECTS

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Abstract:
In the past two decades, studies in the lab (using animals) and in the clinic have demonstrated that numerous pathologic conditions of the body are accompanied by statistically significant changes in the body's cellular and systemic metal metabolism. Anomalies in metal metabolism can be the cause of any chronic disease for which the cause has not yet been determined. Throughout the history of human medicine, coordination compounds based on metals have been utilized to treat a variety of illnesses, including cancer. There have been several metal coordination complexes developed, including those made of Pt, Ru, Au, or Cu, produced, and tested since the discovery of cisplatin in 1965 in an effort to create therapeutically effective and secure medications. When discussing the usage of cytostatic metal complexes, many articles now highlight the most successful examples of pt- and non-pt-based drugs in preclinical and clinical trials. In this review, we aim to provide an overview of coordination compounds and to examine the chemical and biological properties of coordination compounds based on metals. We'll also give a brief description of how these compounds were designed and why they were made, as well as a summary of the physicochemical and biochemical characteristics of metal complexes.

Keywords: Hemoglobin, coordination compounds, Zinc- finger protein, Vitamin B12

INTRODUCTION

The human body consists of many chemical elements, which are the basis for its continuation in life, and most of the From bones, hair, and even in its various organs, first of all These elements are already present in its composition, and an essential part Muscles, teeth, blood, and ultimately every organ of the body, and some other elements enter the body through Through food, water and air. The lack of nutrients causes many problems and diseases, and its increase causes many problems There are also problems, so it must be maintained in a proportion appropriate to the needs of the body, and it is worth noting that there are twenty-four Those elements that are included in the composition of the genetic code "DNA," chemically and without which there is no human life, especially In very small proportions, the human body contains many trace elements.There are some chemical elements in the body[1].The most important of these elements are: Oxygen; Oxygen constitutes about sixty percent of the human body, which is Very large[2] .Carbon; One of the most important chemical elements for the human body at all; Because of every biological molecule, It is a major part It also enters into the composition of the genetic code. In the body, and enters into the installation of the genetic code[3].Hydrogen; It is found in all living cells, and it is a very important element. Nitrogen; It is included in the genetic code.Phosphorous: It is mainly included in the composition of the bones, and it is also included in the composition of the genetic code[4]. Arsenic; Its main function is to revitalize the body, but large amounts of it cause poisoning. Bromine; It is one of the highly toxic chemical elements and it is found in the body in very small proportions, and it also works to discourage desire. It is found in many sources of food as it enters the body when ingested. Cobalt; It is part of vitamin B12 .It is one of the chemical elements that are very necessary for the nervous system. Calcium; enters into the structure of bones and teeth. Copper; found in bones and muscles. Dysprosium; It is found in most of the internal organs of the body, such as the kidneys and liver, and in the bones as well[5]. Europium ; It is found in the body in very small quantities Fluorine; found in bones and teeth. Germanium; It is very important for the immune system, although it is found in the body in very small quantities. Iodine; It is essential for the thyroid gland, as it enters into the manufacture of hormones. Lithium; It is important for the functioning of the nervous system. Molybdenum: It is involved in the synthesis of liver enzymes. Nickel;

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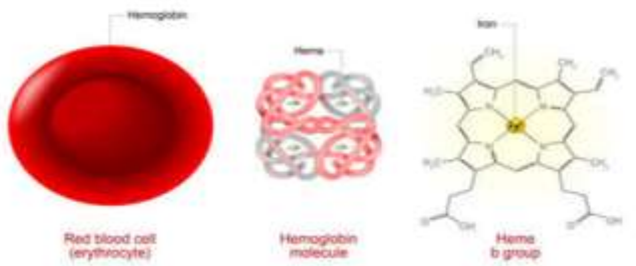
The body needs it in small quantities.Rubidium; Needed by the body in very small amounts. Selenium; It is very important for the body, although it needs it in small quantities, and it is included in the composition of the hair, testicles, and kidneys. Tolium; Found in the liver and kidneys, it is a toxic metal.Uranium; It is found in very small amounts in the bones. Vanadium; An essential element for the body.Yttrium; It is found in breast milk. Zinc: It is found in the semen of men, and it is involved in the composition of hair and nails especially men[6 ,7]. Iron; The importance of iron to the human body is the formation of hemoglobin in the body, which gives blood its red color Dark. It transports oxygen as a carrier of oxygen from cell to cell within the human body. Strengthening Muscles: as iron supplies the muscles with protein for their health. Useful for brain functions and intelligence, by supplying the brain With the necessary oxygen, which supplies it with blood. Prevents anemia, as iron intake in sufficient quantities prevents anemia[8].The amount of iron cures chronic diseases such as kidney disease. Iron intake before menstruation reduces Menstrual complications and menstrual pain. Helps strengthen hair and prevents it from falling out, proper nutrition helps to hair grow. Adequate iron intake highlights nail and skin health symptoms. Iron helps pregnant women to The formation of hemoglobin is necessary for the growth of the fetus, the pregnant mother must consume iron in foods rich in iron for the growth of the fetus fetus. These elements exist in the form of coordination compounds or otherwise, but what concerns us in our research is the compounds Coordination is like hemoglobin[9,10].

HEMOGLOBIN

A protein complex that contains iron found inside red blood cells, It transports oxygen, carbon dioxide, and nitric oxide as well as giving blood its red color. All animals produce hemoglobin, however it has a less intricate structure. All of the body's cells receive oxygen via hemoglobin from the lungs or gills, where the blood is oxidized. Hemoglobin saturated with oxygen is known as oxygenated hemoglobin, and when hemoglobin releases oxygen in the cells of the body, it captures carbon dioxide, a product of cellular respiration, and then transports it to the lungs, where It is expelled through the process of breathing outside the body. When hemoglobin is saturated with carbon dioxide, it It is known as oxygenated carbonic hemoglobin[11,12]. Nitric oxide is a third gas that hemoglobin absorbs and releases in addition to oxygen and carbon dioxide. Nitric oxide is important for controlling blood pressure because it affects the diastole and blood vessel pressure, which increases blood flow. As a result, Hemoglobin regulates the amount of nitric oxide, which in turn regulates how much blood vessels dilate and constrict[13]. There is hemoglobin Most of it is in red blood cells and makes up about 53% of its weight, and for red blood cells to pick up the right amount Of oxygen, it should contain the right amount of hemoglobin. Hemoglobin, in turn, depends on the iron component for him . Iron deficiency hemoglobin deficiency leads to anemia called anemia. He holds Hemoglobin is 20 times larger than oxygen, but some chemical compounds such as monoxide are present Carbon combines directly with hemoglobin to prevent oxygen from combining with hemoglobin, resulting in cases of suffocation. Red blood cells degrade after around 120 days, either in the spleen or during the circulatory cycle [14]. Hemoglobin returns to its original components, including iron, as it enters the new red blood cells formed in the marrow orthotics; When a vein or artery is cut, such as in a wound, the red blood cells work out to the tissues where it disintegrates where hemoglobin turns into a yellow substance, which is the color responsible for the appearance of bruises. Serious disorders like anemia or anemia are brought on by changes in hemoglobin content. There is another disease, but it depends on the genetic makeup of a risk also known as thalassemia[15]. The structural form of hemoglobin show in figure 1.



(Fig .1) :The chemical structure of hemoglobin

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ISSN: 2749-3644

And there is another type of hemoglobin protein that is found only during development fetal changes, which is the globin-gamma protein and hemoglobin proteins, like all proteins, are translated from during the process of translating DNA through special genes, there are 4 pure protein-alpha genes and 2 genes Specific to protein-beta and despite the difference in the number of genes, they are produced in equal quantity to be normal hemoglobin. And after the formation of proteins, they are produced in an equal amount and bound together and organized into blood cells red to the end of its life cycle[16].

Relationship of hemoglobin to different blood groups:

Blood cells consist of hemoglobin and hemoglobin is found in a solution inside the red blood cell, and this is the cell is surrounded by a membrane to keep hemoglobin inside the cell. And known blood groups, B, A ,O and Rh are the properties of the membrane that surrounds the red blood cell. This can be easily represented by a balloon red and blue are different colors on the outside, but inside they have the same water content[17].

HOW DOES HEMOGLOBIN IMBALANCE OCCUR

The components of hemoglobin are the same in all individuals, and the gene responsible for translating hemoglobin is also the same. but it can be a change occurs in a gene, and this change can occur naturally and is called a mutation, and it is rare the occurrence and this change leads to a change in the hemoglobin formed through the translation process and leads to obtaining an abnormal hemoglobin. And when this permanent change in the gene leads to pass this gene mutated to offspring through the parents, and this is the case in diseases that It results from a hemoglobin of disorder. It is noteworthy that most mutations hemoglobin does not lead to problems, but a change in hemoglobin protein leads to a change in the behavior of hemoglobin and thus, it causes diseases, the most famous of which are sickle cell anemia and thalassemia[18] .

HEMOGLOBIN GENE DAMAGE

Genes can suffer damage and become unable to produce normal amounts of hemoglobin, usually one from the genetic sites, either alpha or beta, which harms them, but the two do not occur together. For example: one of the globin-beta genes, which are counted 2 can be damaged and thus be a genetic site one on chromosome 11 is active, thus affecting the amount of protein globin-beta and thus, this will lead to an imbalance in the amounts of alpha and beta hemoglobin. And this imbalance leads to the emergence of a serious disease called thalassemia[19].

HEMOPROTEINS

Hemoproteins perform a wide range of biological tasks, including as the detection of dinuclear gases, chemical catalysis, diatomic gas transport, and electron transfer. In transport electron or oxidation chemistry, heme iron serves as an electron source or sink. The porphyrin molecule also functions as an electron donor in peroxidase processes. The gas bonds to heme iron, which is used to move or detect diatomic gases. The binding of the chemical invading into heme iron causes modifications in the surrounding proteins during the detection of diatomic gases[20]. While most peroxidases migrate between (Fe III) and (Fe IV) and hemeproteins contribute to mitochondrial oxidation, oxidative stress reduction, and the cycle between (Fe II) and iron III, diatomic gases, such as (Fe II), are typically only lowly related to the structure . Before the emergence of molecular oxygen, it has been hypothesized that the initial evolutionary purpose of hemoproteins was electron transfer in metabolic pathways photosynthesis in early sulfur-like organisms[21]. Apoproteins alter the heme macrocycle environment within a matrix protein to produce amazing functional variety. For instance, particular amino acid residues close to the heme molecule are responsible for hemoglobin's capacity to properly transport oxygen to tissues. When the pH is high and the carbon dioxide content is low, hemoglobin binds to oxygen in the lungs in an opposite manner. Hemoglobin will release oxygen into the tissues when the scenario is reversed (decreased temperature, acidity, and carbon dioxide concentrations). According to this phenomena, the acidity and carbon dioxide concentration have an inverse relationship with the oxygen affinity of hemoglobin. The Bohr effect is what it is called[22]. The innate regulation of the globin chain, which results in the histidine residue next to the heme group becoming positively charged under acidic conditions (produced by carbon dioxide dissolved in working muscles, for example), is the molecular mechanism underlying this effect. Figure 2 illustrates the structure and function of heme[23].

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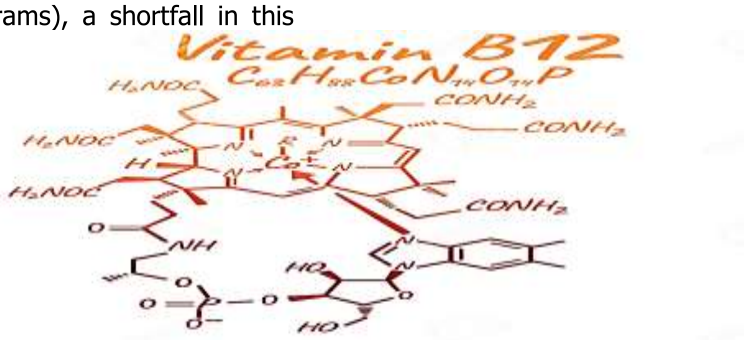
(Fig.2) :Structure and function of heme

VITAMIN B12

Also called cobalamin, it is a water soluble vitamin that is important for the normal functioning of the brain and nervous system. It contributes to the production of blood. One of the eight B vitamins is it. It is derived from animals, just like poultry, red meat, and liver. The amount needed daily is approximately 5 micrograms, and since the liver stores a substantial amount of it (about 5 milligrams), a shortfall in this vitamin typically occurs from an inability to absorb it rather than a shortage in diet. It is believed that the vitamin is safe to consume in amounts that are within suggested ranges. Studies that have not revealed any impacts are also available . B12 is safe when consumed orally negative for taking doses greater than the recommended doses and the figure 3 shows the structural structure of B12[24].



(Fig.3):The structural structure of B12

VITAMIN B12 VITAL IMPORTANCE

The creation of thymidine triphosphate, one of the components of DNA, requires vitamin B12, which is essential for DNA synthesis and therefore the vitamin is important for the maturation of red blood cells and is also required for the manufacture of the myelin sheathing of nerve fibers and the addition of methylation to homocysteine to convert it to methionine. gastric gland cells secreted (Glycoprotein) a protein added to carbohydrates It is absorbed towards the end of the ileum with the aid of the enzyme trypsin thanks to a substance called intrinsic factor that attaches to the vitamin to prevent it from being digested. Due to its role in the creation of red blood cells, vitamin B12 is also used to treat a lack of hemoglobin[25].

VITAMIN B12 SOURCES IN FOOD

beef, eggs, dairy products, and liver and legumes such as wheat and barley. But it must be known that eating foods containing on meat, it does not guarantee that there will be no vitamin B12 deficiency. The main culprit is the gastric enzyme responsible for separating B12 and protein[26].

SYMPTOMS OF B12 DEFICIENCY

The classic clinical symptoms of vitamin B12 deficiency include anemia, fatigue, weight loss, and loss of sensation and vibration.The lesser-known symptoms of vitamin B12 deficiency, not only specific to the disease, but equally common. Symptoms of vitamin B12 deficiency include sleep disturbances, double vision, impotence and other autoimmune disorders (utoimmune A). In addition, elevated (hyperhomocysteinemia), various disorders the risk of heart disease (especially among adults, may be secondary digestive tract (decreased appetite, intestinal hypermotility, flatulence, constipation), fertility problems (both sexes), and possible impairment the immune system) specifically by the action of chemotaxis - and the activity of T cells[27].

World Bulletin of Public Health (WBPH)
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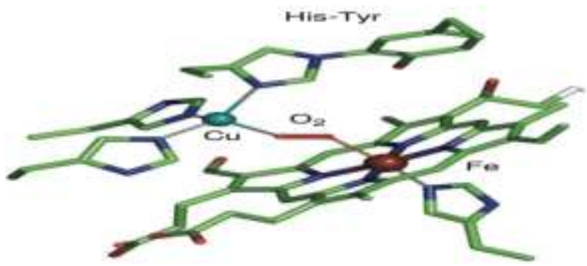
Volume-13, August 2022
ISSN: 2749-3644

TREAT VITAMIN B12 DEFICIENCY

The treatment of vitamin B12 deficiency is easy and cheap: intramuscular administration of vitamin B12 injections to correct the deficiency and fill Inventory. There are many procedures (one injection daily for two weeks, or one injection per week for 4-6 times, and later- right .There are also medicines to be given by mouth, sucking under the tongue, or ointment to spread on the membrane for most patients, it is not necessary to take the vitamin orally, with the addition of several other vitamins sufficient to correct the deficiency, but treatment of vitamin B12 deficiency is able to prevent disease progression in people with high risk condition[28].

THE ENZYME CYTOCHROME C OXIDASE

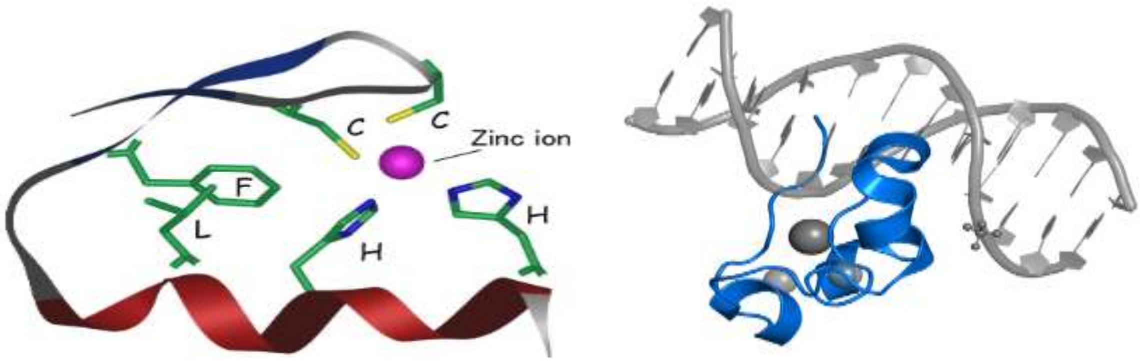
In the chain of electron transport, cytochrome is the sole electron acceptor. It adds four electrons and four protons in order to reduce O2 to water, catalyzing the reaction. Four protons are pumped across the inner mitochondrial membrane as a result of this decrease, helping to provide the proton gradient necessary for ATP generation. The mechanism is not yet resolved. motivational factors, but several mechanisms have been proposed. Prototyping vehicles are also used to try to replicate the process catalytic activity of this enzyme. Pumping protons through CcO is also a very complex process that has yet to be solved mechanistically. Loathing regardless, the data currently indicate a reasonable path for thrust pumping. The figure 4 shows the chemical composition of it[29].



(Fig.4):The chemical composition of Cytochrome C Oxidase.

ZINC- FINGER PROTEIN

A zinc finger is a tiny protein motif that functions as a fold stabilizer by coordinating one or more zinc ions (Zn^{+2}). IIEN was initially created and categorized as a protein to describe the finger-like appearance of a putative transcription factor structure. The structural families that comprise zinc finger proteins (zinc finger proteins) are varied. There are various kinds of zinc fingers, each of which has a structure that distinguishes it from other secondary structures like Greek keys or hairpins. Examples of such distinctive 3D proteins include Cys2His2, Cys4, and Cys6, which are used to identify particular classes of zinc finger proteins. The identification of coordination linkages between zinc ions or the fundamental structure of a protein can also be used to identify the three-dimensional structure. Despite their immense diversity, the vast majority of these proteins typically serve as reactive units that bind. Changes in structure mostly affect how a certain protein binds to other molecules, including DNA, RNA, proteins, and other small helpful compounds. Figure 5 depicts many forms of this protein.[30].



(Fig.5): some different types of Zinc finger protein

World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-13, August 2022
ISSN: 2749-3644

IMPORTANCE AND RELEVANCE

Proteins with these shapes are usually involved in cell proliferation, DNA structure creation, and developmental regulation maintenance of circadian rhythms, the movement of DNA, and the regulation of countless operons bacterial transcription initiation itself . A typical structural motif found in many DNA binding protein regions is the zinc finger. About 3% of all proteins include it, and it serves a number of purposes outside boosting or inhibiting a particular gene. It is one of many fields that have been developed to address the issue of certain nucleic acid sequences[31]. an ion's coordinates Zinc and protein work together to stabilize the alpha helix, which may recognize DNA in a particular way. The coordination of zinc ions and a particular interaction with nucleic acids (such as DNA or RNA) are requirements shared by these domains, but how the protein exploits this connection to carry out its biological tasks depends on the structure of the other domains. zinc finger regions from combining zinc ions on the side chains of cysteine and histidine (in the "classic zinc finger") However, there are more strange variations) to set up a brief alpha helix and two demo sites[32]. By guiding side chains towards the distinctive functional groups at the edges of the DNA bases, the zinc finger ("finger") binds with hydrogen bonds solely with the right DNA base, binding the DNA in a sequence-specific manner. This allows it to fit exactly into the main groove of DNA. Here are some of the diverse ways that zinc is utilized by finger domain proteins in cells [33,34]:

1- Up to 9 zinc fingers on the transcription factor TFIIIA engage with the DNA's sequence. It encourages the transcription of the R rRNA.5 gene while attracting RNA polymerase.

2. By preventing access to additional transcription factors that would improve transcription, the zinc finger proteins SLUG and SNAIL bind to DNA in a box-E pattern and suppress transcription electron cathodes.

3- The DNA repair protein PARP has two zinc-finger domains that preferentially bind to single-strand break sites and a catalytic field.

4-Tristetraprolin, also referred to as (ZFP36), is a transitional regulator that binds to zinc fingers. sequences of elements targeted for metabolism that are rich in the 3 UTR of mRNAs. ZAP antiviral that is protein-bound binds to particular viral mRNA sequences and draws in RNA. Translation occurs before the exosome is broken down. These protein structures are typically used in cell growth, which produces acid structure [35].

Superoxide dismutase

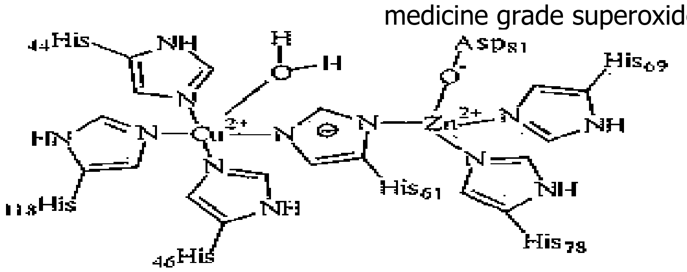
It is an enzyme that catalyzes the conversion of superoxide dismutase to oxygen and hydrogen peroxide, and is also known by the short name superoxide dismutase (EC 1.15.1.1). As a result, it is regarded as a crucial enzyme in practically every cell's antioxidant defense mechanism[36].

Function

This crucial enzyme's primary role is to restore cell viability and slow down the rate of cell deterioration. It eliminates some types of roots or fractures. As this enzyme aids in the process of using copper, zinc, and manganese, free radicals—also known as superoxides—are the most prevalent and maybe the most harmful of all species. Additionally, as people age, their levels of this enzyme tend to gradually decline as their generation of free radicals increases. This enzyme's potential as an anti-aging medication is now being researched. Currently[36].

Types

This enzyme comes in two varieties—one with copper and the other with zinc—and each one acts to safeguard a different area of the cell. The first copper protects the cytoplasm of the cell, which contains the free cracks caused by its erosion and rent, from damage.While containing the genetic outside, the cells assemble in the protection of mitochondria serving as a site for energy production and the figure 6 shows medicine grade superoxide dismutase[37].



(Fig.6): medicine grade superoxide dismutase

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The biological and clinical aspects of some coordination compounds

A key class of medications used to treat cancers consists of medicinal compounds that include metalDespite the fact that numerous metal-containing medications based on gold, ruthenium, gallium, titanium, and iron are in preclinical and clinical trials phases I and II, carboplatin, oxalyplatin, and picoplatin are still the most effective anticancer agents used in clinical practice. Many serious adverse effects, including nephrotoxicity, neurotoxicity, ototoxicity, and myelosuppression, are associated with the therapeutic use of platinum-based medications. Antitumor medications Co, Cu, Zn, and Fe are believed to be less toxic than their platinum counterparts because they are endogenous metals. Inhibiting proteasome activity, DNA deterioration, reactive oxygen species (ROS) production, DNA intercalation, and telomerase activity, and paraptosis are only a few of the diverse methods through which copper-containing coordination compounds operate as promising anticancer therapeutics [38].

Copper coordination compounds

Because copper ions are redox active and biogenic, which offer a variety of biological activity pathways, Coordination compounds containing copper are of high interest. By adjusting the donor and ligand atoms, The pharmacological features of metal complexes can be tailored. In addition to being effective as antibacterial, antituberculosis, antimalarial, antifugal, and anti-inflammatory medications, Coordination compounds with copper are efficient anticancer agents, providing an affordable and secure replacement for traditional chemotherapy that contains platinum. The hallmark of Alzheimer's disease amyloid-(A) and other malignant diseases, such as head and neck cancer, can both be detected by PET imaging with 64Cu-labeled coordination compounds[39].

Lanthanide Coordination Compounds

The coordinating chemistry of lanthanides substantially aids in comprehending the principles of application, notably in biological and medical systems, which is pertinent to biological, biochemical, and health-related aspects. Lanthanides are being used more and more frequently as an effective anticancer substance as well as a diagnostic and prognostic probe in clinical diagnostics. The capacity of chelating agents to change the behavior of the lanthanide ions they bind to in biological systems is their most crucial characteristic. Chelation also significantly changes the lanthanide ions' biodistribution and excretion profile [40]. Complexes of the lanthanide polyamino carboxylate and chelate are employed in magnetic resonance imaging as contrast-enhancing agents. In order to create novel various sorts of particular MRI contrast agents and their conjugated MRI contrast agents with improved relaxivity and similar physiological effects to pharmaceuticals, lanthanide chelates were combined with antibodies and other tissue-specific compounds. For musculoskeletal and cerebrospinal imaging, contrast agent aided MRI is particularly useful due to a number of unique properties[41].

Biological role of zinc

More than twenty metalloenzymes in the human body each contain 2 to 3 g of the biometal zinc. Mammals must have zinc for proper growth and development (carbohydrase, alcohol dehydrogenase, Cu-Zn superoxide dismutase, etc).The human immune system is strengthened by the zinc ion, Copper (II), and Cobalt (II) ions. If enough zinc is ingested into the human body at dosages more than the advised daily intake, adverse effects, such as anomalies of iron depots and a reduction in the life expectancy of erythrocytes, which results in anemia and increased usage, may happen. According to evidence from the literature, zinc exposures larger than 800 mg/day result in a considerable rise in serum levels of amylase and lipase as well as a rise in blood glucose levels. The amino acids and proteins' O-donor atoms, and other biomolecules serve as the primary O-donor atoms through which the Zinc (II) ion of the d10 electron how configuration affects various biomolecule components due to its size and physical-chemical characteristics. It also creates molecule combinations with a coordination number of four at the same time. The content of the ligand can be obtained in(a M : L = 1:4 ratio, or 1: 2) ,with the potential include molecules from the solvent, based on the ligand's denticity[42.43]

Biological role of cobalt

As a microelement, cobalt helps metaloenzymes (methyltransferase and methionine transferase) transfer during the metabolism of proteins and amino acids. Co promotes the utilization of iron in bone marrow cells through vitamin B12, which is crucial for the formation of erythrocytes. The body's ability to absorb Co from food relies on the individual's diet, for example, containing amino acids reduces absorption while an iron shortage improves it. Additionally, Co(II) ions induce cell death and, in higher doses, necrosis combined with inflammation. Furthermore, this metal is carcinogenic effects. A Co^{+2} ion with a d 7 electron arrangement is easily able to engage with the

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molecules' molecular components and generate coordinated complex particles numbers 4, 6, and N donor atoms. [44]

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