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RISKS RELATED TO THE USE OF DIETARY SUPPLEMENTS IN THE LIGHT OF INSUFFICIENT LEGAL REGULATIONS AND LOW PUBLIC AWARENESS

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Abstract. In recent years, we have observed a dynamic development of the dietary supplements (SD) market in Poland has undergone a period of significant expansion and evolution. This is facilitated by the form of the products, the declared properties and the method of presentation, which includes advertising in mass media such as radio, television, press and the Internet. SDs contain mainly vitamins and minerals, as well as amino acids, fatty acids, fibre and other plant products. Their popularity and widespread use may raise a number of doubts. In Polish and European legislation, dietary supplements are classified as foodstuffs. Consequently, they are not subjected to the same rigorous testing procedures as medical products, which include assessments of potential interactions, side effects and durability. A substantial body of evidence attests to the fact that dietary supplements may contain undeclared substances or substances in doses that differ from those indicated by the manufacturer. It is therefore imperative to implement suitable quality standards and to highlight the issues pertaining to the regulatory framework governing dietary supplements.

Keywords: dietary supplements; public awareness; illegal sources; Poland.

INTRODUCTION

Dietary supplements (SDs) are a broad category of products containing "dietary ingredients" such as vitamins, minerals, herbs, botanicals, amino

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acids, fatty acids, and others, which may be used individually or in combination. They are intended to be consumed to supplement the diet and meet basic nutritional needs and are categorized according to their function or type. Consumers are offered a large number of products, brands and preparations, distributed through many different marketing channels [Djaoudene, Romano, Bradai, et al. 2023, 3320]. Growing consumer awareness regarding nutrition, health and well-being is driving the growth of the dietary supplements (SD) market globally. The global SD market size was estimated at 164.0 billion USD in 2022 and is expected to grow at a compound annual growth rate (CAGR) of 9.0% from 2023 to 2030. Consuming products with a high nutritional content is considered in many countries as a symbol of high social status.[1] Additionally, sales of dietary supplements increased dynamically during the COVID-19 pandemic in most countries, including Poland. Approximately 50-75% of the population take them routinely, and almost half of them regularly [Hamulka, Jeruszka-Bielak, Górnicka, et al. 2021, 54]. Concerns about dietary supplements are that there is insufficient data to support their widespread use. Numerous scientific studies have demonstrated their beneficial properties, as well as some adverse and even toxic effects. Therefore, it is necessary to introduce global quality standards and pay more attention to the regulatory challenges related to SD [Djaoudene, Romano, Bradai, et al. 2023, 3320].

1. DIETARY SUPPLEMENTS IN POLAND

Article 3(3)(39) of the Act of 25 August 2006 on food and nutrition safety[2] defines the concept of dietary supplement in the Polish law. According to the Act, a dietary supplement is a food product intended to supplement a normal diet, being a concentrated source of vitamins or minerals or other substances having a nutritional or other physiological effect, single or complex, placed on the market in a form enabling dosing, in the form of: capsules, tablets, dragees and other similar forms, sachets of powder, ampoules of liquid, dropper bottles and other similar forms of liquids and powders intended for consumption in small, measured unit quantities, excluding products having the properties of a medicinal product within the meaning of pharmaceutical law. In Polish and European Union legislation, dietary supplements are classified as food/foodstuffs. However, it should be noted that due to their purpose and form, these are not products commonly

[1] Dietary Supplements Market Size, Share & Trends Analysis Report By Ingredient (Vitamins, Botanicals), By Form (Tablets, Soft gels), By End – user, By Application, By Type, By Distribution Channel, By Region, And Segment Forecasts, 2023-2030, https://www.grandviewresearch.com/industry-analysis/dietary-supplements-market [accessed: 29.09.2024].

[2] Journal of Laws of 2023, item 448.

used to nourish the human body, which are usually derived from agricultural products. They can only supplement the normal human diet, not replace it. At the same time, the concept of a "normal diet" has not been defined in any way. The literature indicates that the standard of a "normal diet" is a derivative of nutritional standards, i.e. standards developed in medical sciences defining demand and its variables [Łata 2022, 119-135]. The condition for introducing SD on the market is the notification to the Chief Sanitary Inspector by the manufacturer and the presentation of the product label design [Starek, Gumułka, and Dąbrowska 2023, 1650]. In 2007, the first product in the "dietary supplement" category was registered in the territory of the Republic of Poland. Since then, the number of dietary supplements introduced to the market has been systematically increasing. In the years 2017-2020, the Chief Sanitary Inspector received 62,808 notifications, while in 2021 there were 21,993. According to the report of the Polish Economic Institute, published in 2019, as many as 72% of Poles declared taking dietary supplements. Almost half of the respondents confirmed the regular use of this type of products. It is worth noticing that SDs are consumed by people without any clinical signs or symptoms of nutrient deficiency, and their effectiveness in such conditions is questioned. Nearly 40% of the respondents were convinced that the effectiveness of SDs is being tested and assessed. Half of the respondents believed that dietary supplements are subject to a similar control regime as medicines. Moreover, consumers did not distinguish between dietary supplements and over-the-counter (OTC) drugs or even prescription drugs [Kowalska-Olczyk 2023, 169-78]. The SD form (e.g. capsules, tablets) and the fact that their main place of sale is a pharmacy make consumers attribute medical properties to them. In fact, the requirements and marketing authorization procedures for medicinal products and SDs differ significantly. SDs are classified as foodstuffs and should not be used as a substitute for medicines [Starek, Gumułka, and Dąbrowska 2023, 1650]. Dietary supplements are eagerly used by people not only because of their easy availability, but also because of the circulating "medical myths" about the possibility of replacing drugs in some diseases. Potential consumers purchasing various vitamin preparations are often unaware of their composition or content of active substances. The diversity of preparations available on the market results from the fact that legal requirements for dietary supplements are less stringent than for drugs. The above facts prove the low awareness of Polish society regarding SDs. Attention is also drawn to the low safety of dietary supplements, resulting from insufficient supervision of these products, lack of restrictive controls before new dietary supplements enter the market and insufficient legal protection of consumers [Kowalska-Olczyk 2023, 169-78]. The imprecise definition of a dietary supplement results in frequent attempts to change the status of some medical products to dietary supplements, dictated by the desire to exempt them

from the Pharmaceutical Law[3] which introduces significant restrictions on the functioning of pharmaceuticals on the market [Olszewski 2010].

2. SELECTED MINERALS IN DIETARY SUPPLEMENTS – ROLE IN THE HUMAN BODY AND THE EFFECTS OF DEFICIENCY AND EXCESS

Minerals, next to vitamins, are among the most popular ingredients of dietary supplements. Mineral ingredients and their chemical forms that may be used for SDs are determined by legal regulations. Minerals that may be present in dietary supplements include: calcium, magnesium, iron, copper, iodine, zinc, manganese, sodium, potassium, selenium, chromium, molybdenum, fluorine, chlorine, phosphorus, boron and silicon [Jarosz, Rychlik , Stoś, et al. 2020]. SDs play an important role in preventing nutrient deficiencies in the human body, reducing the risk of developing some chronic diseases. Deficiency of macro- and microelements may lead to morphological or physiological changes that cause deterioration of the body's ability to function, reduced resistance to stress, increased sensitivity to the harmful effects of other environmental factors, disturbances in growth, development or life expectancy [Bojarowicz and Dźwigulska 2012a, 433-41]. However, it should be remembered that incorrect and unjustified intake of SDs may cause serious health disorders. The most important way to maintain health and reduce the risk of diseases (malignant tumors, cardiovascular diseases, obesity, diabetes and others) is a balanced diet containing all the necessary nutrients in appropriate proportions. The decision to take SDs to support pharmacotherapy or prevent lifestyle diseases should be consulted with a doctor or dietitian [Jarosz, Rychlik, Stoś, et al. 2020].

The effects of deficiency, but also excess of selected minerals in the human body are summarized below.

2.1. Iron

Iron (Fe) is intimately involved in a number of biological processes in the human body, including oxygen transport by hemoglobin in red blood cells, DNA synthesis, cellular respiration and electron transfer, as well as general metabolism [Ravingerová, Kindernay, Barteková, et al. 2020, 7889]. Iron deficiency remains one of the major nutritional disorders worldwide, and low iron intake and/or bioavailability are now the leading causes of anemia [Liberal, Pinela, Vívar-Quintana, et al. 2020, 1871]. The most characteristic symptoms of anemia are: pale mucous membranes and conjunctiva,

[3] Act of 6 September 2001, the Pharmaceutical Law, Journal of Laws of 2024, item 686.

black spots in the corners of the mouth, rough skin, brittle hair and nails, decreased physical fitness and ability to concentrate, and immune deficits. Anemia in the first and second trimester of pregnancy increases the risk of premature delivery and the birth of a child with low birth weight [Wojtasik, Jarosz, and Stoś 2017, 203-28]. The unique characteristics that make iron valuable for standard cellular functions also make it able to catalyze reactions that lead to the formation of reactive oxygen species (ROS), which occur when iron levels are very high. Therefore, although iron is an essential trace element in the human body, it can also be toxic when present in excessive concentrations [Liberal, Pinela, Vívar-Quintana, et al. 2020, 1871]. The increase in free radical production, caused by Fe excess increases the of risk cancer and coronary heart disease. There are no cases of iron toxicity observed in food. Acute poisoning has been observed in children due to an overdose of iron from pharmaceutical preparations. The first symptoms of iron poisoning are nausea, diarrhea and vomiting. Then, disorders of the cardiovascular system, central nervous system, kidneys, liver and circulatory system appear [Wojtasik, Jarosz, and Stoś 2017, 203-28].

2.2. Calcium

Calcium (Ca) is a bioelement necessary for the proper functioning of the human body. It influences many intracellular and extracellular processes and is necessary for the development, growth and maintenance of bones and the stability of the cellular cytoskeleton [Ciosek, Kot, Kosik-Bogacka, et al. 2021, 506]. Correct calcium levels bring many health benefits, such as lowering blood pressure, reducing hypertensive disorders during pregnancy, preventing osteoporosis and colon adenomas, and lowering cholesterol levels [Cormick and Belizán 2019, 1606]. The consequence of chronic calcium deficiency in adults is osteomalacia and an increased risk of osteoporosis, and in children – rickets. Ca deficiencies also cause increased body excitability, neurological disorders, tetany, and increased blood pressure. Excessive calcium intake may cause kidney diseases (failure, urolithiasis, milk-alkaline syndrome), vascular calcification, damage to the structure of organs or disturbances in the functioning of various systems in the body, as well as an increased risk of cardiovascular diseases and prostate cancer, or disturbances in the absorption of other minerals, e.g. iron, magnesium and zinc [Wojtasik, Jarosz, and Stoś 2017, 203-28].

2.3. Magnesium

Magnesium (Mg) is a nutrient essential for maintaining important physiological functions. This ion plays a key role in cellular homeostasis and organ functioning. Mg is a cofactor in over 600 enzymatic reactions and is necessary for the activity of protein kinases, glycolytic enzymes,

phosphorylation processes and ATP-related reactions [Barbagallo, Veronese, and Dominguez 2021, 463]. It takes part in the synthesis of RNA and DNA, the metabolism of proteins, carbohydrates and lipids. It plays an important role in the stability of cell membranes, bone and calcium metabolism, and the functioning of the nervous and immune systems. Symptoms of Mg deficiency are common non-specific. Additionally, the clinical diagnosis of Mg deficiency is problematic because its concentration in serum does not reflect the total content in the body. Mg deficiency is associated with a number of diseases, such as neurological diseases (headaches, convulsions, stroke), circulatory system diseases (arrhythmia, preeclampsia, heart failure), respiratory diseases (bronchial asthma, chronic obstructive pulmonary disease) and depression. Recent research suggests that chronic Mg deficiency may be responsible for an increased risk of overweight and obesity, insulin resistance and type 2 diabetes, hypertension, lipid metabolism disorders and atherosclerosis [Pelczyńska, Moszak, and Bogdański 2022, 1714; Alawi, Majoni, and Falhammar 2018, 9041694]. Excessive supply of magnesium may occur when consuming large amounts of products enriched with this ingredient and dietary supplements. Large doses of magnesium salts have laxative properties and their chronic consumption may cause poisoning. Adverse reactions include alkalosis, dehydration, breathing difficulties, and changes in the heart's electrocardiogram, sleep disorders, muscle weakness and disorientation [Jarosz, Rychlik, Stośet al. 2020].

2.4. Zinc

Zinc (Zn) is an essential trace element for human health, known for its role as a regulatory, structural and catalytic component of at least 3,000 proteins, including enzymes and transcription factors. Approximately 10% of the human proteome is associated with Zn ions to regulate gene expression, DNA metabolism, chromatin structure, cell proliferation, maturation, death, immune responses and antioxidant defense [Maret 2013, 82-91]. Efficient homeostatic systems precisely regulate intracellular concentrations of this bioelement. However, disturbed Zn homeostasis is important in the pathogenesis of some chronic diseases, such as cancer, diabetes, depression, Wilson's disease, Alzheimer's disease and other age-related diseases [Costa, Sarmento-Ribeiro, and Gonçalves 2023, 4822]. Recent studies have shown the important role of zinc in the fight against COVID-19. Zinc was found to prevent SARS-CoV-2 from entering cells by downregulating the expression of ACE-2 receptors and inhibiting the SARS-CoV-2 RNA-dependent RNA polymerase. Zinc, thanks to its anti-inflammatory properties, also prevents the cytokine storm that occurs after SARS-CoV-2 enters the cell [Imran, Fatima, Alzahrani, et al. 2022, 1227].

The daily requirement for Zn according to the Institute of Nutrition and Food is 5 mg for infants up to 1 year of age, 10 mg for children aged 1 to 9, girls and women 10-13 mg, pregnant women 12-16 mg, breastfeeding women 16-21 mg, boys and men 14-16 mg daily. It is supplied to the body mainly through the alimentary route, with food of plant and animal origin, and to a lesser extent through the respiratory system and skin [Gertig and Przysławski 2006; Szcześniak, Grimling, and Meler 2014]. Zinc deficiencies cause skin lesions, problems with proper wound healing, weakened senses of taste and smell, weakened immune system and increased susceptibility to infections. The excess of this microelement is manifested by symptoms such as: abdominal pain, diarrhea, nausea and vomiting, headaches, disturbed copper metabolism in the body, reduced iron absorption, reduced HDL levels in the blood, as well as disturbed functioning of the heart and pancreas [Abendrot, Merks, and Kalinowska 2019, 510-18].

2.5. Chrome

Chromium (Cr) can exist in various oxidation states: Cr(0), Cr(III) and Cr(VI), with Cr(III) and Cr(VI) being relatively stable and largely dominant. While Cr(III) is an essential trace element for human health, found in soil and rocks (easily absorbed by plants), hexavalent chromium is mainly an industrial pollutant. Cr(VI) compounds are widely used as pigments for textile dyes, paints, inks, plastics, corrosion preventives and wood preservatives. Cr(VI) is classified by IARC (International Agency for Research on Cancer) as a human carcinogen (class I) [Genchi, Lauria, Catalano, et al. 2021, 638]. Cr(III) is a trace element that facilitates the metabolism of carbohydrates and lipids. It plays an important role in glucose homeostasis as a critical cofactor for insulin action and as a component of the glucose tolerance factor [Chen, Kan, Ratnasekera, et al. 2022, 2687]. Cr(III) improves the activity of insulin by binding to it and intensifying its action approximately threefold [Genchi, Lauria, Catalano, et al. 2021, 638]. The results of cross-sectional and case-control studies prove that people with diabetes have lower serum chromium levels compared to healthy people. Decreased plasma Cr levels have also been observed in patients with cardiovascular diseases (e.g. coronary heart disease, myocardial infarction). Additionally, plasma chromium levels have been found to be negatively correlated with blood pressure and low-density lipoprotein levels [Chen, Kan, Ratnasekera, et al. 2022, 2687].

Due to the suggested ability of Cr to control carbohydrate-lipid metabolism and to reduce body weight, it is often used as an ingredient of supplements used in the treatment of obesity [Juśkiewicz, Ognik, Fotschki, et al. 2023, 3962]. Trivalent chromium compounds are also popular ingredients of SDs used by diabetics [Staniek, Król, and Wójciak 2020, 3070]. The most popular chromium compounds included in SD include: chromium

picolinate, chromium histidinate, chromium dinococysteinate and chromium bound to niacin. Cr deficiency can cause blood sugar spikes, elevated cholesterol and blood pressure. In addition, it may cause reduced resistance to infections, atherosclerosis, hormonal disorders, nervous system disorders and fatigue. However, a too high level of chromium may lead to pathological conditions. Long-term exposure to Cr(III) may cause skin allergies and cancer. Moreover, the accumulation of dietary supplements based on Cr(III) may cause genotoxic effects [Genchi, Lauria, Catalano, et al. 2021, 638].

3. INTERACTIONS BETWEEN DIETARY SUPPLEMENTS CONTAINING MINERALS AND DRUGS

Medicine packaging contains important information about the product and its potential side effects. However, the packaging of dietary supplements often lacks information about side effects, contraindications to use, as well as interactions that may occur when using a given SD with prescription or over-the-counter drugs [Bojarowicz and Dźwigulska 2012b, 442-47]. Additionally, patients often do not provide information about the SDs they take during consultations with a doctor or pharmacist, which may result in serious health risks [Stępień, Niewiarowski, and Harasimiuk 2019, 51-59]. Drug interactions occur when the pharmacological effects of a given drug are altered by the presence of another drug or xenobiotic, as well as bioactive ingredients in food or beverages, and other chemicals. Clinically significant interactions pose a health risk because they can influence the outcome of treatment and even cause life-threatening side effects of medications. Traditionally, interaction mechanisms are classified as pharmacokinetic or pharmacodynamic, depending on the nature of the interaction [Petric, Žuntar, Putnik, et al. 2021, 33; Thanacoody 2019, 53-65]. Pharmacodynamic interactions occur when two preparations (dietary supplements and/or drugs) are administered simultaneously, with one product influencing the action of the other without changing its concentration in the body. These types of interactions occur less frequently than pharmacokinetic interactions, in which the interaction is caused by a changed concentration of the active substance in the body [Kreft 2015, 127-35]. The bioelements that are most often included in SDs and are the most important from the point of view of drug interactions are iron (Fe), calcium (Ca) and magnesium (Mg) [Abendrot, Merks, and Kalinowska-Lis 2019, 510-18].

3.1. Iron

Drug interactions of iron-containing SDs may occur in many patients and involve a large number of therapies. Iron ions cause a significant reduction in the bioavailability of many drugs, such as: tetracycline, tetracycline

derivatives (doxycycline, methacycline and oxytetracycline), penicillamine, methyldopa, levodopa, carbidopa and ciprofloxacin. The primary mechanism of these drug interactions is the formation of iron-drug complexes (chelation or binding of iron by the drug involved). Also many other important and commonly used drugs, such as thyroxine, captopril and folic acid, form stable complexes with iron [Campbell and Hasinoff 1991, 251-55].

3.2. Calcium

Calcium, like most minerals, may reduce the absorption and effect of most antibiotics, including: tetracyclines and fluoroquinolones used in respiratory and urinary tract infections. The reduction in the concentration of antibiotics in the blood can reach up to 50%, which is associated with the lack of effectiveness of the treatment. Moreover, calcium ions may increase the toxicity of cardiac glycosides (digoxin and methyldigoxin) used in cardiac arrhythmias. When using calcium supplements and calcium channel blockers (e.g. verapamil) to treat hypertension, blood pressure should be monitored regularly. This mineral may reduce the effect of the drug [Bojarowicz and Dźwigulska 2012b, 442-47].

3.3. Magnesium

Magnesium ions contained in SDs may form complex compounds with low solubility (bioavailability), reducing the effect of pharmaceuticals such as: anticoagulant drugs (e.g. ticlopidine), antifungal drugs (ketoconazole), antipsychotic and anxiolytic drugs (chlorpromazine, clonazepam), cardiac glycosides (digoxins), methyldigoxin, antihypertensive drugs (e.g. captopril) and antibacterial drugs (tetracyclines). They may also increase the bioavailability of bronchodilators (theophylline) or drugs used in Parkinson's disease (levodopa), increasing the risk of side effects such as nausea, vomiting, heart disorders, headaches and insomnia [Abendrot, Merks, and Kalinowska-Lis 2019, 510-18].

4. THREATS RESULTING FROM THE LACK OF QUALITY CONTROL OF DIETARY SUPPLEMENTS

Dietary supplements, unlike medical products, are not subject to stringent quality requirements. This means that people using this type of preparations are not sure whether they contain the declared active substance and whether this substance is present in the amount declared by the manufacturer [Stępień, Niewiarowski, and Harasimiuk 2019, 51-59]. Differences can be found both in different products containing a given ingredient and in

different batches of the same supplement from one manufacturer [Starek, Gumułka, and Dąbrowska 2023, 1650]. Additionally, there is a risk of the presence of substances in the preparations that are prohibited for dietary supplements. The pharmaceutical availability of active substances is also undetermined [Stępień, Niewiarowski, and Harasimiuk 2019, 51-59].

In many countries, the illegal production of counterfeit medical products and dietary supplements (including products containing false information about their composition, origin, action and use) is increasing, especially in online offers and in non-pharmacy markets (markets, oriental medicine clinics, gyms). There is also more documented information about hospitalizations and deaths of people who used preparations of unknown origin purchased from illegal sources [Fijałek, Sarna, Błażewicz, et al. 2010, 227-35].

Quality studies of dietary supplements indicate numerous irregularities. The analysis of slimming preparations revealed the presence of sibutramine, monodesmethylsibutramine and didesmethylsibutramine, which are prohibited by Polish law. Preparations for athletes, which, according to the manufacturer's declaration, should contain vitamins and amino acids, contain anabolic steroids and beta-methylphenylethylamine contamination – a substance with an effect similar to amphetamine. In preparations with a declared effect on relieving joint pain and neuralgia, the presence of the corticosteroid dexamethasone and phenylbutazone, classified as non-steroidal anti-inflammatory drugs with a very strong effect, was found [Stępień, Niewiarowski, and Harasimiuk 2019, 51-59].

As a result of microbiological purity tests of dietary supplements conducted at Poznań University of Medical Sciences, it was found that 6.5% of 1,165 tested samples of preparations produced by pharmaceutical plants in Wielkopolska did not meet the applicable requirements. The most common abnormalities concerned the presence of aerobic bacteria and fungi. In several cases, the presence of Escherichia coli bacteria, causing infections of the digestive and urinary systems, was detected [Ratajczak, Kubicka, Kamińska, et al. 2015, 383-87].

CONCLUSION

Dietary supplements are a category of products intended for consumption to supplement the diet as well as to meet basic nutritional needs. In recent years, there has been a trend of increased consumption of dietary supplements, although there is still insufficient data to support their widespread use. Numerous studies indicate both the positive impact of taking dietary supplements, as well as the unfavourable and even toxic effects of taking them. This is mainly related to the lack of strictly defined indications

for taking dietary supplements and, above all, to their classification as foodstuffs, which results in the lack of obligation to test them for interactions, potential side effects and durability. Attention is drawn to the low safety of dietary supplements, resulting from insufficient supervision of these products, lack of strict controls before new dietary supplements enter the market, and insufficient legal protection of consumers. Attention should also be paid to the low public awareness of the effects of taking dietary supplements to the insufficient research on their effectiveness and to the need to take them. Many people still see dietary supplements as substitutes for medicines, even though dietary supplements, unlike medical products, are not subject to strict quality requirements. This means that people using this type of preparations cannot be sure whether they actually contain the declared active substance or whether this substance is present in the amount declared by the manufacturer. Additionally, patients often do not provide information about the dietary supplements they take during consultations with a doctor or pharmacist, which may result in serious health risks, including- among others – the possibility of interactions that may occur when using a given SD with prescription or over-the-counter drugs.

In connection with the above, attention should be paid to the need of introducing appropriate quality standards and to changing legal regulations regarding dietary supplements, so as to increase control over their quality and the effects of taking them. It is also necessary to provide information aimed at increasing public awareness of the properties of dietary supplements, their composition, as well as the content of active substances.

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