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Review Article

Biological role and food sources of biogenic metals

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Abstract

The biogenic metals (Na, K, Mg, Ca, Mn, Fe, Co, Cu, Zn and Mo) and their compounds are widely studied. Basic multidisciplinary research in medicinal inorganic chemistry and bioinorganic chemistry contributes to the development of pharmaceuticals with potential future medical application, therapeutics, and the health benefits therein. Consideration and research to control the action of biogenic chemical elements and their compounds in the living organisms are crucial for their possible useful application and the key to circumventing their toxicity. The biogenic metals have various physical and chemical properties consistent with their location in the periodic table, that is why their biological roles are different. Their typical chemical properties involve the formation of coordination complexes and oxidation-reduction reactions. The current review focuses upon the functions of biogenic metals in living systems, their food abundance, including the utility of these elements and their compounds in medicinal therapy and diagnosis.

1. Introduction

Chemical elements and their compounds found in biological systems obey homeostatic criteria. Homeostasis, the maintenance of chemical elements and compounds at optimal physiological levels, represents a complex interactive system involving many elements and the biological energy supply. Interactions between deficiencies and excesses of elements and compounds interfere with homeostasis and may cause disease problems in the living organisms.

Biogenic metals essential to life forms include ten vital elements which can be divided into next major categories: (1) macroelements (Na, K, Mg, Ca); (2) trace elements (Cu, Zn, Fe); and (3) ultra-trace metals (Mn, Mo, Co). Chemical elements in the biosphere have different distribution in the intracellular or extracellular space. Consequently, among the biogenic metals, Na, Ca, Cu, Mo are extracellular, and K, Mg, Fe, Co, Zn, Mn are intracellular elements. It is not known exactly how these elements were chosen by primitive lifecycle and during the evolution stages. Most probably they were selected because of their abilities to accomplish certain structural functions or to provide specific reactivities. For instance, iron was selected by evolutionary forces because of its ability to bind oxygen in a reversible fashion.

We seem to be preoccupied with controlling energy from dietary intake of proteins, fats, and sugars but pay correspondingly very little attention to the biogenic metals' intake that make metabolism possible, or to their presence in the human body. Due to the high reactivity and catalytic potential of biogenic metal ions, their levels in the human diet and environment are an important factor for health, for causing diseases or affecting their progression, and for influencing healthy ageing.

The s-elements of the IA group of the periodic table are so-called alkali metals (lithium, sodium, potassium, rubidium, cesium, and francium). They exhibit many of the physical properties typical for metals, though their densities are lesser than those of other metals. The only electron in their outer shell is loosely bound, thus their atoms can easily lose the valence electron turning into uni-charged cations. They have the largest atomic radii, the lowest ionization energies and electronegativities of the elements in their corresponding periods. All this results in their strong metallic properties and very high reactivities. The alkali metal ions are least capable of forming coordination compounds.

The alkaline earth metals are the elements located in the IIA group of the periodic table. They possess many of the typical properties of metals showing low electron affinities and low electronegativities. These elements have two electrons in the external shell that can be easily lost. Their atomic radii are smaller than that of the alkali metals. The two valence electrons are not tightly bound to the nucleus, so the alkaline earths readily lose them thus forming divalent cations.

The transition metals occupy the middle parts of the long periods in the periodic table between the main groups on the left and the groups on the right-hand side. With the exception of IA group metals and the slightly lesser exception of IIA group metals, there is a tendency for transition metals to form complex compounds with electron donor functional groups of bioligands, forming covalent bonds between the central metal cation and the ligands. Another typical chemical property of the biogenic d-elements and their compounds is their affinity to participate in oxidation-reduction reactions due to their variable oxidation states in the respective compounds. The biogenic transition metal ions are the best-recognized constituents of a great number of enzymes, hormones, different proteins, vitamins and various essential biologically active compounds.

There have been numerous very useful reviews about the behavior of biogenic metals in biological systems [1-22]. The papers referenced in this topic are good sources for understanding and answering the questions discussed.

The current review shows the results from a search on the Web of Science (WOS) database (Clarivate Analytics) with different keywords including ‘biogenic metal’, ‘biological role’, ‘food sources’. These results show the number of references returned for different combinations of keywords.

2. Biological role of biogenic metals and their compounds

2.1. Sodium and potassium

Of the alkali metals the most important biogenic metals are sodium and potassium, which maintain the charge and osmotic balance.

Sodium is found in excessive abundance in the juicy vegetables, and is present in practically all kinds of food. Sodium salts, particularly NaCl, are found almost everywhere in all the biological materials. Sodium is a vital element for life, as is potassium, and these two elements maintain a fixed balance within the cell structures. Most of the biological functions of sodium salts are the consequence of the dominant role of sodium cations. The salinity presence in soils is often harmful to plant growth. Sodium ions easily replace calcium and other important ions in clay complexes, converting the clay to a sticky mass; water filtration is thus considerably reduced, and the soil basicity rises distinctly. Fish's tolerance to changes in salinity is quite remarkable. Various marine bacteria tolerate a salt concentration of up to 25%. The smallest sodium requirement for mammals is around 0.05% of the diet, corresponding to 1-2 grams of salt per day, resulting in an average Na content of living body tissues of around 0.24% [23]. The sodium content in the different tissues shows a wide variation, for example the blood contains approximately 0.62% NaCl, while the skin has a Na content of less than 0.1%. In of the body there is a strict connection between the salt content and water balance, the low intake of salt causes loss of water. Large quantities of sodium are usually lost by sweating through the skin, and substantial amounts are excreted in the urine. Without sodium, the human cells could not get the nutrients needed for survival. Sodium allows the living bodies to maintain the correct blood chemistry and the precise amount of water in the blood. Sodium also allows the muscles to contract normally. The body needs sodium to digest the food. Normal functioning of the human nervous system is also dependent on sodium.

The sodium content of foods is quite variable and depends on both the food source. Animal foods certainly contain more sodium. Foods naturally low in sodium are fruit, vegetables, oils, and cereals, with their content ranging from traces to ~20 mg/100 g, with few exceptions [24]. Meat and fishery products naturally contain from 40 to 120 mg/100 g, but some shellfish, such as mussels and oysters, contain up to 500 mg/100 g. Whole milk contains ~50 mg/100 g. Bread may contain only traces to several hundred milligrams of sodium per 100 g (~1.5–2 g of salt). The sodium content of some traditional meats and cheeses is extremely high (up to 2500 mg/100 g), and so also is that of many frozen foods (up to 700 mg/100 g) [25].

Potassium is an extremely important element to cells in the human body. Each organism has a strictly maintained K level and a relatively fixed K-Na ratio. Potassium is the main cation inside the living cells, and sodium is the most abundant cation in the extracellular fluids. Potassium is an important ingredient of fertilizers. In the plant kingdom, this element is one of the three key elements that make plant life possible. The other two are nitrogen and phosphorus, known as N-P-K crucial plant nutrients. The potassium content in plants is significantly different, but it is normally in the range of 0.5-2.0%. In the human body, the ratio of potassium between the cells and plasma is almost 27:1. The K content in the muscle tissue is around 0.3%, whereas that of blood serum is approximately 0.01-0.02%. There is strong evidence of a negative association between dietary potassium and blood pressure, and some evidence of negative associations between dietary potassium and cardiovascular and kidney disease. Blood pressure lowering is particularly associated with high potassium and low sodium diets [26-28].

The normal dietary requirement is around 3.3 grams of potassium per day, nevertheless the ingestion of more than 20 grams of potassium leads to serious physiological effects. Excess potassium can be excreted in the urine, and by sweating.

Important dietary sources of potassium include fruit and vegetables (including rice, potatoes, legumes and wholegrains), dairy products, and animal proteins. Worldwide, diets are low in potassium compared to dietary guidelines. Interventions focused on increasing dietary potassium will have major benefits including improvements in diet, reducing non-communicable disease and enhancing planetary health [29,30].

When potassium is added as a preservative during processing, it is usually as potassium chloride, whereas it is usually present in fruit and vegetables as potassium citrate [31].

Sodium and potassium ions work together in the body to maintain the fluid balance in cells, blood plasma and extracellular fluids. In order to regulate the intracellular and extracellular concentrations of Na^+ und K^+ it is essential that these cations can cross the cell membrane. This trans-membrane transport is passive (through diffusion) or active by the use of the Na^+/K^+-specific pump. The passive transport is hydrophilic (along ion channels) or hydrophobic (by ionophores). Ion channels are trans-membrane protein molecules, which play a primary role in regulating cellular excitability Their selectivity for K^+ and Na^+ is realized by geometrical factors. Ionophores are macrocyclic compounds with oxygen containing functional groups, forming stable complexes specifically with Na^+ or K^+ *in vivo*. The selectivity for Na^+ and K^+ is determined by the size of the functionalities. Sodium and potassium food sources are presented in Figs. 1 and 2.

Among the complex compounds sodium nitroprusside $Na_2[Fe(CN)_5NO]$ is a medication which serves to lower blood pressure, since it relaxes the muscles of blood vessels [32,33].

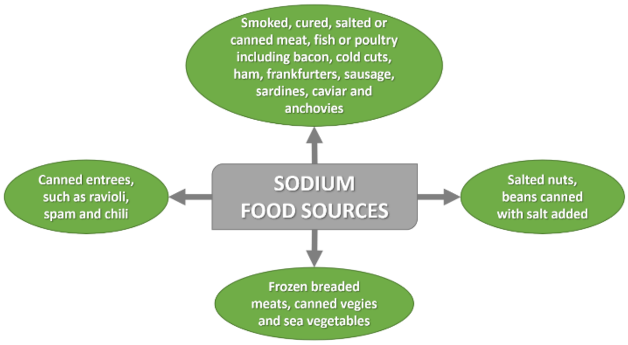

Figure 1. Sodium food sources [23-25]

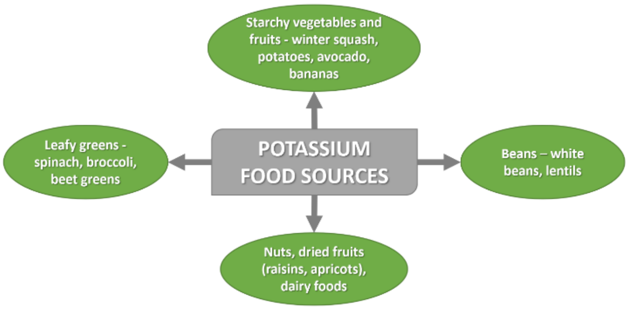

Figure 2. Potassium food sources [29-31]

2.2. Magnesium and calcium

Magnesium is an element that is required by the living bodies for the proper growth, formation and function of bones and muscles. It prevents some heart and high blood pressure disorders. Magnesium helps convert the food into energy and is important for the proper absorption of calcium and potassium. This important element also helps the brains function normally and prevents depression. Magnesium is essential in allowing human body to control insulin levels in blood. It can be injected into patients' veins in emergency situations such as acute asthma or acute heart attacks being effective in treating numerous heart and lung diseases.

Foods high in magnesium amounts include fish, lean meat, dairy products, seeds, whole grains and dark-green leafy vegetables. Magnesium plays many important biochemical and physiological functions in plants, affecting both yield of their biomass and/or edible parts. Hence, fast growing plants require a high supply of Mg, mainly via externally applied fertilizers, which will sustain their rate of growth. The growing concern about low Mg concentrations in plant products can be significantly mitigated through soil and/or foliar application of Mg fertilizers. In order to produce Mg-rich food, it is necessary to build up an effective strategy for Mg management in soils and providing adequate plant nutrition for sustaining normal human health [34-36]. It is ascertained that magnesium content in fruits and vegetables dropped in the last years, and about 80% of this metal is lost during food processing. As a consequence, a large percentage of people all over the world does not meet the minimum daily magnesium requirement [37].

Magnesium participates in the phosphate (energy) metabolism activating molecules (kinases, ATPases, phosphatases, enolases, isomerases, protein synthases and polymerases) and triggering activation paths.

Calcium is a macronutrient and one of the most abundant biogenic metals in the human body. This vital element is important for maintaining strong bones, teeth, and proper blood pressure; for controlling muscle growth and brain impulses; for making blood clot; for digesting food and making body energy. Its deficiency can lead to serious complications. Low soluble calcium compounds (carbonates and phosphates) are incorporated into exo- and endo-skeletons, for instance bone (calcium hydroxy phosphate) and sea shells (calcium carbonate). In addition, calcium cations have a vital role as co-factors in hydrolases and a structure function in proteins resembling Zn^{2+}. Calcium cation is predominantly an extracellular cation. The exchange between the extra- and intracellular space is achieved by Ca-ATPases. Malfunctions of Ca metabolism lead to the deposition of insoluble calcium compounds (phosphate, oxalate, steroids) in the blood vessels thus causing calcification. The food presenting the highest levels of Ca are dairy, fish and cereal products [38-43]. Food sources of magnesium and calcium are given in Figs. 3 and 4.

The complexes of alkaline and alkaline earth cations have small stability constants, except for Mg. The charge density of Mg^{2+} is particularly higher than that of Ca^{2+}. The larger the charge density, the higher is the capacity of the cation to polarize the respective ligand. Mg^{2+} cations form stable complexes with N-donor ligands, for example chlorophyll. The complexes of Mg^{2+} are both thermodynamically and kinetically more stable than those of Na^{+}, K^{+} and Ca^{2+}.

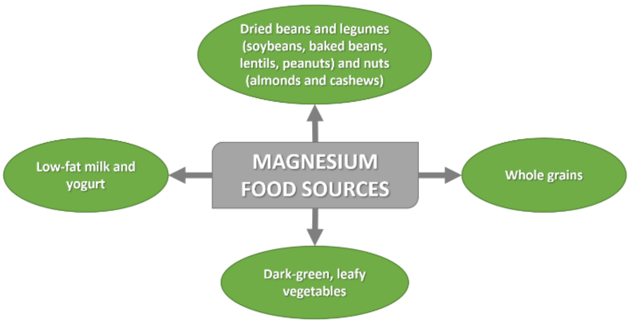

Figure 3. Magnesium food sources [34-37]

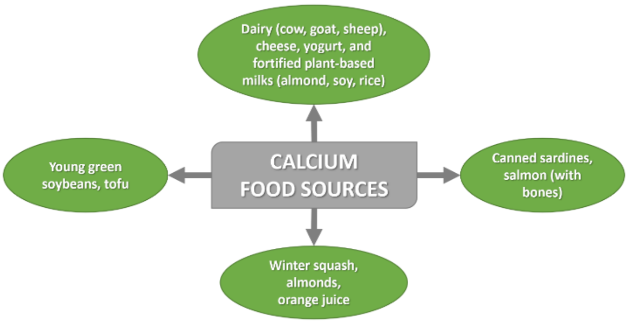

Figure 4. Calcium food sources [38-43]

The amounts existing in the body and the daily demand of the physiologically relevant alkaline cations Na^+ and K^+, and alkaline earth cations Mg^{2+} and Ca^{2+} are listed in Table 1.

Table 1. Amounts and daily demand of Na^+, K^+, Mg^{2+} and Ca^{2+} [23-43]

	Na^+	K^+	Mg^{2+}	Ca^{2+}
Amounts present in the human body (g/70 kg weight)	105	140	35	1050
Daily demand (g)	1.1-3.3	2.0-5.0	0.3-0.4	0.8-1.2

There are prominent differences in the intracellular and extracellular amounts of Na^+, K^+, Mg^{2+} and Ca^{2+}, summarized in Table 2 along with the data for erythrocytes and blood plasma. Maintaining the correct concentration gradients is of key importance for the proper specific functions, for instance controlling the cell membrane potentials and osmotic pressure, activating the signal transductions and enzymes. Medications of magnesium and calcium are common antacid drugs and these elements are constant constituents in many supplements [44-47].

Table 2. Concentrations of Na^+, K^+, Mg^{2+} and Ca^{2+} (*mM*) in the intracellular and extracellular fluids [23-43].

	Na^+	K^+	Mg^{2+}	Ca^{2+}
Intracellular in erythrocytes	11	92	2.5	0.1
Blood plasma	152	10	50	10
Intracellular amount	10	155	15	0.001
Extracellular amount	142	4	0.9	2.5

2.3. Transition biogenic metals

Transition metals function in a number of different ways in biological systems depending on their location. Transition metal ions that exist in single oxidation states, such as zinc(II), function as structural elements in zinc fingers and superoxide dismutase, similarly to the IIA main group ions, as triggers for protein activity like Ca^{2+} ions. Transition biogenic metals that exist in various oxidation states serve as electron carriers (iron in cytochromes or in Fe-S clusters of nitrogenase); as mediators of oxygen transport (iron in hemoglobin or copper in hemocyanin); in enzyme catalysis (copper in SOD or Fe and Mo in nitrogenase).

2.3.1. Manganese

Manganese is an extremely important element which is involved in the production of energy, bone growth and cell reproduction, supports the immune system and regulates blood sugar levels. This element supports blood clotting with vitamin K. It helps to control the effects of stress with the B-complex vitamins. As manganese is extremely rare but vital element, humans can easily get enough from a good balanced diet [48-52]. Foods that contain high amounts of manganese include avocados, berries, whole grains, nuts and seeds, egg yolks, green leafy vegetables and legumes, Fig. 5.

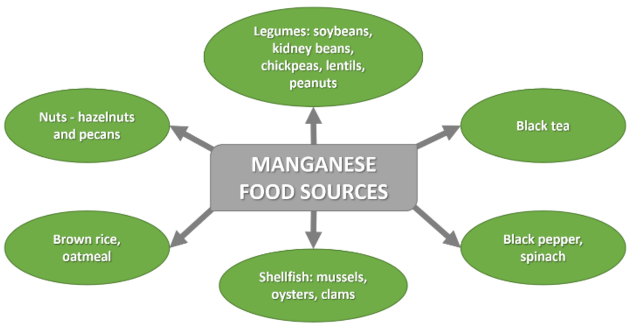

Figure 5. Manganese food sources [48-52]

Manganese is a constituent of the active centers of numerous enzymes (acyltransferase, pyruvate carboxylase, superoxide dismutase, arginase, cholinesterase, glycosyl transferase, peroxidase etc.). Despite its variable oxidation states, manganese is found in living organisms predominantly in the Mn(II) and Mn(III) complexes with O- and N-donor bioligands and a typical coordination number of 6. Manganese coordination compounds are used in photodynamic therapy, as MRI contrast agents and may represent potential drugs with high specificity [53-55].

2.3.2. Iron

This element has many physiological functions in the body, being the most abundant transition metal in human organisms. It is important for keeping a healthy immune system, for digesting the food. The iron obtained from the diet is an essential part of hemoglobin which carries oxygen in the body. Iron deficiency anemia is one of the most common nutritional diseases, and can be prevented by a balanced diet.

The body cannot synthesize iron and must acquire it. Food is the only natural source of iron, and the mineral is ingestible in supplement form. Dietary iron has two primary forms: heme and nonheme. All plant-derived and animal-derived foods contain nonheme iron, while heme iron is found only in the foods derived from animals, mainly meat, fish, poultry, and eggs. Heme iron has a higher bioavailability and is absorbed easier without the need for absorption-enhancing cofactors. Nonheme Fe, which is the most important dietary source in vegetarians, shows lower bioavailability. Its absorption depends on the balance between dietary enhancers and inhibitors and body Fe stores.

Around 25% of dietary heme Fe and 17% of dietary nonheme Fe get absorbed. Consequently, less than one-fifth of the amount of dietary Fe gets absorbed by the body. Many foods contain iron, including eggs, red meats (beef, veal, lamb, pork), offal (liver, kidney, pate), fish (salmon, tuna, sardines), Fig. 6, [56-60].

Figure 6. Iron food sources [56-60]

When taken up with the food iron is mostly present and gets into the gastro-intestinal tract in its ferric Fe^{3+} form. In the small intestines ferric iron is reduced to its ferrous Fe^{2+} form. Only in this oxidation state iron can be absorbed by the epithelium cells of the mucosa. For transfer to the blood serum, reoxidation to Fe^{3+} is necessary. The oxidation of Fe^{2+} to Fe^{3+} in the mucosa is catalyzed by a Cu enzyme ceruloplasmin. Iron possesses specific biologically suitable properties which are less presented by the other transition metals - variability between the +2 and +3 oxidation states; formation of hexa-aqua iron cations – typical Brønsted acids; changeability between high- and low-spin states; flexibility to the donating ligand nature, coordination numbers and geometries; tendency to form oligo- and polymers. The anticancer activity of iron coordination complexes with a variety of biologically active ligands (thiosemicarbazones, antitumor antibiotic Bleomycin etc.) have been reported [61-65].

2.3.3. Cobalt

Cobalt is a vital element that is part of vitamin B-12 (cobalamin), a coenzyme which is essential in the formation of nucleic acids, proteins, etc., as well as for the proper digestion of the food. Vitamin B-12 is required for the normal formation of red blood cells. It helps vitamin C perform its functions and prevents nerve damage. Vitamin B-12 deficiency can prevent the red blood cells from carrying enough oxygen from the lungs to the different parts of the body, causing anemia and irreversible nerve damage. This vitamin can be stored in the body. That is why, it is easy to get enough of it in the diet and deficiencies are very rare, mainly vegetarians are at risk because vitamin B-12 is found only in animal sources (eggs, cheese, milk, fish and red meat), Fig. 7, [66-69].

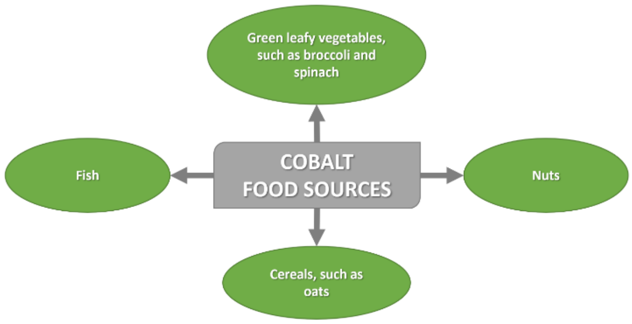

Figure 7. Cobalt food sources [66-69]

Excessive levels of cobalt can also be harmful causing respiratory, hematological hepatic, cardiovascular, renal effects. Exposure to cobalt is also possible through food and drinking water.

Cobalt compounds are known as excellent mimics of some metalloenzymes. Many of them are widely studied for the development of antitumor agents, enzyme inhibitors, drug delivery devices, and agents for positron emission tomography [70-74].

Nickel is a transition metal with a variety of essential applications. It is supposed of being an essential metal for human nutrition, although definitive evidence has not yet established its essentialness to humans. Patients with certain liver and kidney diseases are known to have low levels of nickel. Nickel excess in the body is associated with a high incidence of thyroid disease, heart disease and cancer. Food sources of nickel are nuts, chocolate, fruits and vegetables. Meats are typically low in nickel. It is known to be an essential trace element for several species of animals (chickens and rats). Bacteria use nickel to make enzymes [75].

2.3.4. Copper

Copper is found in both plants and animals, where many Cu-containing proteins have been isolated (hemocyanins, ceruloplasmin, cerebrocuprein, erythrocuprein, hepatocuprein). There are numerous copper-containing enzymes: ascorbic acid oxidase; cytochrome oxidase; tyrosinases, etc.

Copper is critically significant for many of human body functions. It helps protect the cells. It is important for keeping blood vessels elastic and flexible; for the regulation of blood pressure, pulse, healing; for the brain functions. Copper is found in food sources, such as legumes, nuts, seeds, organ meats, and whole grains. Total body copper is 100–200 mg, being higher in brain, liver, and kidneys; most of serum copper is bound to ceruloplasmin. Deficiency of Cu results from major burns, renal replacement therapy, parenteral nutrition, and gastric bypass procedures [76-78]. Copper deficiency in the diet include symptoms of anemia, arthritis and other medical complications. Importantly, copper interacts with Fe and Zn in the process of intestinal absorption, thus intake of each element and the body status may influence the absorption of the others [79-81]. Copper is mainly found in dried beans, almonds, soybeans, peas, broccoli, garlic, whole-wheat products, seafood, Fig. 8, [76-81].

Recent research is devoted to numerous vital properties of copper compounds, for instance protecting ability against cancer and heart disease, improving the immune system and many others [82-85] as well as their radiopharmaceutical application as diagnostic imaging and targeted radiotherapy agents [86,87].

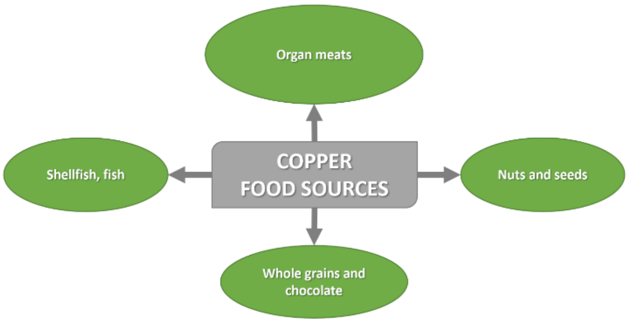

Figure 8. Copper food sources [76-81]

2.3.5. Zinc

Zinc is recognized as an essential biogenic metal for plants, animals and humans with very important and multiple body functions. In zinc proteins, Zn^{2+} takes over either a catalytic or a structural function. Zinc helps the body construct and maintain DNA. It is needed for the growth and repair of tissues, particularly connective tissues like ligaments and tendons. Teeth, nails, bones, skin and hair could not grow without zinc. Zinc is an important element for a healthy immune system, for the release and use of hormones in the body, for the brains to work properly.

Zinc deficiency in the diet can have serious effects on human health with typical symptoms encompassing disturbance of growth, arthritis-related health problems, break-down of the immune system and loss of taste, mental apathy and damage to reproductive organs. Zinc deficiency occurs from an inadequate diet, inadequate absorption, altered demand, or increased losses. Zinc replacement corrects deficiency in weeks; prolonged therapy may result in toxicity. There appears a relationship between the intake and levels of copper and zinc with respect to cardiovascular health and neurodegenerative diseases [88-90]. The best food sources of zinc include whole wheat bread, seafood and animal meat, Fig. 9, [90-93].

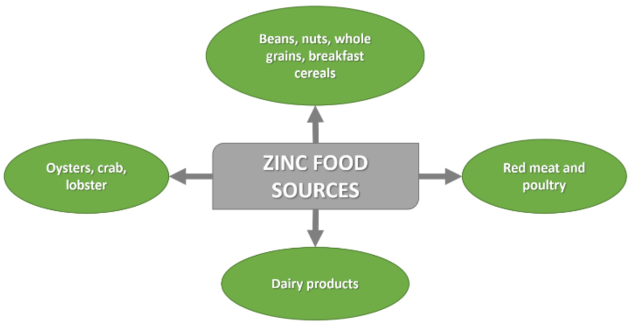

Figure 9. Zinc food sources [89-93]

The daily requirement for zinc is commonly satisfied by the nutrients. The toxicity of zinc is very low and poisoning is rare. Both zinc and its salts are well tolerated.

The amphoteric metal Zn is stable due to passivation in air. In water solutions, Zn^{2+} exists in the form of $[Zn(H_2O)_6]^{2+}$, a typical Brønstedt acid. Zn^{2+} forms complexes mainly with coordination numbers of 4, which are tetrahedral or square planar, 5 (square-pyramidal geometry) and 6 (octahedral geometry). Zinc is not redox active (d^{10}), distinct from iron, copper, manganese and molybdenum.

A number of zinc coordination compounds with organic ligands have therapeutic uses. Some of them have been evaluated for their photodynamic activities [94].

2.3.6. Molybdenum

Molybdenum is supposed to be a necessary trace element in animal diets, but its functions have not been completely established. This element exhibits different oxidation states and variable coordination numbers, thus showing various biological actions. It is found in all tissues of the living body, but tends to be the most concentrated in the kidneys, liver, skin and bones. Molybdenum deficiency in the diets can cause mouth and gum disorders and can contribute to getting cancer. The refined and processed foods lead to Mo deficiency, characterized by anemia, loss of appetite and weight, and stunted growth in animals.

The best dietary contributors of molybdenum are legumes, grains, and nuts. Bioavailability of molybdenum is fairly high but depends on form, with molybdenum preparations having greater bioavailability than food-bound Mo. Molybdenum deficiency and toxicity are rare, possibly because of the body's ability to adapt to a wide range of molybdenum intake levels. At low intakes of Mo, the fractional transfer of molybdenum from plasma to urine is lower and a greater fraction is deposited into tissues, and at high intakes of Mo, the opposite occurs [95,96] The amount of Mo in plant food varies significantly and depends on the mineral content of the soil. The best food sources of molybdenum are beans, dark green leafy vegetables, legumes (peanuts and peas), and grains, Fig. 10, [95-98]. Hard tap water can also supply molybdenum to the diet.

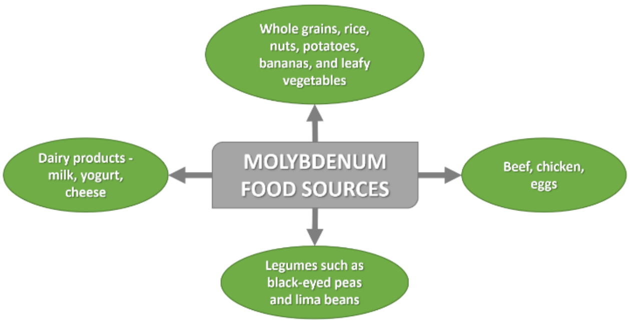

Figure 10. Molybdenum food sources [95-98]

Molybdenum is a trace element that functions as a cofactor for at least 4 enzymes: sulfite oxidase, xanthine oxidase, aldehyde oxidase, and mitochondrial amidoxime reducing component. In each case, molybdenum is bound to a complex, multiring organic component called molybdopterin, forming the entity molybdenum cofactor [97-99]. Mo-containing enzymes catalyze the oxidation-reduction reactions of small molecules and the lack of these enzymes leads to serious pathologies. The development of molybdenum coordination compounds as anticancer agents has been recently reviewed [100,101].

In addition to the above-described biogenic metals, which biological effects are widely studied and established, there is lots of information in the medical and biochemical literature about the activity of almost all the trace metals in the living organisms.

4. Conclusions

In this review, the biogenic metals are discussed in the context of their chemical behavior, biological role and food sources. Elements present in the form of free ions are readily ionized and ultimately get absorbed entirely by the body. Transition metals readily form stable covalent complexes and normally interact as parts of biomacromolecules (proteins, enzymes, hormones) according to their chemical characteristics and oxidation states. Although many vital elements and their compounds are required at some dosage for the organism's survival, these elements and the respective compounds may be deleterious if taken in overly large doses or if present in excess. At high concentrations they can disturb important biochemical processes, constituting an important threat for the health of plant and animals. Knowledge of chemistry and biology of biogenic metals combines.

many research fields of biochemistry, toxicology and pharmacology. Introducing metal ions into the biological systems may be carried out for therapeutic or diagnostic purposes. From a therapeutic viewpoint, considerable research efforts are being exerted to the development of biogenic metal-based compounds as potential diagnostic or therapeutic agents.

Authors' contributions

Irena Kostova has contributed alone

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Conflicts of interest

The author declares that there is no conflict of interest regarding the publication of this paper.

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