Trace elements in the human body

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CHAPTER: 1 INTRODUCTION

1. Introduction

1. 1 Trace Elements in Biological System:

In recent years scientists from a variety of disciplines have directed their attention in an aggressive manner to a long neglected area of biochemical research i. e. the role of trace elements for the etiology of disease.

Most of the elements present in the periodic table are considered to be trace elements. They are defined as various chemical elements that occur in very small amounts in the body of organisms (and are referred to as trace elements). These elements are essential for many physiological and biochemical processes. A trace element is anelementin a sample that has an averageconcentrationof less than 100parts per million(ppm) measured in atomic count or less than 100 micrograms per gram (1). Similarly, if the body needs less than 100 milligram (mg) of an element in a day then it is labelled as a trace element. However, their concentrations may be as low as less than 100 mg of 1 kilogram (kg) of body weight or 65 kg of a body weight of an adult should not contain more than 7 gram (gm) of a trace element (2).

1. 2. Role of Trace Elements in Human Body:

All living organisms possess a certain amount of various trace elements in their body in order to process their body functions properly. It is incredibly important that optimum balance level of these elements in every organ, tissue and cell of the human body is maintained that serves as a primary reason to keep an organism healthy and functional. These trace elements can be in any chemical form such as inorganic salts or as biochemical agents. The trace elements are ubiquitously distributed all over the earth crest. They play several roles in human body. (However, their role varies,) such as (the element) iron, which is important for the transportation of oxygen in the body, whereas calcium is the basic component of the bones. Both plants and animals require them for their proper functioning, growth, and propagation of their life (3).

It is evident that the trace elements are present in the human body in very minute quantity, and if the processes of supply and demand are interrupted due to any reason for example, the intake of these elements is not sustained up to an adequate amount, or the metabolic disorder fails to absorb these elements up to the required limit for a chemical reaction (and) the body becomes deficient of these trace elements. In case of deficiency, the body uses its reserves, but these reserves have to be replenished. The trace elements are the components of various enzymes, hormones and are a part of complicated physiological and biological mechanisms, through which a body generates other biochemicals, and proteins which help a range of systems to come out of this demanding state of affairs unscathed. This ability of a body to keep the level of its nutrients and chemical agents within optimum range despite its supply is called homeostasis. This critical process provides the body sufficient support in order to sustain that pressure, which builds up due to the deficiency of trace elements. However, a lot of damage occurs within the body during this turmoil. The frequency of these types of episodes leads the body towards the development of many diseases and makes it vulnerable for the formation of various disorders.

Lifestyle, environmental exposure, and diet can directly influence the concentration of trace elements in the body. There are numerous and essential metabolic activities which can not be instigated without the presence of these trace elements. Such functions may include protein metabolism, red blood cell production, development of healthy bones and teeth. It may also include growth that depends on thyroid hormones, and proper functioning of nerves and muscle (functions). Furthermore, fertility, maintenance of the integrity of cell membranes, hair coat growth, and electrical stabilization of the cell (electrically) involves directly or indirectly certain trace elements for their proper functioning. Additionally, trace elements serve as a component of B-12, which is critical for proper heart functions, regulation of heart beat, and pigmentation. The trace elements are also required for some other functions that carried out inside the body of organism such as reproduction, maintenance of fluid balance, (aid in) intercellular communication (which is) needed for structure of most proteins and crucial for proper energy processing in the body,(reproduction, act as catalyst,) etc. Another example of such deficiencies or excessiveness of the amount of trace elements can be seen in iodine intake, where such a deficiency (or excess (ive)) can cause goiter (an enlarged thyroid gland). This trace element is efficiently concentrated by thyroid glands in fish, amphibians, reptiles, birds, and mammals for the distinctive purpose of producing thyroid hormones (4).

It is stated that selenium can be stored in the cells of body and then become part of the victuals series. It starts when carnivorous grazed in the fields where soil is reach with selenium and consequently the growing crops have received a great amount of selenium and eventually high selenium levels become the part of the body of the animals. Initially, selenium was considered to be a toxic element, however with the progression of scientific research and refined consensus has led to the strong belief that selenium is not toxic, and it is essential to several functions in the human body. Such as selenium acts as an antioxidant and sometimes it is present an integral constituent of enzyme glutathione peroxidase (5-6). Regular cellular metabolism is responsible for most of the production of reactive oxygen species (ROS) in normal cells. Therefore, ROS are neutralized, engaged, or destroyed by the action of antioxidants. Similarly, the malignant cells also contribute in production of ROS and demonstrate the low levels of antioxidant enzyme in the blood of most cancer patients (7). Beyond, the optimum limit of chromium in the blood of an organism can be linked with onset of diabetes and cardiovascular disease as well (8).

Similarly, selenium influences the development of copious degenerative diseases, and its deficiencies among human beings as well as animals are being recognized worldwide as it has some association with number of pathologies (9).

1. 3 The Concept of Essentiality:

Those elements that are indispensable, necessary, and incredibly important for the metabolisms of living organisms are called essential elements. It has been widely accepted and established fact that without the presence of these essential trace elements no biochemical metabolism can be initiated properly, and (on the other hand) the outcome of these chemical reactions does not meet the requirements. Consequently, the concept of ‘ essentiality’ is a leading cause for scientists today to focus their efforts in this field. Furthermore, explore the circumstances through collected data to discern actual facts and reasons for the significance of trace elements required in several metabolic activities in animals. However, special attention must be directed towards how their low or high blood levels, can initiate the development of disease, and the optimum blood levels of these trace elements necessary for the metabolic processes to proceed in a proper manner. This is important because some trace metals which are necessary for growth of an organism may be harmful if their specific concentration is even slightly raised.

The essential trace elements act as catalyst and the body of an organism can not produce them itself. The only source of these elements in the body is our diet. However, the presence of most of these elements is higher animals is just an expression of geochemical origin or the indicator of environmental contaminations. All cells receive their nourishment from extracellular fluid. The activities of all these trace elements biologically furbish optimal implementation by commencing a series of metabolic reactions in each cell. A lack of any step in the series can lead from mild to severe problems to the health of an organizm.

The following elements such as zinc (Zn), copper (Cu), selenium (Se) chromium (Cr), cobalt (Co), iodine (I), manganese (Mn), and molybdenum (Mo) are considered to be as essential elements for human body. Although they play incredible roles such as being active sites of enzymes, or control the bioactivity of the metabolism though these elements are present in very small amount of the total body weight. The core consequences of low levels of trace elements are the reduced activities of the concerned enzymes. An element is recognized as essential when it has a well defined function as a stabilizer, structural, hormonal or an enzymatic cofactor, when it is always present in tissues and organs in well precise concentration range. When it induces reproducible physiological effects, and when it is possible to prevent and treat consequences due to its deficiency through its supplementation.

The effects of the essential elements cannot be completely eradicated by any other element. Nevertheless, another concept of essentiality defines an element as essential when a deficient intake produces an impairment of function. The elimination of an essential trace element produces similar physiological or structural abnormalities apart from type of variety. The restoration of these essential trace elements invalidates or precludes respective abnormalities. Consequently, these abnormalities are accompanied by specific biochemical changes that can be prevented or remedied when the deficiency is prevented and remedied and restore the physiological level of that element. The symptoms of deficiency (is) disappear(s) and body functions becomes normal (10-11). Therefore, the physiological levels are restored and the symptoms which indicate such deficiencies are also vanished and the body functions return to their normal state.

Trace elements are essential components of biological structures. To deal with this necessity, biological systems have developed the ability to recognize a metal and deliver it to the target without allowing the metal to participate in toxic reactions. Proteins are primarily responsible for such recognition and transport, and prevent most of the associations of trace elements with other molecules that leads to undesirable chemical modiï¬cations of these molecules (12).

1. 4. The Transition Metal: Chromium:

Chromium is the basic element used in various industrial processes such as paint, construction, chrome plating, (and the) production of stainless steel as well as leather tanning, wood preservation, textile dyes and pigments. Besides the use of chromium in varieties of industries, trivalent (Cr (III)) and hexavalent (Cr (VI)) chromium compounds are thought to be the most biologically imperative (13-14). For example, the Cr (III) is an essential dietary mineral in low doses. It is required to potentiate insulin for the normal glucose metabolism (15-16). Since 1971, the International Agency for Research on Cancer (IARC) has been interested to categorize carcinogens and ascertain occupational association with high rate of cancer risk. Some chemicals used in shoe, tire, and furniture manufacturing, as well as nickel refining, diesel fuel, and dry cleaning have been classified as “ probable ” carcinogens. Arsenic, asbestos, benzene, benzidine, chromium, 2-Naphthylene, oils, and vinylchloride show occupational exposures causally associated with cancer in humans.

1. 4. 1. Chromium Metabolism:

The chemistry of chromium is very interesting and complicated because of having the capability of possessing various oxidation states. However, chromium (III) and (VI) are the most stable forms that exist in our environment. The chromium (III) and chromium (VI) inter-conversion is influenced by numerous factors, such as the concentrations and type of chromium species, nature of oxidizing or reducing agents. Moreover, the electrochemical behavior of the oxidation and reduction reactions, ambient temperatures and pressure, amount of light, sorbents, acid-base reactions, complexing agents, and precipitation and chemical reactions may also play a pivotal roll in support of establishing a specific chromium oxidation state in certain environmental conditions. Chromium can react directly at the site of contact or be absorbed through human tissue. A very important difference is observed that chromate ion (Cr (VI)) slips away through cellular membranes at an exceedingly faster rate than chromium (III) species (17). Chromium (III) combines directly to transferrin, an iron-transporting protein in the plasma after entering the body from an exogenous source. In contrast, chromium (VI) is immediately engaged by erythrocytes after absorption and is reduced to chromium (III) inside the cell. Apart from the source, chromium (III) is extensively distributed within the body and measured for most of the chromium both in plasma or tissues. It has been expounded that the reduction of chromium (VI) does not occur in the plasma. Chromium (VI) enters cells through the phosphate and sulfate anion-exchange carrier pathway. However, most chromium (III) present in the blood stream and is substantially bound to amino acids, and with other organic acids. The plasma proteins, such as globulins may also an attractive target for chromium (III) though a portion of it remains in plasma for an extended period of time as well (18).

The blood provides a major carrier service for the delivery of chromium to other parts and organs of the body. The substantial concentration of chromium was discovered as a protein-complex in various parts of the human body such as bone marrow, lungs, lymph nodes, spleen, kidney, and liver, though the highest levels of chromium remains in the lungs (19-20). Excretion of chromium takes place primarily through kidneys, with the release of maximum concentration and without leaving traces of it in the organs. However, almost 10% of an absorbed dose is eliminated by biliary excretion. Nevertheless, minute quantities delivered to hair, nails, milk, and sweat. Chromium usually cleared from blood within hours whereas eradication from the organs of body is not prompt as the half life of chromium is several days. In a study chromium (VI) was administered to volunteers and it was observed that it removed more rapidly from the body than chromium (III) (21).

The reduction of chromium (VI) to chromium (III) has been extensively investigated and it has been observed that the consumed hexavalent chromium is vigorously reduced to the trivalent form by the action of chemicals present in stomach such as gastric fluid (22). However the results of another study show that chromium (VI) is reduced to the chromium (III) form in the red blood cells (RBCs) as well (23). Moreover, during reduction to the trivalent form, chromium may interact with cellular macromolecules, including DNA (18) or it may be released slowly from the cell (24).

After conducting a series of experiments a group of scientists purposed various routs (routes) by which conversion of chromium (VI) to chromium (III) can occurs inside the body of an organism. They discovered that as soon as chromium (VI) enters inside the cell it is immediately incorporated by cellular reductants and converts chromium (VI) to the trivalent form. The reductants may consist of ascorbic acid, glutathione, and flavoenzymes. The example of glutathione is cytochrome P-450 glutathione reductase and the example of flavoenzymes is riboflavin. However, inter-conversion of one oxidation state to another oxidation of chromium instantly occurs when reducing agent is ascorbate instead of glutathione. At some point during the process of conversion from one oxidation to another oxidation state chromium is capable of producing many other types of unstable complexes as well as free radicals such as hydroxyl group (*OH) and single atom of oxygen ($^1O_2$). Besides the production of oxidants, the presence of DNA abrasions were also observed during this series of experiments. For example these abrasions may consist on oxidative damage of DNA, and production of 8-oxo-deoxyguanosine etc. However, it is still mystery whether to characterize the formation of various intermediate chromium complexes as potential carcinogen with respect to chromium (VI) (25-26).

1. 4. 2. Chromium Deficiency:

Chromium deficiency has been associated with many factors such as impaired glucose tolerance, fasting hyperglycemia, glucosuria, elevated body fat percentage, decreased lean body mass, maturity-onset diabetes, cardiovascular disease, decreased sperm count, and impaired fertility etc (27). A recent comparative study revealed that supplement chromium (III)-picolinate is an excellent source of chromium towards its own deficiency as compared to chromium (III)-niacin (19). However there is a long list of fresh food and nuts that are available in the market that are considered to be a rich source of chromium (III) such as cereals, spices, fresh vegetables, meats, and fish etc.

1. 4. 3. Chromium Toxicity:

Generally the toxicity of an element is measured on the basis of its lethal dose, where the tolerance limit of the body is exhausted and the consequences of high levels of particular element appear in the form of signs, symptoms, and medical impairments. These elements are estimated for their toxicity or carcinogenic potential exclusively by measuring their levels present in the blood of an organism for instance, tin and lead. However, chromium is exceptional among the list of carcinogens due to its versatile nature of retaining various oxidation states such as chromium (IV), chromium (V), chromium (IV), and chromium (III) etc. Therefore, chromium oxidation states have also been taken into account for the evolution of chromium carcinogenicity. For example, consideration of a hazardous waste material is dependent on the concentration of chromium present in the form of chromium (VI) while the other forms of chromium are classified as non carcinogens, according to the United States Environmental Protection Agency (USEPA). Furthermore, it has been recommended that the measurement of toxic levels of chromium is also reliant on the availability of biological form of chromium (28).