

Assesment Of Some Vital Minerals And Their Impact On Human Health: A Perspective Review On Medical Geology

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Abstract

The goal of this study is to evaluate the literature on the subject of medical geology's use of minerals, emphasizing the significance and connections between geological elements and human health. An analysis of earlier studies on the subject of interest was undertaken using the results of a document-based qualitative study that clarified the geologic origins and movement of harmful components in the environment that expose humans through intake of food and water. This was done taking into account the growing interest between the health and geoscience communities in the topic. Medical geology proposes a collaboration between two unrelated fields of expertise, such as Earth sciences and biomedical sciences, and it has been established that the growth of science and technology has facilitated the creation of new research avenues requiring interdisciplinary work with the participation of experts from many disciplines of expertise. Numerous factors are taken into account, including the relationship between environment and health, which is crucial for a wide audience, including students, researchers, geologists and biomedical experts, legislators, and the general public. It has been established that the development of science and technology has facilitated the creation of new research avenues requiring interdisciplinary work with the participation of experts from many disciplines of expertise. Medical geology proposes a collaboration between two unrelated fields of expertise, such as Earth sciences and biomedical sciences. The link between the environment and health is one of many considerations, and it is vital for a large audience, including learners, scholars, geologists and biological specialists, politicians, and the general public.

Keywords: Medical geology, health, diseases, toxicity, minerals.

1. Introduction

The use of vitamin, mineral, and other supplemental nutrition-based therapy has significantly increased in the US. In keeping with this trend, several healthcare practitioners are considering incorporating these therapies into their clinics. For those accustomed to conventional healthcare settings, this may be unfamiliar territory, but many patients who have been utilizing supplements for self-medication are already familiar with it. In addition to providing an overview of the most current pertinent research on the use of essential vitamins and minerals in the treatment of diabetes, this article aims to explain how micronutrient demands are determined. The impact of minerals and vitamins on human health is a subject of profound significance, as these essential nutrients are integral to the proper functioning and well-being of our bodies. Minerals and vitamins play diverse and indispensable roles in supporting numerous physiological processes and biochemical reactions, ensuring optimal growth, development, and overall vitality. Minerals, such as calcium, iron, magnesium, zinc, and potassium, are essential for a range of bodily functions. They contribute to the structural integrity of bones and teeth, regulate muscle contractions, maintain fluid balance, and act as co-factors in enzymatic reactions vital for

metabolic processes. On the other hand, vitamins, including A, B-complex, C, D, E, and K, are organic compounds that serve as co-enzymes, facilitating crucial biochemical reactions and supporting various bodily systems. The absence or deficiency of minerals and vitamins can lead to significant health challenges. For instance, inadequate calcium intake may result in weakened bones and osteoporosis, while iron deficiency can cause anemia and impaired oxygen transport. Vitamin deficiencies can manifest as a compromised immune system, skin disorders, impaired vision, and cognitive decline. Conversely, maintaining adequate levels of minerals and vitamins is essential for fostering optimal health. A balanced intake of these nutrients can promote healthy growth and development, support cardiovascular health, enhance cognitive function, and boost the body's immune response, fortifying it against infections and diseases. In this exploration of the effects of minerals and vitamins on human health, we will delve into the specific roles of various nutrients and their impact on our well-being. By understanding the significance of these essential elements and their interactions within the body, we can make informed decisions about our diets and lifestyles to optimize our health and lead a vibrant and fulfilling life. Throughout this journey, we will emphasize the importance of

striking a balance in nutrient intake and highlight evidence-based practices to maximize the positive effects of minerals and vitamins on human health.

Minerals and vitamins play a wide range of vital roles in our systems. The nutrition community first concentrated on avoiding deficient illnesses like scurvy, pellagra, and rickets by comprehending the functions of micronutrients. As nutritional science became more understood, it became clear that these nutrients have considerably larger impacts. We now know that micronutrients are essential for controlling gene expression, metabolism, and the onset and progression of a number of chronic illnesses [1]. With more knowledge, it is also possible to personalize dietary advice to each person's particular genetic profile, potentially boosting the advantages and beneficial effects of medical nutrition therapy.

The human body requires trace levels of minerals and trace elements, which are micronutrients. They do, however, display well-defined biological roles. Widespread issues with human health are linked to deficiencies in certain micronutrients. The emphasis of this review article is on a few of these mineral and trace element deficits and how they affect insulin resistance and diabetes. Depending on the makeup of the food, various populations have quite variable levels of trace elements. Numerous micronutrient deficiencies afflict considerable segments of the population in numerous Asian nations. Local dietary variations in selenium, zinc, copper, iron, chromium, and iodine are present in both industrialized and developing nations, mostly as a result of malnutrition and reliance on traditional diets.

Insulin resistance and an imbalance in glucose homeostasis may result from these deficits and, in rare instances, excesses of critical trace elements. Iodine, selenium, zinc, calcium, chromium, cobalt, iron, boron, and magnesium deficiency are the major problems, affecting at least one billion people worldwide. The effects of micronutrient deficiencies on diabetes and insulin resistance in individuals of various racial backgrounds from regions of Asia, Africa, and North America are examined in this review, which includes a variety of cohort and case-controlled studies, observational and laboratory-based studies, randomized controlled trials, and studies with significant results. Changes in the levels of these micronutrients in the individuals' urine and serum might indicate a trajectory toward oxidative stress and metabolic changes, providing information about illnesses.

2. Review of Literature

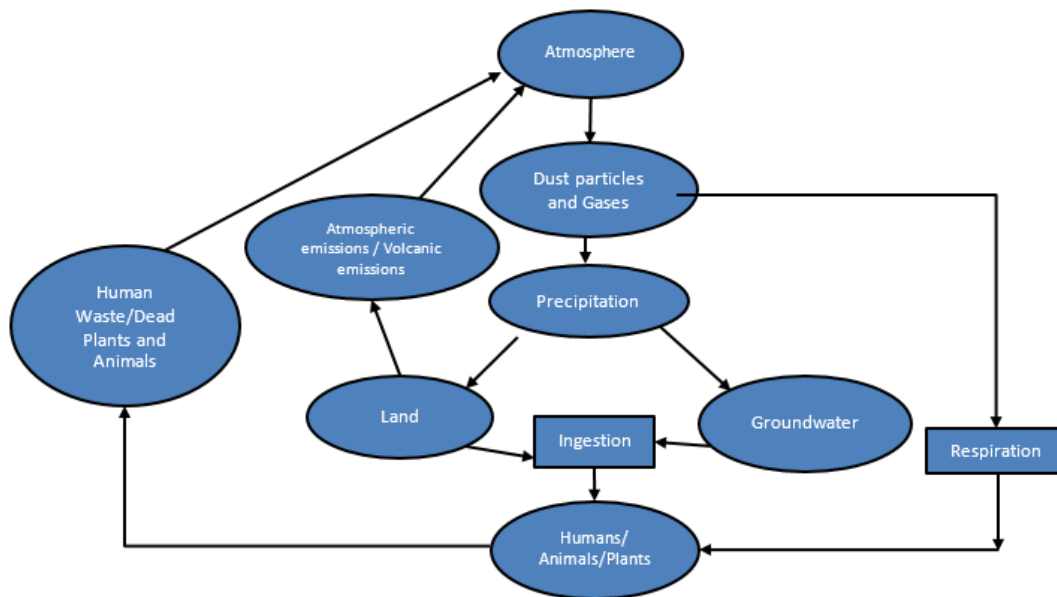
The body requires minerals and trace elements as key micronutrients for normal function. These

components are extremely beneficial for physiological processes [1]. Minerals and trace elements are necessary cofactors for a variety of enzymes and are also crucial for a number of biological processes. Additionally, they serve as stabilizing elements in proteins and enzymes. Some trace elements control important biological processes by binding to the receptor site on the cell membrane or altering the structural characteristics of the receptor to prohibit specific molecules from entering the cell [2]. Micronutrients have two purposes: they maintain healthy cellular architecture and they block additional pathways that might cause disease [3]. These essential micronutrients have significant physiological effects and are linked to diabetes [4,5].

Reputable sources, such as scientific results and clinical data from diabetes research, are used to identify crucial micronutrient deficiency/overload. However, because there are so many contradictory studies, it might be difficult for doctors to advise diabetics on diet [6]. Due to improvements in diagnosis, management, and research, diabetes patients now live longer, which has corresponded with a rise in the aged population overall. Diabetes alters the trace element-related antioxidant enzymes [7]. Diabetes mellitus has been shown in several cohort studies to alter the homeostasis of trace elements [8]. Early component abnormalities may severely hinder insulin metabolism [9,10,11]. The majority of cohort studies either focus on a single factor or a few ones.

Organic acids, macro elements, vitamins, and trace elements make up the four primary subcategories of micronutrients. Chloride, calcium, phosphorus, magnesium, sodium, potassium, and iron are the main macroelements. On the other hand, several trace elements, including as cobalt, boron, chromium, copper, sulfur, iodine, zinc, and molybdenum, increase insulin action by activating insulin receptor sites [14]. Numerous macro and trace elements' mechanisms of action are changed in type 2 diabetes mellitus (T2DM), and these trace elements play specific roles in the development and progression of T2DM [15]. This review covers a wide range of laboratory-based research, observational studies, cohort and case-controlled studies, randomized controlled trials, and publications with significant findings. This thorough examination compiles research on people from North America, Asia, and Africa with a variety of ethnic backgrounds. Overall, this work lends credence to the hypothesis that trace element deficiencies may be connected to oxidative stress, which occurs before insulin resistance or diabetes, either directly or indirectly.

Minerals Transport Cycle



3. Results and Discussions

4.1 Micronutrients

Our bodies require trace amounts of vitamins and minerals known as micronutrients for various activities. They generally perform the roles of essential cofactors and coenzymes for metabolic processes. As a result, they support key cellular processes including glycolysis, the citric acid cycle, lipid metabolism, and amino acid metabolism that are essential for life and the production of energy [1]. Even minor deficient levels might lead to severe illness states. Research has been done on micronutrients as potential treatments and preventative measures for both type 1 and type 2 diabetes as well as for common complications of diabetes [2,3]. The limitations of noninvasive assessment procedures are the cause of the difficulty in detecting micronutrient levels. The actual quantities of nutrients available in essential nutrient pools might not be adequately reflected by common approaches, such as measuring plasma nutrient levels. Additionally, nutritional assessment databases and methods are frequently not completely trustworthy [1-4]. Due to these methodological limitations, it has been challenging for researchers to plan and carry out micronutrient supplement studies that are targeted at people with deficiencies who are most likely to benefit from supplements. As a result, research on how micronutrients affect people with diabetes has shown a diversity of results.

The use of diverse populations of diabetic patients with different biochemical origins, variations in glycemic control, variations in the doses and forms of micronutrients used, variability in study length, lack of control for the dietary contribution of micronutrients, and use of various biochemical assays and methods of analysis are additional

research variables that may also be involved in the discrepancy in study findings [1-4]. We won't have any definitive data until these methodological issues are resolved, most likely. Dietary reference intakes (DRIs) are the foundation of current dietary recommendations. The RDAs that were previously in use have been replaced by DRIs, which were developed in 1998. The RDA, Adequate Intake (AI), Estimated Average Requirement (EAR), and Tolerable Upper Intake Level (UL) are the four numbers that make up the DRIs.

The quantity of nutrients deemed essential to satisfy the needs of almost all healthy people is known as the recommended daily allowance (RDA). It works well when utilized as an intake aim objective. However, because the RDA is, by definition, far greater than the needs of many people, intakes that are below the RDA are not necessarily insufficient. The AI is used in place of the RDA for nutrients for which there is presently insufficient scientific data to develop one. The EAR is the amount of nutrient intake deemed sufficient to meet the demands of 50% of healthy individuals in a certain life stage or gender group. It works well for figuring out whether a nutritional deficiency is probable. There is a 50% probability that a diet will be insufficient if it falls below the EAR for a particular nutrient. For there to be a true deficit, there has to be supporting clinical and biochemical evidence. The UL is the most amount of nutrients consumed without experiencing any unfavorable side effects. It is based on healthy population individuals who are more prone to develop poisoning. Regular daily nutritional intake from diet and supplements is the basis for the UL. It is most suited for determining the amount of nutrients consumed on a daily basis that are likely to have major negative side effects.

4.2 Chromium

To maintain a normal rate of glucose metabolism, you require the trace element trivalent chromium (Cr^{3+}). Experimental chromium deprivation results in impaired glucose tolerance, however it improves with chromium supplementation [5]. Determining clinical chromium deficiency is difficult since there is no valid biochemical biomarker of chromium status [2, 5]. Studies on the effects of chromium on glycemic control, dyslipidemia, weight loss, body composition, and bone density have been conducted [4,5]. The current AIs for chromium are 25 g for females and 35 g for males. There isn't a standardized UL. Previously, it was believed that a daily consumption of up to 200 g was safe and adequate. Intakes of between 20 and 30 g/day are regarded as usual in the US [5].

Although there are various risk factors for micronutrient deficiencies, it is not shown that patients with diabetes have higher rates of deficiency. Low-calorie diets, becoming older, and hyperglycemia and glycosuria are a few of them. Pregnancy, breastfeeding, stress, illness, physical trauma, and prolonged intense activity are other variables that may raise chromium needs [4,5]. Chromium is necessary for the proper regulation of insulin, which in turn keeps the body's blood sugar under control. Thus, maintaining enough chromium levels is crucial. The three most common ailments in the US—diabetes, high blood pressure, and obesity—are caused by insufficient chromium intake, poor food choices, and a sedentary lifestyle. High blood sugar levels might result from a chromium deficiency. If you have a chromium deficiency, which is quite uncommon, it could be worth a go. If you have been told you have renal problems, stay away. Supplementing with chromium may aggravate the condition and further harm the kidneys. Ever since chromium (Cr) was identified as an important trace metal in 1955 [45], it has been known to significantly increase glucose tolerance by lowering insulin resistance. Chinese investigations revealed that supplemental Cr reduced T2DM patients' levels of insulin, cholesterol, blood sugar, and hemoglobin A1C in a dose-dependent manner [46].

Nutritional chromium enhances insulin sensitivity and blood lipid levels [47]. Most diets do not provide the 50 mg of Cr per day that is advised. Insufficient Cr is a factor in the signs and symptoms of diabetes and cardiovascular diseases [48]. In those with hypoglycemia, hyperglycemia, diabetes, and hyperlipidemia, chromium raises their glucose and insulin levels while having little to no effect on the control group. In addition to raising insulin sensitivity, cell sensitivity, and insulin internalization, chromium enhances insulin binding,

receptor number, and insulin receptor enzymes [49].

According to many studies on the effects of chromium supplementation on lipid levels and glucose metabolism, individuals who do not have diabetes were not impacted by the effects of chromium on lipid or glucose metabolism, but diabetic patients' glucose metabolism was significantly enhanced [66]. Cr promotes increased insulin binding, receptor quantity, and phosphorylation. A comparative study done in China and the US found that individuals with mild glucose intolerance only need 200 mg/day of Cr supplementation, as opposed to those with higher glucose tolerance and diabetes [67].

According to Rajendran et al., there is a connection between serum Cr levels and T2DM. They asserted that a decrease in Cr levels was caused by the metabolic response to oxidative stress in T2DM patients. In this study, 42 newly diagnosed T2DM patients were divided into two groups: well-managed (HbA1c 7.0%) and uncontrolled (HbA1c > 7.0%). Serum Cr concentration was assessed in both groups. T2DM patients with uncontrolled glucose levels exhibited lower serum Cr levels (0.065 0.03 g/L vs. 0.103 0.04 g/L, p 0.05) compared to the control group. It was statistically significant that the HbA1c and serum Cr levels were adversely associated ($r = -0.6514$, p 0.0001). After 40 years of age, both groups' chromium levels decreased due to advancing age (p 0.05) [68]. Oral chromium picolinate treatment was shown to reduce hyperglycemia-mediated oxidative stress in a different investigation using an experimental diabetic rat model [69].

4.3 Cobalt

One of the most prevalent elements in the crust of the planet is cobalt. Of the 70 naturally occurring minerals, it is one. Its origins are both human and natural. Common natural causes include soil and rock erosion and weathering. The usage of phosphate fertilizers on soil, cobalt-containing trash, and the combustion of fossil fuels are examples of anthropogenic sources [146]. Cobalt in drinking water has no established acceptable limit [135,136]. While most foods contain cobalt, there is often little of it in groundwater. Given that it is a component of the crucial vitamin B12, it can have both negative and positive impacts on human health. Although it has been determined to cause cancer in animals, the USEPA has not listed it as a carcinogenic substance [137]. According to a number of studies, typical cobalt serum concentrations are less than 0.5 g/L. Saker et al. demonstrated that cobalt chloride (CoCl_2)'s glucose-lowering impact reduced gluconeogenesis in diabetic rats [39]. In diabetic rats' visceral organs, cobalt alone or together with ascorbate lowers lipid

peroxidation [40]. Compared to their contemporaries without diabetes, T2D patients' serum cobalt levels decreased. By reducing oxidative stress, cobalt therapy also improved nephropathy and heart function in a rat model of type 2 diabetes [41].

The investigations conducted on humans to compare the cobalt levels in diabetes patients with appropriate controls are insufficient. In one Pakistani investigation, males in five age groups—diabetic and non-diabetic—were the subjects [42]. In contrast to other research done on streptozotocin (STZ) treated Type 1 diabetic rats, they observed a greater mean cobalt content in diabetic patients after doing a multi-element serum analysis. In comparison to healthy people, Flores et al. found that diabetes patients had considerably greater

serum concentrations of Al, Cd, Cu, Mn, Hg, and Ni, and significantly lower serum concentrations of Cr, Co, and V [43]. 76 individuals, ranging in age from 52 to 8 years, had their levels of trace elements in the blood and urine of healthy and diabetic participants compared to healthy participants. According to the study, diabetic patients had lower urine levels of Cd, Co, Pb, Mn, Mo, Ni, and Se and higher amounts of Cr, As, Cu, and Zn compared to healthy people. Only the changes in Cd and Zn, though, were statistically significant [43]. Hexamine cobalt chloride, at a concentration of 2 mM, has been shown to prevent mouse pancreatic islet cells from secreting 22.2 mM of glucose-induced insulin without affecting glucose metabolism or Ca influx into the cytosol [44].

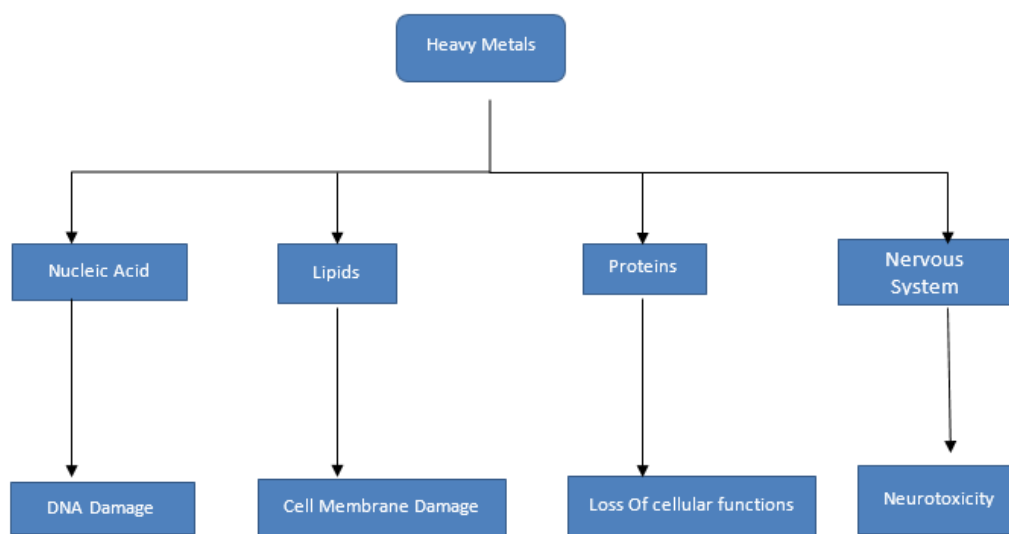


Figure: Flow chart of the effect of human health through minerals

4.4 Vanadium

The Scandinavian goddess associated with beauty, youth, and shine is whence vanadium gets its name. Black pepper, dill, parsley, mushrooms, and shellfish are a few excellent dietary sources of vanadium, but it's important to keep in mind that up to 90% of the vanadium taken from these sources is not absorbed by the body. Most recent studies have concentrated on vanadium's capacity to mimic or enhance insulin activity. Vanadyl sulfate is a notable vanadium form that has showed biological importance by favorably altering a number of factors including glucose tolerance, cholesterol levels, bones, and teeth. Bodybuilders and those with diabetes frequently take vanadyl sulfate because of its ability to imitate insulin.

4.5 Iodine

Reduced thyroid hormone synthesis can cause increased thyroid stimulating hormone (TSH) release and thyroid gland hypertrophy as a result of iodine deficiency [70]. According to a recent study, consuming too much iodine may impair the capacity of islet cells to survive and secrete insulin.

Endoplasmic reticulum stress and the activation of pro-apoptotic proteins may be responsible for this impact [71]. Energy metabolism must be regulated properly by the thyroid, and poor thyroid function can have a big impact on blood glucose management in diabetics. Thyroid illness is more likely to affect those with diabetes mellitus [72,73].

Iodine status and urine iodine levels were examined in individuals with type 2 diabetes mellitus (T2DM) in a clinical investigation conducted in Saudi Arabia. According to the findings, T2DM patients had considerably lower urine iodine concentrations than healthy control persons [74]. Insulin resistance (IR), which has been linked to increased thyroid volume and nodule prevalence in individuals with metabolic syndrome [75,76], is a contributing factor to impaired glucose metabolism. Another investigation found that treating hyperthyroidism in people with diabetes mellitus reduced the prevalence of diabetes [77]. Additionally, a research on people with pre-diabetes, T2DM, and normal glucose metabolism in a region with mild to severe iodine deficiency discovered that people with

impaired glucose metabolism had larger thyroid volumes and nodule prevalence [78]. In example, hypothyroidism affects more women than males, and diabetes and hypothyroidism have been linked in an American Indian community. According to the study, women are more likely than males to have diabetes and hypothyroidism. Additionally, hypothyroidism was more prevalent in women 60 years of age and older, suggesting that diabetes and American Indian women are more likely to cohabit [79].

4.6 Copper

Copper is naturally found in both surface and groundwater, often in complex forms or as particulate matter [142]. It is important to note that copper toxicity can have severe consequences, ranking after mercury and cadmium in terms of adverse impact [143]. A noteworthy concern arises from the potential coincidence of ozone layer depletion and dietary copper deficiency, which may increase the risk of skin cancer in humans. The recommended daily intake of copper for adults typically ranges from 1 to 3 mg, with drinking water contributing 0.1 to 1 mg per day in most cases. The drinking water standard for copper is set at 0.05 to 1.5 mg/L [136]. Copper is an essential trace mineral crucial for various enzymatic reactions within the human body. The brain, bones, kidneys, and liver harbor the highest concentrations of copper in humans.

Copper has demonstrated beneficial therapeutic effects in preventing cardiovascular disease and treating arthritis. Even though there is scientific proof that copper may be absorbed through the skin and chelated to another compound with potential anti-inflammatory properties, some doctors are dubious about the effectiveness of wearing copper bracelets, despite the fact that it has been a traditional treatment for arthritis. Only Trace Minerals includes 2 mg of copper, which is within the healthy daily range of 1.5 to 3 mg for dietary copper. Unless therapeutic zinc concentrations (over 80 mg) are being taken, it is crucial to limit copper intake to no more than 3 to 4 mg per day since excessive copper can produce free radicals. When copper supplementation is already enough based on hair or blood tests and excess fructose is not ingested, the body just needs a little amount of copper to support biological functions.

4.7 Manganese

Manganese is a prevalent element found in various types of rocks and can be detected in both surface and groundwater, with higher concentrations often present in groundwater. It originates from both natural and human sources. Geogenic sources stem from the weathering of manganese-bearing minerals and rocks, while anthropogenic contributions result from industrial effluent,

domestic sewage, and leachate from landfills, which release manganese into the groundwater. While essential for human health, the average daily dietary intake of manganese is approximately 1.8 mg [141]. The established limits for manganese in groundwater are typically set at 0.1 mg/L and 0.4 mg/L [135,136].

4.8 Boron

Each capsule of Only Trace Minerals has 3 mg of boron. Although there is no precise Recommended Daily Allowance (RDA) for boron, this important trace element is required for turning vitamin D into its active form and is critical for supporting healthy bones and joints. Boron significantly affects estrogen levels, especially in postmenopausal women. According to a research, eating 3 mg of dietary boron per day boosted levels of estradiol and decreased urine calcium loss by up to 44%. It is essential to assess the need for additional estradiol through blood testing, as some postmenopausal women may require it. Unfortunately, obtaining sufficient boron from the average diet is challenging due to its scarcity in soil and subsequently low levels in food, even though fruits and vegetables are primary sources of boron. Boron, as a micronutrient, plays diverse and significant roles in metabolism. It contributes to bone development and regeneration, promotes wound healing, influences sex hormone production, aids in vitamin D metabolism, and supports the absorption and utilization of calcium and magnesium.

Research on rats has indicated that dietary boron affects plasma insulin concentrations, reducing levels in boron-supplemented rats compared to boron-deficient ones. Interestingly, boron deficiency does not seem to impact plasma glucose concentrations and is independent of magnesium or dietary vitamin D status. Boric acid, a form of boron, has been found to inhibit calcium release, which affects insulin release and brain function. Moreover, boron appears to impact metabolic regulation and enzymatic systems related to triglyceride levels, as shown in animal studies. In a cell model, boric acid and sodium pentaborate pentahydrate were found to inhibit adipogenesis and suppress the expression of adipogenesis-related genes and proteins, indicating potential roles in controlling adipose tissue growth. Additionally, boron treatment has shown antioxidant effects and preservation of pancreatic beta cells in diabetic animals. However, a study on normal and diabetic pregnancies did not find a significant correlation between maternal boron levels and lipid profiles.

4.9 Molybdenum

Molybdenum plays a critical role in the functioning of numerous enzymes and acts as a coenzyme for essential enzymatic processes. Some of these enzymes are involved in detoxifying alcohol and

sulfur, as well as contributing to the production of uric acid. Furthermore, molybdenum has been associated with potential cancer prevention and the prevention of dental cavities. Maintaining adequate molybdenum levels is important to avoid allergic reactions to sulfites, which are commonly present in the average diet. On average, most individuals consume approximately 2 to 3 mg of molybdenum daily, while those who consume beer and wine may have up to 10 mg daily. The acceptable limit for molybdenum in drinking water is set at 0.07 mg/L. Molybdenum has shown no significant negative interactions with other nutrients or drugs and is generally considered safe, except when taken in extremely high doses exceeding 100 mg per kilogram of body weight. In practical terms, this would amount to an astonishing 7000 mg for a person weighing 154 pounds. Only Trace Minerals contains a more appropriate and safe amount of molybdenum, providing 250 mcg per capsule.

4.10 Zinc

Zinc is an indispensable element found in every cell and serves as a vital component of over 200 enzymes in the body. Its significance lies in supporting proper cell division and participating in more enzymatic reactions than any other mineral. Zinc plays a crucial role in the functioning of various hormones, including thymic hormones, sex hormones, growth hormone, and insulin. For adults, the Recommended Dietary Allowance (RDA) for zinc is 15 mg per day. A deficiency of zinc can lead to various symptoms, such as impaired wound healing, night blindness, growth retardation, mouth ulcers, a white coating on the tongue, and white spots on the fingernails. Additionally, zinc is essential for maintaining healthy vision, taste, and smell. In the human body, zinc is primarily stored in muscle tissue, with significant amounts found in various organs and tissues, including white blood cells, red blood cells, bone, skin, kidney, liver, pancreas, retina, and the prostate gland. It plays a crucial role in supporting healthy male sex hormones and prostate function, and zinc levels can be measured in white blood cells to assess its status in the body. Severe clinical disorders include connective tissue disease, rheumatoid arthritis, impotence/infertility, inflammatory bowel disease, alcoholism, night blindness, mental illness, and acne have all been linked to zinc deficiency.

Additionally, zinc is necessary for a strong immune system. A lack of T cells, a drop in thymic hormone levels, and problems with vital white blood cell activities can all be brought on by low zinc levels. However, with the right zinc dosage, these effects can be reversed. Additionally, zinc directly inhibits some viruses, including those that cause the common cold. To maintain excellent health, a daily zinc intake of 15 to 80 mg is sufficient. 20 mg of zinc are present in Only Trace Minerals, providing more

of this important mineral than is generally present in multi-nutrient supplements. Only Trace Minerals must not be taken with milk products, calcium supplements, or magnesium supplements. If Only Trace Minerals is taken without meals, some people with sensitive stomachs can suffer minor discomfort.

4.11 Calcium

Calcium has a big impact on both insulin secretion and resistance [25]. Skeletal muscles, cardiac muscles, platelets, and erythrocytes all experience a breakdown in cell regulation as a result of diabetes' impact on calcium homeostasis. This change in homeostasis may play a significant role in adequate insulin secretion and action, as well as a number of vascular issues [26,27]. The onset of type 2 diabetes (T2DM) is correlated with fluctuations in calcium and vitamin D levels, according to a 2007 study by Pittas et al. The incidence of T2DM or metabolic syndrome was found to be slightly correlated with low vitamin D status, calcium intake, and dairy consumption. Blood 25-hydroxyvitamin D (25-OHD) levels and the prevalence of metabolic syndrome and type 2 diabetes (T2DM) were examined, and the findings revealed inverse associations between the incidence of T2DM or metabolic syndrome for highest vs lowest combined vitamin D and calcium consumption. When provided as supplements, these two nutrients improved glucose metabolism and decreased the deleterious effects of hyperglycemia [28]. Two small group studies revealed various serum calcium levels. A research conducted in Baghdad with 30 participants aged 30 to 70 years revealed elevated blood calcium levels and a marked decline in parathyroid levels [29]. An Indian research, however, found that diabetes individuals had considerably lower blood calcium levels than non-diabetic controls. Furthermore, a negative link between elevated serum calcium levels and plasma blood glucose levels was seen [30]. According to this, people with uncontrolled hyperglycemia and diabetes are more likely to develop hypocalcemia than healthy individuals [31].

There aren't many cohort studies looking at raised blood calcium levels as indicators of poor glucose metabolism, but one of them found a higher risk of diabetes in people with higher serum calcium concentrations. In 77 patients of T2DM, the study revealed an overall rise in blood calcium levels throughout follow-up. These findings are consistent with cross-sectional studies that have previously shown that diabetic patients have higher serum calcium levels than non-diabetics. This association remained significant even after calcium supplement users and people with abnormal calcium levels were excluded, proving that elevated serum calcium levels are linked to an increased risk of T2DM [32]. A second study in Korean patients confirmed the correlation between the incidence of the metabolic

syndrome and diabetes and higher blood calcium levels (p 0.001). This relationship was unaffected by age, sex, BMI, serum creatinine, phosphorus, parathyroid hormone (PTH), 25-OHD levels, usage of tobacco or alcohol, exercise, total calorie intake, calcium intake, or salt intake [33]. According to research, calcium levels and the development of diabetes are intricately linked. Reduced -cell function is associated with abnormal calcium regulation, which can also have an effect on oxidative stress and impaired glucose homeostasis. High cytosolic calcium concentrations may be linked to insulin resistance, according to studies conducted in cell culture [34, 35]. Dietary calcium consumption has been shown to delay the onset of T2D in earlier dose-dependent meta-analyses of cohort studies [37,38].

4.12 Iron

The bidirectional relationship between iron metabolism and glucose homeostasis is becoming more well acknowledged, and iron plays a key role in glucose metabolism [80]. A significant factor influencing glucose metabolism may be impaired iron absorption. Serum ferritin concentrations in persons with type 2 diabetes mellitus (T2DM) may have an impact on insulin sensitivity, viscosity, oxidative damage, and vascular resistance. Both blood ferritin levels and body mass index (BMI) may be used independently as predictors in a glucose tolerance test [81]. According to a study on pregnant women without anaemia or diabetes mellitus before 20 weeks of gestation and tested again at 28 3 weeks of gestation, those who were diagnosed with gestational diabetes mellitus (GDM) had significantly higher concentrations of serum ferritin, iron, transferrin saturation, and post-natal haemoglobin, pointing to a link between higher iron stores and glucose intolerance [82].

HazardousMinerals	Source	Health effects
Radioactive Minerals (U or Th)	Radioactive minerals in soil and groundwater	Renal failure, Liver effects, genotoxicity, neuroendocrine effects
Crocidolite	Blue Asbestos	Lung diseases, including cancer
Hydroxyapatite	Bones and teeth	Form deposits in heart valves and arteries , arthritis.
Erionite	Fibrous zeolite	Malignant mesotheliomas in humans
Phenacite	Beryllium containing dust	Poisoning
K-feldspar	U and Pb containing soil	Lung cancer, nausea, irregular heartbeats.
Chrysotile	White asbestos	Hardening of lung tissues, difficulty in breathing
Quartz	Fine particulate	Respiratory effects (silicosis or silicotuberculosis), lung cancer.
Fluorite	Major fluoride minerals	Severe bone disorder
Pyrite	Acid mine waters with sulfide mine tailings	heavy metal poisoning
Galena	Lead in groundwater	Neurotoxicity and cardiovascular diseases

According to cross-sectional research, diabetes patients have higher transferrin saturation levels than non-diabetics, and these higher levels are linked to lower C-reactive protein and higher fasting plasma glucose levels [84]. A decreased ratio of transferrin receptors to ferritin was also associated with an increased risk of type 2 diabetes in healthy women, according to results of another study [85]. Because of the well-known pro-oxidant properties of iron, having high levels of iron in the body increases the risk of type 2 diabetes [86]. High body iron reserves, indicated by circulating ferritin levels, have been associated in epidemiological studies to type 2 diabetes and other insulin-resistant conditions [87]. Phlebotomy, which lowers body iron levels, has been demonstrated to increase insulin sensitivity in people, suggesting a link between iron overload and the risk of developing diabetes [88]. Studies looking at the role of iron in gestational diabetes mellitus (GDM) have discovered that women with GDM have higher

serum ferritin, iron, transferrin saturation, and haemoglobin levels than those without GDM [89]. In addition, women with managed diabetes had a higher frequency of anaemia than males did [90], which was related to both poor glycemic control and gender differences. While not many markers of iron metabolism are known, ferritin has been identified as a significant factor associated with T2DM. Transferrin saturation (TSAT) and iron were inversely associated with T2DM, indicating the potential association of secondary iron metabolic markers in the progression of the disease [91]. In 2015, iron's influence on glucose metabolism on multiple levels was confirmed [80].

4.13 Selenium

Dietary selenium (Se) is an essential micronutrient required for the synthesis of selenoproteins, which play critical roles in various biological functions, including antioxidant and cytoprotective properties. Some studies suggest that Se supplementation may

be beneficial in preventing metabolic diseases, including type 2 diabetes (T2DM) [110].

The association between serum Se levels and diabetes was examined using a cross-sectional examination of a sample of U.S. people. A control group, diabetics receiving insulin therapy, and diabetics with a fasting plasma glucose level of 126 mg/dL were all included in the study. The study discovered that diabetics had a mean serum Se differential of 2.1 ng/mL compared to controls (95% CI 0.4-0.8, $p = 0.02$) after controlling for age, sex, race, and BMI. The findings showed a direct link between elevated blood Se levels and the incidence of diabetes. To avoid diabetes, the research did not offer any particular advice on Se supplementation or limitation [111, 112]. On the other hand, Se treatment at 0.2 mol/L in drinking water for 3 weeks led to decreased blood glucose levels and enhanced lipid metabolism in a research employing non-obese diabetic mice [113]. Another cross-sectional investigation examined the relationship between dietary selenium consumption and diabetes in middle-aged and elderly Chinese individuals (5423 participants). According to the study's findings, there is a strong positive link between dietary selenium consumption and the prevalence of diabetes. Similarly, a cross-sectional analysis of over 8876 U.S. adults aged 20 and above under the National Health and Nutrition Examination Survey revealed a positive association between higher serum selenium levels and the prevalence of diabetes [110,111,114,115]

4. Conclusions

The findings of this medical geology review unequivocally emphasize the vital role of minerals and vitamins in maintaining human health. From bolstering immune function to aiding in essential biochemical processes, these micronutrients play an integral part in our overall well-being. As we have explored the relationship between geological factors and the presence of minerals in the environment, it becomes apparent that understanding these connections can have significant implications for public health initiatives and targeted interventions. Through an in-depth analysis of the impact of minerals and vitamins on human health, this medical geology review highlights the intricate relationship between geological processes and nutrition. The research underscores the importance of incorporating geoscience perspectives into public health strategies, particularly in regions where certain minerals and vitamins are deficient or excessive in the environment. By identifying such connections, we can work towards the development of tailored interventions to address deficiencies and mitigate potential health risks associated with excess mineral exposure. This comprehensive medical geology review establishes a strong foundation for recognizing the crucial role minerals

and vitamins play in the maintenance of human health. The intricate interplay between geological factors and nutrition underscores the need for multidisciplinary collaboration between geologists, nutritionists, and healthcare professionals. Armed with this knowledge, we can implement evidence-based strategies to optimize micronutrient intake, enhance public health outcomes, and improve the overall quality of life for diverse populations across the globe.

The evidence presented in this medical geology review underscores the significance of minerals and vitamins in promoting human health and preventing various nutritional deficiencies. It highlights the importance of adopting a holistic approach to healthcare, incorporating geological factors into the equation to better understand the geographical distribution of essential nutrients. By acknowledging the impact of the environment on our nutritional status, we can develop targeted interventions and policies that empower individuals to make informed dietary choices, leading to healthier and more sustainable lifestyles.

Conflict of interest

All authors declare no competing interests.

References

- [1]. Abbas, W. A., Al-Zubaidi, M. A., & Al-Khazraji, S. K. (2011). Estimation of serum calcium and parathyroid hormone (PTH) levels in diabetic patients in correlation with age and duration of disease. *Clinical Chemistry and Laboratory Medicine*, 49, S365.
- [2]. Ablikim, M., Achasov, M. N., Albayrak, O., Ambrose, D. J., An, F., An, Q., Bai, J. Z., Ferroli, R. B., Ban, Y., Becker, J., et al. (2014). Observation of a charged (DD^*) \pm mass peak in $e^+ e^- \rightarrow \pi DD^*$ at $\sqrt{s} = 4.26$ GeV. *Physical Review Letters*, 112, 022001. <https://doi.org/10.1103/PhysRevLett.112.022001>
- [3]. Abou-Seif, M. A., & Youssef, A.-A. (2004). Evaluation of some biochemical changes in diabetic patients. *Clinica Chimica Acta*, 346, 161-170. doi: 10.1016/j.cccn.2004.03.030
- [4]. Abraham, A. S., Brooks, B. A., & Eylath, U. (1992). The effects of chromium supplementation on serum glucose and lipids in patients with and without non-insulin-dependent diabetes. *Metabolism*, 41, 768-771. [https://doi.org/10.1016/0026-0495\(92\)90318-5](https://doi.org/10.1016/0026-0495(92)90318-5)
- [5]. Afkhami-Ardekani, M., & Rashidi, M. (2009). Iron status in women with and without gestational diabetes mellitus. *Journal of Diabetes and its Complications*, 23, 194-198. doi: 10.1016/j.jdiacomp.2007.11.006

- [6]. Agency for Toxic Substances and Disease Registry. (2002). Toxicological profile for copper (draft for public comment). Public Health Service, U.S. Department of Health and Human Services, Atlanta, G.A.
- [7]. Agency of Toxic Substances and Disease Registry. (2020).
- [8]. Al-Attas, O. S., Al-Daghri, N., Alkharfy, K. M., Alokail, M. S., Al-Johani, N. J., Abd-Alrahman, S. H., Yakout, S. M., Draz, H., & Sabico, S. (2012). Urinary Iodine is Associated with Insulin Resistance in Subjects with Diabetes Mellitus Type 2. *Experimental and Clinical Endocrinology & Diabetes*, 120, 618–622. doi: 10.1055/s-0032-1323816
- [9]. Aly, H. F., & Mantawy, M. M. (2012). Comparative effects of zinc, selenium, and vitamin E or their combination on carbohydrate metabolizing enzymes and oxidative stress in streptozotocin-induced diabetic rats. *European Review for Medical and Pharmacological Sciences*, 16, 66–78.
- [10]. Anderson, R. A. (1997). Nutritional factors influencing the glucose/insulin system: Chromium. *Journal of the American College of Nutrition*, 16, 404–410. <https://doi.org/10.1080/07315724.1997.10718705>
- [11]. Anderson, R. A. (1998). Chromium, glucose intolerance, and diabetes. *Journal of the American College of Nutrition*, 17, 548–555. <https://doi.org/10.1080/07315724.1998.10718802>
- [12]. Anderson, R. A., Polansky, M. M., Bryden, N. A., Roginski, E. E., Mertz, W., & Glinsmann, W. (1983). Chromium supplementation of human subjects: Effects on glucose, insulin, and lipid variables. *Metabolism*, 32, 894–899. [https://doi.org/10.1016/0026-0495\(83\)90203-2](https://doi.org/10.1016/0026-0495(83)90203-2)
- [13]. Anil Kumar, V. S. P. D., Jaiprabhu, J., & Krishnan, R. (2014). Serum copper and zinc levels significance in type 2 diabetic patients. *Journal of Medical Science and Technology*, 3, 79–81.
- [14]. Anil, C., Akkurt, A., Ayturk, S., Kut, A., & Gursoy, A. (2013). Impaired glucose metabolism is a risk factor for increased thyroid volume and nodule prevalence in a mild-to-moderate iodine-deficient area. *Metabolism*, 62, 970–975. doi: 10.1016/j.metabol.2013.01.009
- [15]. Anjum, A. (2012). Comparative study on calcium, magnesium, and cobalt in diabetic and non-diabetic patients (males) in Punjab, Pakistan. *African Journal of Biotechnology*, 11, 7258–7262.
- [16]. Aune, D., Norat, T., Romundstad, P. R., & Vatten, L. J. (2013). Dairy products and the risk of type 2 diabetes: A systematic review and dose-response meta-analysis of cohort studies. *The American Journal of Clinical Nutrition*, 98, 1066–1083. <https://doi.org/10.3945/ajcn.113.059030>
- [17]. Badran, M., Morsy, R., Soliman, H., & Elnimr, T. (2016). Assessment of trace elements levels in patients with type 2 diabetes using multivariate statistical analysis. *Journal of Trace Elements in Medicine and Biology*, 33, 114–119. <https://doi.org/10.1016/j.jtemb.2015.10.006>
- [18]. Bakken, N. A., & Hunt, C. D. (2003). Dietary boron decreases peak pancreatic in situ insulin release in chicks and plasma insulin concentrations in rats regardless of vitamin D or magnesium status. *The Journal of Nutrition*, 133, 3577–3583. <https://doi.org/10.1093/jn/133.11.3577>
- [19]. Balk, E., Tatsioni, A., Lichtenstein, A. H., Lau, J., & Pittas, A. G. (2007). Effect of Chromium Supplementation on Glucose Metabolism and Lipids: A systematic review of randomized controlled trials. *Diabetes Care*, 30, 2154–2163. <https://doi.org/10.2337/dc06-0996>
- [20]. Bandeira, V. D. S., Pires, L. V., Hashimoto, L. L., De Alencar, L. L., Almondes, K. G. S., Lottenberg, S. A., & Cozzolino, S. M. F. (2017). Association of reduced zinc status with poor glycemic control in individuals with type 2 diabetes mellitus. *Journal of Trace Elements in Medicine and Biology*, 44, 132–136. doi: 10.1016/j.jtemb.2017.07.004
- [21]. Barbagallo, M., & Dominguez, L.-J. (2007). Magnesium metabolism in type 2 diabetes mellitus, metabolic syndrome, and insulin resistance. *Archives of Biochemistry and Biophysics*, 458, 40–47. doi: 10.1016/j.abb.2006.05.007
- [22]. Bleys, J., Navas-Acien, A., & Guallar, E. (2007). Selenium and diabetes: More bad news for supplements. *Annals of Internal Medicine*, 147, 271–272. doi: 10.7326/0003-4819-147-4-200708210-00177
- [23]. Bleys, J., Navas-Acien, A., & Guallar, E. (2007). Serum Selenium and Diabetes in U.S. Adults. *Diabetes Care*, 30, 829–834. doi: 10.2337/dc06-1726
- [24]. Blumberg, D., Bonetti, A., Jacomella, V., Capillo, S., Truttman, A. C., Lüthy, C. M., Colombo, J. P., & Bianchetti, M. G. (1998). Free circulating magnesium and renal magnesium handling during acute metabolic acidosis in humans. *American Journal of Nephrology*, 18, 233–236. doi: 10.1159/000013342
- [25]. Bureau of Indian Standard. (2012). Drinking water specification. New Delhi.
- [26]. Caglar, G. S., Çakal, G. Ö., Yüce, E., & Pabuccu, R. (2012). Evaluation of serum boron levels and lipid profile in pregnancies with or without gestational diabetes. *Journal of Perinatal Medicine*, 40. <https://doi.org/10.1515/jpm.2011.121>

- [27]. Calabrese, E. J., Canada, A. T., & Sacco, C. (1985). Trace elements and public health. *Annual Review of Public Health*, 6, 131–146. <https://doi.org/10.1146/annurev.pu.06.050185.001023>
- [28]. Cao, J., Vecoli, C., Neglia, D., Tavazzi, B., Lazzarino, G., Novelli, M., Masiello, P., Wang, Y.-T., Puri, N., Paolucci, N., et al. (2012). Cobalt-protoporphyrin improves heart function by blunting oxidative stress and restoring NO synthase equilibrium in an animal model of experimental diabetes. *Frontiers in Physiology*, 3. <https://doi.org/10.3389/fphys.2012.00160>
- [29]. Cefalu, W. T., Rood, J., Pinsonat, P., Qin, J., Sereda, O., Levitan, L., Anderson, R. A., Zhang, X. H., Martin, J. M., Martin, C. K., et al. (2009). Characterization of the metabolic and physiologic response to chromium supplementation in subjects with type 2 diabetes mellitus. *Metabolism*, 59, 755–762. <https://doi.org/10.1016/j.metabol.2009.09.023>
- [30]. Chen, C., Jiang, W., Zhong, N., Wu, J., Jiang, H., Du, J., Li, Y., Ma, X., Zhao, M., Hashimoto, K., et al. (2014). Impaired processing speed and attention in first-episode drug-naive schizophrenia with deficit syndrome. *Schizophrenia Research*, 159, 478–484. <https://doi.org/10.1016/j.schres.2014.09.005>
- [31]. Chen, S., Itoh, Y., Masuda, T., Shimizu, S., Zhao, J., Ma, J., Nakamura, S., Okuro, K., Noguchi, H., Uosaki, K., et al. (2015). Subnanoscale hydrophobic modulation of salt bridges in aqueous media. *Science*, 348, 555–559. <https://doi.org/10.1126/science.aaa7532>
- [32]. Chen, Z. C., & Ma, J. F. (2015). Improving nitrogen use efficiency in rice through enhancing root nitrate uptake mediated by a nitrate transporter, NRT1.1B. *Journal of Genetics and Genomics*, 42, 463–465. <https://doi.org/10.1016/j.jgg.2015.08.003>
- [33]. Cheng, Y., Ma, W., Li, X., Miao, W., Zheng, L., & Cheng, B. (2011). Polyamines stimulate hyphal branching and infection in the early stage of *Glomus tunicate* colonization. *World Journal of Microbiology & Biotechnology*, 28, 1615–1621. <https://doi.org/10.1007/s11274-011-0967-0>
- [34]. Coban, F. K., Ince, S., Kucukkurt, I., Demirel, H. H., & Hazman, Ö. (2014). Boron attenuates malathion-induced oxidative stress and acetylcholinesterase inhibition in rats. *Drug and Chemical Toxicology*, 38, 391–399. <https://doi.org/10.3109/01480545.2014.974109>
- [35]. Cooppan, R., & Kozak, G. P. (1980). Hyperthyroidism and diabetes mellitus. An analysis of 70 patients. *Archives of Internal Medicine*, 140, 370–373. doi: 10.1001/archinte.1980.00330150084021
- [36]. De Vega, R. G., Fernández-Sánchez, M. L., Fernández, J. C., Álvarez Menéndez, F. V., & Sanz-Medel, A. (2016). Selenium levels and Glutathione peroxidase activity in the plasma of patients with type II diabetes mellitus. *Journal of Trace Elements in Medicine and Biology*, 37, 44–49. doi: 10.1016/j.jtemb.2016.06.007
- [37]. Derakhshanian, H., Javanbakht, M., Zarei, M., Djalali, E., & Djalali, M. (2017).
- [38]. Dessordi, R., Spirlandeli, A. L., Zamarioli, A., Volpon, J. B., & Navarro, A. M. (2017). Boron supplementation improves the bone health of non-obese diabetic mice. *Journal of Trace Elements in Medicine and Biology*, 39, 169–175. <https://doi.org/10.1016/j.jtemb.2016.09.011>
- [39]. Dibaba, D. T., Xun, P., Fly, A. D., Yokota, K., & He, K. (2014). Dietary magnesium intake and risk of metabolic syndrome: A meta-analysis. *Diabetic Medicine*, 31, 1301–1309. doi: 10.1111/dme.12537
- [40]. Djurhuus, M., Klitgaard, N., Pedersen, K., Blaabjerg, O., Altura, B., Altura, B., & Henriksen, J. E. (2001). Magnesium reduces insulin-stimulated glucose uptake and serum lipid concentrations in type 1 diabetes. *Metabolism*, 50, 1409–1417. doi: 10.1053/meta.2001.28072
- [41]. Doğan, A., Demirci, S., Apdik, H., Bayrak, O. F., Gulluoglu, S., Tuysuz, E. C., Gusev, O., Rizvanov, A. A., Nikerel, E., & Sahin, F. (2017). A new hope for obesity management: Boron inhibits adipogenesis in progenitor cells through the Wnt/ β -catenin pathway. *Metabolism*, 69, 130–142. <https://doi.org/10.1016/j.metabol.2017.01.021>
- [42]. Dongiovanni, P., Ruscica, M., Rametta, R., Recalcati, S., Steffani, L., Gatti, S., Girelli, D., Cairo, G., Magni, P., Fargion, S., et al. (2013). Dietary Iron Overload Induces Visceral Adipose Tissue Insulin Resistance. *The American Journal of Pathology*, 182, 2254–2263. doi: 10.1016/j.ajpath.2013.02.019
- [43]. Eikhenberger, E. (1993). Relationships between the demand for and toxicity of metals in aquatic ecosystems. In *Some issues of the toxicity of metal ions*. International Programme on Chemical Safety. Mir, Moscow, 62–87.
- [44]. El Dib, R., Gameiro, O. L. F., Ogata, M. S. P., Módolo, N. S. P., Braz, L. G., Jorge, E. C., ... & Nascimento, P. D. (2015). Zinc supplementation for the prevention of type 2 diabetes mellitus in adults with insulin resistance. *Cochrane Database of Systematic Reviews*, CD005525. doi: 10.1002/14651858.CD005525.pub3

- [45]. El-Zebda, G. A. (n.d.). Significance of serum levels of copper and zinc in Type II diabetic, hypertensive, and diabetic hypertensive patients in Gaza City. Available online: <http://library.iugaza.edu.ps/thesis/69220.pdf>
- [46]. Estakhri, M., Djazayery, A., Eshraghian, M. R., Jalali, M., Karamizadeh, Z., Chamari, M., & Milani, M. P. (2011). Serum Zinc Levels in Children and Adolescents with Type-1 Diabetes Mellitus. *Iranian Journal of Public Health*, 40, 83–88. [PMC free article]
- [47]. Fernandez-Real, J.-M., López-Bermejo, A., & Ricart-Engel, W. (2002). Cross-talk between iron metabolism and diabetes. *Diabetes*, 51, 2348–2354. doi: 10.2337/diabetes.51.8.2348
- [48]. Fernandez-Real, J.-M., McClain, D., & Manco, M. (2015). Mechanisms Linking Glucose Homeostasis and Iron Metabolism Toward the Onset and Progression of Type 2 Diabetes. *Diabetes Care*, 38, 2169–2176. doi: 10.2337/dc14-3082
- [49]. Flores, C. R., Puga, M. P., Wrobel, K., Garay-Sevilla, M. E., & Wrobel, K. (2011). Trace elements status in diabetes mellitus type 2: Possible role of the interaction between molybdenum and copper in the progress of typical complications. *Diabetes Research and Clinical Practice*, 91, 333–341. <https://doi.org/10.1016/j.diabres.2010.12.014>
- [50]. Foster, M., & Samman, S. (2012). Zinc and Regulation of Inflammatory Cytokines: Implications for Cardiometabolic Disease. *Nutrients*, 4, 676–694. doi: 10.3390/nu4070676
- [51]. Gagandeep, D. S. J., Shailaza, S., & Rahul, R. (2015). Evaluation of Trace Elements and Glycated Hemoglobin in Type 2 Diabetes Mellitus. *World Journal of Pharmacy and Pharmaceutical Sciences*, 4, 940–947.
- [52]. Gaur, S., et al. (2012). Biological effect of heavy metal in drinking water samples of western Uttar Pradesh region in India. *Journal of Technical Research and Applications*, 2(5), 100–106.
- [53]. Gierach, M., Gierach, J., & Junik, R. (2014). Insulinooporność a choroby tarczycy. *Endokrynologia Polska*, 65, 70–76. doi: 10.5603/EP.2014.0010
- [54]. Gijsbers, L., Ding, E. L., Malik, V. S., De Goede, J., Geleijnse, J. M., & Soedamah-Muthu, S. S. (2016). Consumption of dairy foods and diabetes incidence: A dose-response meta-analysis of observational studies. *The American Journal of Clinical Nutrition*, 103, 1111–1124. <https://doi.org/10.3945/ajcn.115.123216>
- [55]. Glinsmann, W. H., Feldman, F. J., & Mertz, W. (1966). Plasma Chromium after Glucose Administration. *Science*, 152, 1243–1245. <https://doi.org/10.1126/science.152.3726.1243>
- [56]. Hamilton, E. I. (1994). The biochemistry of cobalt. *Science of the Total Environment*, 150(1-3), 7–39. doi: 10.1016/0048-9697(94)90126-0. PMID: 7939612.
- [57]. Hans, C. P., Chaudhary, D. P., & Bansal, D. D. (2002). Magnesium deficiency increases oxidative stress in rats. *Indian Journal of Experimental Biology*, 40, 1275–1279.
- [58]. Hassan, S. A. E. (2016). Serum calcium levels in correlation with glycated hemoglobin in type 2 diabetic Sudanese patients. *Advances in Diabetes and Metabolism*, 4, 59–64.
- [59]. Hata, A., Doi, Y., Ninomiya, T., Mukai, N., Hirakawa, Y., Hata, J., Ozawa, M., Uchida, K., Shirota, T., Kitazono, T., et al. (2013). Magnesium intake decreases Type 2 diabetes risk through the improvement of insulin resistance and inflammation: The Hisayama Study. *Diabetic Medicine*, 30, 1487–1494. doi: 10.1111/dme.12250
- [60]. Henquin, J.-C. (2011). The dual control of insulin secretion by glucose involves triggering and amplifying pathways in β -cells. *Diabetes Research and Clinical Practice*, 93, S27–S31. [https://doi.org/10.1016/S0168-8227\(11\)70010-9](https://doi.org/10.1016/S0168-8227(11)70010-9)
- [61]. Huth, C., Beuerle, S., Zierer, A., Heier, M., Herder, C., Kaiser, T., Koenig, W., Kronenberg, F., Oexle, K., Rathmann, W., et al. (2015). Biomarkers of iron metabolism are independently associated with impaired glucose metabolism and type 2 diabetes: The KORA F4 study. *European Journal of Endocrinology*, 173, 643–653. doi: 10.1530/EJE-15-0631
- [62]. Hwang, D. Y., Seo, S., Kim, Y., Kim, C., Shim, S., Jee, S., ... & Lee, S. (2007). Selenium acts as an insulin-like molecule for the down-regulation of diabetic symptoms via endoplasmic reticulum stress and insulin signaling proteins in diabetes-induced non-obese diabetic mice. *Journal of Biosciences*, 32(4), 723–735. doi: 10.1007/s12038-007-0072-6
- [63]. IOM. (2001). Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc. Institute of Medicine (US) Panel on Micronutrients. National Academies Press, Washington DC.
- [64]. IPCS. (1998). Copper. Environmental Health Criteria 200. International Programme on Chemical Safety. World Health Organization, Geneva.
- [65]. Jansen, J., Karges, W., & Rink, L. (2009). Zinc and diabetes—Clinical links and molecular mechanisms. *Journal of Nutritional Biochemistry*, 20, 399–417. doi: 10.1016/j.jnutbio.2009.01.009

- [66]. Jiang, R., Manson, J. E., Meigs, J. B., Ma, J., Rifai, N., & Hu, F. B. (2004). Body Iron Stores in Relation to Risk of Type 2 Diabetes in Apparently Healthy Women. *JAMA*, 291, 711–717. doi: 10.1001/jama.291.6.711
- [67]. Kanchana, N., & Saikumar, P. (2014). Serum calcium levels in type 2 diabetes mellitus. *IOSR Journal of Dental and Medical Sciences*, 13, 1–3. <https://doi.org/10.9790/0853-13820103>
- [68]. Kao, W. H., Folsom, A. R., Nieto, F. J., Mo, J. P., Watson, R. L., & Brancati, F. L. (1999). Serum and dietary magnesium and the risk for type 2 diabetes mellitus: The Atherosclerosis Risk in Communities Study. *Archives of Internal Medicine*, 159, 2151–2159. doi: 10.1001/archinte.159.18.2151
- [69]. Kashiv, Y., Austin, J. R., Lai, B., Rose, V., Vogt, S., & El-Muayed, M. (2016). Imaging trace element distributions in single organelles and subcellular features. *Scientific Reports*, 6, 21437. <https://doi.org/10.1038/srep21437>
- [70]. Kawasaki, N., Matsui, K., Ito, M., Nakamura, T., Yoshimura, T., Ushijima, H., & Maeyama, M. (1985). Effect of calcium supplementation on the vascular sensitivity to angiotensin II in pregnant women. *American Journal of Obstetrics and Gynecology*, 153, 576–582. [https://doi.org/10.1016/0002-9378\(85\)90482-X](https://doi.org/10.1016/0002-9378(85)90482-X)
- [71]. Kazi, T. G., Afridi, H. I., Kazi, N., Jamali, M. K., Arain, M. B., Jalbani, N., & Kandhro, G. A. (2008). Copper, Chromium, Manganese, Iron, Nickel, and Zinc Levels in Biological Samples of Diabetes Mellitus Patients. *Biological Trace Element Research*, 122, 1–18. <https://doi.org/10.1007/s12011-007-8062-y>
- [72]. Khaliq, H., Juming, Z., & Ke-Mei, P. (2018). The physiological role of boron on health. *Biological Trace Element Research*, 186, 31–51. <https://doi.org/10.1007/s12011-018-1284-3>
- [73]. Khan, T. A., Ahmad, M. H. (n.d.). Trace elements in the groundwater and their probable health effects in a Kali River segment, Ganga Basin. *Indian Journal of Environmental Protection*, 42(9), 1094–1100.
- [74]. Kim, M. K., Kim, G., Jang, E. H., Kwon, H.-S., Baek, K. H., Oh, K. W., Lee, J. H., Yoon, K.-H., Lee, W. C., Lee, K. W., et al. (2010). Altered calcium homeostasis is correlated with the presence of metabolic syndrome and diabetes in middle-aged and elderly Korean subjects: The Chungju Metabolic Disease Cohort study (CMC study). *Atherosclerosis*, 212, 674–681. <https://doi.org/10.1016/j.atherosclerosis.2010.07.005>
- [75]. Kloubert, V., & Rink, L. (2015). Zinc as a micronutrient and its preventive role of oxidative damage in cells. *Food & Function*, 6, 3195–3204. doi: 10.1039/C5FO00630A
- [76]. Koekkoek, W. A., & Van Zanten, A. R. (2016). Antioxidant vitamins and trace elements in critical illness. *Nutrition in Clinical Practice*, 31, 457–474. <https://doi.org/10.1177/0884533616653832>
- [77]. Krisai, P., Leib, S., Aeschbacher, S., Kofler, T., Assadian, M., Maseli, A., Todd, J., Estis, J., Risch, M., Risch, L., et al. (2016). Relationships of iron metabolism with insulin resistance and glucose levels in young and healthy adults. *European Journal of Internal Medicine*, 32, 31–37. doi: 10.1016/j.ejim.2016.03.017
- [78]. Kumari, S., Singh, A. K., Verma, A. K., & Yaduvanshi, N. P. (2014). Assessment and spatial distribution of groundwater quality in industrial areas of Ghaziabad, India. *Environmental Monitoring and Assessment*, 186(1), 501–514. doi: 10.1007/s10661-013-3393-y. PMID: 23996647.
- [79]. Lao, T. T., Chan, P. L., & Tam, K. F. (2001). Gestational diabetes mellitus in the last trimester—A feature of maternal iron excess? *Diabetic Medicine: A Journal of the British Diabetic Association*, 18, 218–223. doi: 10.1046/j.1464-5491.2001.00453.x
- [80]. Li, Y. V. (2013). Zinc and insulin in pancreatic beta-cells. *Endocrine*, 45, 178–189. doi: 10.1007/s12020-013-0032-x
- [81]. Liu, M., Jeong, E.-M., Liu, H., Xie, A., So, E. Y., Shi, G., Jeong, G. E., Zhou, A., & Dudley, S. C. (2019). Magnesium supplementation improves diabetic mitochondrial and cardiac diastolic function. *JCI Insight*, 4. doi: 10.1172/jci.insight.123182
- [82]. Lopez-Ridaura, R., Willett, W. C., Rimm, E. B., Liu, S., Stampfer, M. J., Manson, J. E., & Hu, F. B. (2004). Magnesium intake and risk of type 2 diabetes in men and women. *Diabetes Care*, 27, 134–140. doi: 10.2337/diacare.27.1.134
- [83]. Lu, C. W., Chang, H. H., Yang, K. C., Kuo, C. S., Lee, L. T., & Huang, K. C. (2016). High serum selenium levels are associated with increased risk for diabetes mellitus independent of central obesity and insulin resistance. *BMJ Open Diabetes Research and Care*, 4. doi: 10.1136/bmjdr-2016-000253
- [84]. Ly, L. D., Xu, S., Choi, S.-K., Ha, C.-M., Thoudam, T., Cha, S.-K., Wiederkehr, A., Wollheim, C. B., Lee, I.-K., & Park, K.-S. (2017). Oxidative stress and calcium dysregulation by palmitate in type 2 diabetes. *Experimental and Molecular Medicine*, 49, e291. <https://doi.org/10.1038/emm.2016.157>
- [85]. Maher, M., & Ahmed, S. R. H. (2002). A Study of Serum Magnesium, Zinc, Copper and Glycohemoglobin In Children With Type 1

- Diabetes Mellitus. *Alexandria Journal of Pediatrics*, 16, 285–289.
- [86]. Manal Kamal, M. S., Naglaa, K., & Khadega, A. (2009). Evaluation of trace elements and Malondialdehyde levels in type II diabetes mellitus. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, 3, 214–218. doi: 10.1016/j.dsx.2009.07.007
- [87]. Markou, K., Georgopoulos, N., Kyriazopoulou, V., & Vagenakis, A. (2001). Iodine-Induced Hypothyroidism. *Thyroid*, 11(5), 501–510. doi: 10.1089/105072501300176462
- [88]. McCarty, M. F. (1980). The therapeutic potential of Glucose Tolerance Factor. *Medical Hypotheses*, 6, 1177–1189. [https://doi.org/10.1016/0306-9877\(80\)90140-1](https://doi.org/10.1016/0306-9877(80)90140-1)
- [89]. Meenakshi, P. U. G., & Nayyar, S. B. (2013). Comparative Study of Serum Zinc, Magnesium, and Copper Levels among Patients of Type 2 Diabetes Mellitus with and without Microangiopathic Complications. *Innovative Journal of Medical and Health Science*, 3, 274–278.
- [90]. Mertz, W. (1993). Chromium in Human Nutrition: A Review. *The Journal of Nutrition*, 123, 626–633. <https://doi.org/10.1093/jn/123.4.626>
- [91]. Mertz, W., & Schwarz, K. (1955). Impaired intravenous glucose tolerance as an early sign of dietary necrotic liver degeneration. *Archives of Biochemistry and Biophysics*, 58, 504–506. [https://doi.org/10.1016/0003-9861\(55\)90151-X](https://doi.org/10.1016/0003-9861(55)90151-X)
- [92]. Michalek, A. M., Mahoney, M. C., & Calebaugh, D. (2000). Hypothyroidism and diabetes mellitus in an American Indian population. *The Journal of Family Practice*, 49, 638.
- [93]. Nderstigt, C., Corssmit, E. P., De Koning, E. J. P., & Dekkers, O. M. (2016). Incidence and prevalence of thyroid dysfunction in type 1 diabetes. *Journal of Diabetes and its Complications*, 30, 420–425. doi: 10.1016/j.jdiacomp.2015.12.027
- [94]. Nordberg, M., & Nordberg, G. F. (2016). Trace element research-historical and future aspects. *Journal of Trace Elements in Medicine and Biology*, 38, 46–52. <https://doi.org/10.1016/j.jtemb.2016.04.006>
- [95]. Offenbacher, E. G., Rinko, C. J., & Pi-Sunyer, F. X. (1985). The effects of inorganic chromium and brewer's yeast on glucose tolerance, plasma lipids, and plasma chromium in elderly subjects. *The American Journal of Clinical Nutrition*, 42, 454–461. <https://doi.org/10.1093/ajcn/42.3.454>
- [96]. Ozcan, L., & Tabas, I. (2016). Calcium signaling and ER stress in insulin resistance and atherosclerosis. *Journal of Internal Medicine*, 280, 457–464. <https://doi.org/10.1111/joim.12562>
- [97]. Paolisso, G., & Ravussin, E. (1995). Intracellular magnesium and insulin resistance: Results in Pima Indians and Caucasians. *The Journal of Clinical Endocrinology & Metabolism*, 80, 1382–1385. doi: 10.1210/jcem.80.4.7714114
- [98]. Park, K., Rimm, E. B., Siscovick, D. S., Spiegelman, N., Manson, J. E., Morris, J. S., ... & Mozaffarian, D. (2012). Toenail Selenium and Incidence of Type 2 Diabetes in U.S. Men and Women. *Diabetes Care*, 35, 1544–1551. doi: 10.2337/dc11-2136
- [99]. Peacock, J. M., Folsom, A. R., Arnett, D. K., Eckfeldt, J. H., & Szklo, M. (1999). Relationship of serum and dietary magnesium to incident hypertension: The Atherosclerosis Risk in Communities (ARIC) Study. *Annals of Epidemiology*, 9, 159–165. doi: 10.1016/S1047-2797(98)00040-4
- [100]. Pham, P.-C. T., Pham, S. V., & Miller, J. M. (2007). Hypomagnesemia in Patients with Type 2 Diabetes. *Clinical Journal of the American Society of Nephrology*, 2, 366–373. doi: 10.2215/CJN.02960906
- [101]. Pittas, A. G., Lau, J., Hu, F. B., & Dawson-Hughes, B. (2007). The role of vitamin D and calcium in type 2 diabetes: A systematic review and meta-analysis. *Journal of Clinical Endocrinology and Metabolism*, 92, 2017–2029. <https://doi.org/10.1210/jc.2007-0298>
- [102]. Potter, J. F., Levin, P., Anderson, R. A., Freiberg, J., Andres, R., & Elahi, D. (1985). Glucose metabolism in glucose-intolerant older people during chromium supplementation. *Metabolism*, 34, 199–204. [https://doi.org/10.1016/0026-0495\(85\)90001-0](https://doi.org/10.1016/0026-0495(85)90001-0)
- [103]. Preuss, H. G., & Anderson, R. A. (1998). Chromium update: Examining recent literature 1997–1998. *Current Opinion in Clinical Nutrition and Metabolic Care*, 1, 509–512. <https://doi.org/10.1097/00075197-199811000-00005>
- [104]. Priya, K., Dhas, T. K. M., Sylvia, J., & Rita, M. A. (2015). Selenium and glutathione peroxidase in diabetes mellitus. *International Journal of Pharma Bioscience*, 6, 496–501.
- [105]. Rabinowitz, M. B., Gonick, H. C., Levin, S. R., & Davidson, M. B. (1983). A clinical trial of chromium and yeast supplements on carbohydrate and lipid metabolism in diabetic men. *Biological Trace Element Research*, 5, 449–466. <https://doi.org/10.1007/BF02988938>
- [106]. Rajendran, K., Manikandan, S., Nair, L., Karuthodiyil, R., Vijayarajan, N., Gnanasekar, R., Kapil, V. V., & Mohamed, A. S. (2015). Serum Chromium Levels in Type 2 Diabetic Patients and Its Association with Glycaemic Control. *Journal of Clinical and Diagnostic Research*, 9, OC05–OC08.

- <https://doi.org/10.7860/JCDR/2015/16062.6753>
- [107]. Rajpathak, S. N., Crandall, J. P., Wylie-Rosett, J., Kabat, G. C., Rohan, T. E., & Hu, F. B. (2009). The role of iron in type 2 diabetes in humans. *Biochimica et Biophysica Acta (BBA) - General Subjects*, 1790, 671–681. doi: 10.1016/j.bbagen.2008.04.005
- [108]. Rogowicz-Frontczak, A., Pilacinski, S., Chwiałkowska, A. T., Naskręt, D., & Zozulińska-Ziółkiewicz, R. (2018). Insulin resistance is associated with larger thyroid volume in adults with type 1 diabetes independently from the presence of thyroid autoimmunity. *Scandinavian Journal of Clinical & Laboratory Investigation*, 78, 287–292. doi: 10.1080/00365513.2018.1455221
- [109]. Rosique-Esteban, N., Guasch-Ferré, M., Hernández-Alonso, P., & Salas-Salvadó, J. (2018). Dietary Magnesium and Cardiovascular Disease: A Review with Emphasis in Epidemiological Studies. *Nutrients*, 10, 168. doi: 10.3390/nu10020168
- [110]. Saker, F., Ybarra, J., Leahy, P., Hanson, R. W., Kalhan, S. C., & Ismail-Beigi, F. (1998). Glycemia-lowering effect of cobalt chloride in the diabetic rat: Role of decreased gluconeogenesis. *American Journal of Physiology - Endocrinology and Metabolism*, 274, E984–E991. <https://doi.org/10.1152/ajpendo.1998.274.6.E984>
- [111]. Sales, C. H., Pedrosa, L. F. C., Lima, J., & Lemos, T. (2011). Influence of magnesium status and magnesium intake on blood glucose control in patients with type 2 diabetes. *Clinical Nutrition*, 30, 359–364. doi: 10.1016/j.clnu.2010.12.011
- [112]. Saner, G., Yüksel, T., & Gurson, C. T. (1980). Effect of chromium on insulin secretion and glucose removal rate in the newborn. *The American Journal of Clinical Nutrition*, 33, 232–235. <https://doi.org/10.1093/ajcn/33.2.232>
- [113]. Saris, N. E., Mervaala, E., Karppanen, H., & Lewenstam, A. (2000). Magnesium. An update on physiological, clinical, and analytical aspects. *Clinica Chimica Acta*, 294, 1–26. doi: 10.1016/S0009-8981(99)00258-2
- [114]. Shah, G., Pinna, J. L., Lung, C. C., Mahmoud, S., & Mooradian, A. D. (1994). Tissue-specific distribution of malondialdehyde-modified proteins in diabetes mellitus. *Life Sciences*, 55, 1343–1349. doi: 10.1016/0024-3205(94)00767-5
- [115]. Sharif, A., Younus, S., Baig, K., & Ali, N. H. (2014). Prevalence and Risk of Anemia in Type-2 Diabetic Patients. *Health*, 6, 1415–1419. doi: 10.4236/health.2014.612173
- [116]. Sherman, L., Glennon, J., Brech, W., Klomberg, G., & Gordon, E. (1968). Failure of trivalent chromium to improve hyperglycemia in diabetes mellitus. *Metabolism*, 17, 439–442. [https://doi.org/10.1016/0026-0495\(68\)90066-8](https://doi.org/10.1016/0026-0495(68)90066-8)
- [117]. Siddiqui, K., Bawazeer, N., & Joy, S. S. (2014). Variation in macro and trace elements in the progression of type 2 diabetes. *The Scientific World Journal*, 2014, 461591. <https://doi.org/10.1155/2014/461591>
- [118]. Smith, I. C., & Carson, B. L. (1979). *Trace Metals in the Environment. Volume 1: Thallium*. Ann Arbor Science Publishers Inc., Ann Arbor.
- [119]. Stranges, S., Marshall, J. R., Natarajan, R., Donahue, R. P., Trevisan, M., Combs, G. F., ... & Reid, E. M. (2007). Effects of long-term selenium supplementation on the incidence of type 2 diabetes: A randomized trial. *Annals of Internal Medicine*, 147(4), 217–223. doi: 10.7326/0003-4819-147-4-200708210-00175
- [120]. Stranges, S., Sieri, S., Vinceti, M., Grioni, S., Guallar, E., Laclaustra, M., ... & Krogh, V. (2010). A prospective study of dietary selenium intake and risk of type 2 diabetes. *BMC Public Health*, 10, 564. doi: 10.1186/1471-2458-10-564
- [121]. Subekti, I., Pramono, L. A., Dewiasty, E., & Harbuwono, D. S. (2017). Thyroid Dysfunction in Type 2 Diabetes Mellitus Patients. *Acta Medica Indonesiana*, 49, 314–323.
- [122]. Sujatha P. Trace Elements in Diabetes Mellitus. *J. Clin. Diagn. Res.* 2013;7:1863–1865. doi: 10.7860/JCDR/2013/5464.3335. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
- [123]. Sujatha, P. (2013). Trace elements in diabetes mellitus. *Journal of Clinical and Diagnostic Research*, 7, 1863–1865. <https://doi.org/10.7860/JCDR/2013/5464.3335>
- [124]. Sun, G., Vasdev, S., Martin, G., Gadag, V., & Zhang, H. (2005). Altered calcium homeostasis is correlated with abnormalities of fasting serum glucose, insulin resistance, and β -cell function in the Newfoundland population. *Diabetes*, 54, 3336–3339. <https://doi.org/10.2337/diabetes.54.11.3336>
- [125]. Sun, W., Yang, J., Wang, W., Hou, J., Cheng, Y., Fu, Y., Xu, Z., & Cai, L. (2018). The beneficial effects of Zn on Akt-mediated insulin and cell survival signaling pathways in diabetes. *Journal of Trace Elements in Medicine and Biology*, 46, 117–127. <https://doi.org/10.1016/j.jtemb.2017.12.005>
- [126]. Sun, Z., Wang, X., Chen, J., Duan, P., Wang, J., Liu, Y., & Guo, H. (2017). Effects of iodine excess on islet beta cells (beta-TC-6) function

- and the mechanism. *Journal of Hygiene Research*, 46, 610–614.
- [127]. Sundaram, B., Aggarwal, A., & Sandhir, R. (2013). Chromium picolinate attenuates hyperglycemia-induced oxidative stress in streptozotocin-induced diabetic rats. *Journal of Trace Elements in Medicine and Biology*, 27, 117–121. doi: 10.1016/j.jtemb.2012.09.002
- [128]. Thomas, M., MacIsaac, R. J., Tsalamandris, C., & Jerums, G. (2004). Elevated iron indices in patients with diabetes. *Diabetic Medicine: A Journal of the British Diabetic Association*, 21, 798–802. doi: 10.1111/j.1464-5491.2004.01196.x
- [129]. Thomas, M., MacIsaac, R. J., Tsalamandris, C., Power, D., & Jerums, G. (2003). Unrecognized anemia in patients with diabetes: A cross-sectional survey. *Diabetes Care*, 26, 1164–1169. doi: 10.2337/diacare.26.4.1164
- [130]. Tinkov, A. A., Sinitskii, A., Popova, E., Nemereshina, O., Gatiatulina, E., Skalnaya, M. G., Skalny, A. V., & Nikonorov, A. (2015). Alteration of local adipose tissue trace element homeostasis as a possible mechanism of obesity-related insulin resistance. *Medical Hypotheses*, 85, 343–347. <https://doi.org/10.1016/j.mehy.2015.06.005>
- [131]. Tsubamoto, Y., Eto, K., Noda, M., Daniel, S., Suga, S., Yamashita, S., Kasai, H., Wakui, M., Sharp, G. W. G., Kimura, S., et al. (2000). Hexamminecobalt(III) chloride inhibits glucose-induced insulin secretion at the exocytotic process. *The Journal of Biological Chemistry*, 276, 2979–2985. <https://doi.org/10.1074/jbc.M005816200>
- [132]. Uğurlu, V., Binay, C., Şimşek, E., & Bal, C. (2016). Cellular trace element changes in type 1 diabetes patients. *Journal of Clinical Research in Pediatric Endocrinology*, 8, 180–186. <https://doi.org/10.4274/jcrpe.2449>
- [133]. Uluisik, I., Karakaya, H. Ç., & Koc, A. (2018). The importance of boron in biological systems. *Journal of Trace Elements in Medicine and Biology*, 45, 156–162. <https://doi.org/10.1016/j.jtemb.2017.10.008>
- [134]. Viktorinova, A., Tošerová, E., Križko, M., & Ďuračková, Z. (2009). The altered metabolism of copper, zinc, and magnesium is associated with increased levels of glycated hemoglobin in patients with diabetes mellitus. *Metabolism*, 58, 1477–1482. doi: 10.1016/j.metabol.2009.04.035
- [135]. Vincent, J. B. (2000). Elucidating a biological role for chromium at a molecular level. *Accounts of Chemical Research*, 33, 503–510. <https://doi.org/10.1021/ar990073r>
- [136]. Vrtovec, M., Vrtovec, B., Briski, A., Kocijančič, A., Anderson, R. A., & Radovancevic, B. (2005). Chromium supplementation shortens QTc interval duration in patients with type 2 diabetes mellitus. *American Heart Journal*, 149, 632–636. <https://doi.org/10.1016/j.ahj.2004.07.021>
- [137]. Wang, Z. Q., Qin, J., Martin, J., Zhang, X. H., Sereda, O., Anderson, R. A., Pinsonat, P., & Cefalu, W. T. (2007). The phenotype of subjects with type 2 diabetes mellitus may determine clinical response to chromium supplementation. *Metabolism*, 56, 1652–1655. <https://doi.org/10.1016/j.metabol.2007.07.007>
- [138]. Wei, J., Zeng, C., Gong, Q.-Y., Yang, H.-B., Li, X.-X., Lei, G.-H., & Yang, T.-B. (2015). The association between dietary selenium intake and diabetes: A cross-sectional study among middle-aged and older adults. *Nutrition Journal*, 14, 18. doi: 10.1186/s12937-015-0007-2
- [139]. Wells, I. C., Claassen, J. P., & Anderson, R. J. (2003). A test for adequacy of chromium nutrition in humans—Relation to Type 2 diabetes mellitus. *Biochemical and Biophysical Research Communications*, 303, 825–827. [https://doi.org/10.1016/S0006-291X\(03\)00419-4](https://doi.org/10.1016/S0006-291X(03)00419-4)
- [140]. Wolide, A. D., Zawdie, B., Alemayehu, T., & Tadesse, S. (2017). Association of trace metal elements with lipid profiles in type 2 diabetes mellitus patients: A cross-sectional study. *BMC Endocrine Disorders*, 17, 64. <https://doi.org/10.1186/s12902-017-0217-z>
- [141]. World Health Organization. (2005). *World Health Organization*, Geneva.
- [142]. Xu, J., Zhou, Q., Liu, G., Tan, Y., & Cai, L. (2013). Analysis of Serum and Urinal Copper and Zinc in Chinese Northeast Population with the Prediabetes or Diabetes with and without Complications. *Oxidative Medicine and Cellular Longevity*, 2013, 1–11. doi: 10.1155/2013/635214. [PMC free article]
- [143]. Yildirim, Ö., & Buyukbingol, Z. (2002). Effect of cobalt on the oxidative status in heart and aorta of streptozotocin-induced diabetic rats. *Cell Biochemistry and Function*, 21, 27–33. <https://doi.org/10.1002/cbf.995>
- [144]. Young, V. R. (2003). Trace element biology: The knowledge base and its application for the nutrition of individuals and populations. *The Journal of Nutrition*, 133(Suppl. 1), 1581S–1587S. <https://doi.org/10.1093/jn/133.5.1581S>
- [145]. Zhang, H., Yan, C., Yang, Z., Zhang, W., Niu, Y., Li, X., Qin, L., & Su, Q. (2017). Alterations of serum trace elements in patients with type 2 diabetes. *Journal of Trace Elements in Medicine and Biology*, 40, 91–96. <https://doi.org/10.1016/j.jtemb.2016.12.017>
- [146]. Zhang, Q., Sun, X., Xiao, X., Zheng, J., Li, M., Yu, M., Ping, F., Wang, Z., Qi, C., Wang, T., et al. (2017). Dietary chromium restriction in

pregnant mice changes the methylation status of hepatic genes involved with insulin signaling in adult male offspring. PLoS ONE, 12, e0169889. <https://doi.org/10.1371/journal.pone.0169889>

- [147]. Zofkova, I., Nemcikova, P., & Matucha, P. (2013). Trace elements and bone health. *Clinical Chemistry and Laboratory Medicine*, 51, 1-7. <https://doi.org/10.1515/cclm-2012-0868>