

## DIETARY SUPPLEMENTS – SAFELY AND IN MODERATION

Paulina Gorol



Nowadays many people have problems with applying a proper, balanced diet. This results in increased risk of the deficiencies of nutrients which are important for health. Aware of certain insufficiencies in our everyday diet, we try to “take shortcuts” – instead of properly composed meals and rest, we frequently serve dietary supplements to our organism because we believe that they will grant us health, youth, good looks and infinite vital powers. Correcting nutrition through supplementation seems to be very comfortable and not to require special effort. Moreover, the eagerness to use supplements is strengthened by omnipresent advertisements.

### **A Supplement is not a Medication**

In accordance with the definition included in the act of 25 August 2006 on the safety of food and nutrition, dietary supplements are foodstuffs aimed at supplementing a normal diet. They are a concentrated source of vitamins, minerals or other substances which have a nutritional effect (or other physiological effect). Supplements do not have the properties of a medicinal product as defined in the regulations of pharmaceutical law. The aim of a dietary supplement is, as its name indicates, not the treatment or prevention of diseases, but supplementing the missing nutrients in the organism. The products of this kind should, however, not be the main source of vitamins or minerals, because their overuse may lead to unpleasant health consequences. Dietary supplements have the status of foodstuffs and they are subject to regulations defined in the food law provisions for commonly consumed foodstuffs (detailed information is available at the website of the Chief Sanitary Inspectorate – GIS). Medications, in turn, both compounded and over-the-counter ones, are subject to the regulations of very strict pharmaceutical law and to the control of the Office for Registration of Medicinal Products and the Chief Pharmaceutical Inspectorate.

Before any medication is marketed, its efficacy and safety must be proven. Medications are also subject to continuous quality control already after they enter the market. The introduction of a new supplement to the market requires only informing the Chief Sanitary Inspectorate about such an intention. The manufacturer has to provide information referring to e.g. the product marking and its quantitative and qualitative content<sup>5,12</sup>. The documentation confirming the quality and the declared effects of the supplement is not required. Such a situation frequently makes it possible to sell products of low quality. Controlling supplements already present in the market also takes place in a limited scope<sup>2,14</sup>. As a result, besides supplements which are safe and fulfill their task, we can come across products which contain ingredients which are not permitted and harmful for health or preparations, the quantitative or qualitative content of which is different from the one declared on the label<sup>14</sup>. Therefore we should not use supplements coming from unsure sources, especially bought through the Internet and manufactured by companies which are not renown. If we decide to use supplementation, it is best to buy such products in a pharmacy, where we can obtain the advice of a pharmacist. The threats related to supplementation do not refer only to the quality of the preparation itself. For obvious reasons, using supplements as drug substitutes may be dangerous. As has already been mentioned, supplements do not have a therapeutic effect and may be used only as diet supplementation. However, as indicated by a study carried out in 2014, as much as 41% of Poles did not understand the difference between the properties of medications and supplements<sup>15</sup>. Fortunately, in recent years consumer awareness regarding the above mentioned threats has been increasing, for example, thanks to educational initiatives such as the consumer guide which is available at the webpage of the Chief Sanitary Inspectorate. Unfortunately, the threats related to the biochemistry of supplemented substances are still a rarely discussed topic.

## The Role of Vitamins

Vitamins are indispensable for the proper functioning of the organism. However, many people do not realize that the human organism may react in a bad way to their overdose. Supplementation with vitamins A, E and C is very popular. They are frequently promoted as molecules which ensure health and beauty due to their antioxidant properties. Unfortunately, the fact that their excessive intake may be harmful for health, is frequently omitted.

Vitamin A fulfils many important functions in the organism, e.g. it demonstrates antioxidant action, which results from the vitamin's ability to remove free radicals, it participates in the process of seeing because it is an ingredient of the eye retina pigment, and it is also indispensable for the regeneration of skin, healing of wounds and in the maturing and differentiation of the cells of the immune system. The intake of excessive amounts of vitamin A may, however, lead to the supersaturation of the organism, i.e. hypervitaminosis. Retinoids are not excreted in the urine, their high supply may lead to the accumulation in the organism and to the emergence of dangerous symptoms. The symptoms of hypervitaminosis include general weakness, headaches, loss of appetite, cracking of the lips and hair loss, bone pain also appears. Symptoms of acute intoxication may occur as a result of one-time consumption of very high amounts of vitamin A, hundreds times higher than the recommended dose per day. These symptoms include an increase of intracranial pressure, vomiting, nausea and skin lesions<sup>4</sup>. Another consequence of the excessive supply of vitamin A is a disruption of the absorption of  $\beta$ -carotene and mineral salts from food. The negative consequences of vitamin A hypervitaminosis subside after the discontinuation of use or the reduction of the used dose. Few people realize the fact that high doses of this vitamin should be avoided during pregnancy. Retinoids have a teratogenic effect, i.e. they can disturb the development of the fetus. Pregnant women should not take more than 2 mg (6000 IU) of vitamin A daily<sup>7,10</sup>.  $\beta$ -carotene has antioxidant properties, it beneficially influences the eyes and the immune system. The consumption of a very high amount of this compound is not a significant health threat; however, the results of a study conducted on cigarette smokers were surprising. In smokers, the supplementation of about 20 mg of  $\beta$ -carotene per day increased the risk of lung cancer by 18%, and in alcoholics there was an increase of the risk of intracerebral hemorrhages. Similar results were observed in people exposed to the effect of asbestos. The study results lead to the conclusion that cigarette smoke, asbestos and alcohol, i.e. substances that intensify oxidative

stress, contribute to the prooxidative activity of  $\beta$ -carotene, which in turn leads to the damage of the cells of the organism.

Vitamin E, besides vitamins A and C, also protects the organism against oxidative stress and cell damage caused by free radicals. It takes part in maintaining proper permeability of cell membranes and the reduction of platelet aggregation (sticking together), thus preventing blood clots. Additionally, it influences the proper performance of muscles and sperm production in men. It is also needed by pregnant women, because it is co-responsible for maintaining pregnancy and for the proper development of the fetus. Studies show that the simultaneous use of vitamin E and anticoagulants (e.g. warfarin, acenocoumarol) may increase the risk of bleedings by intensifying the anticoagulant effect<sup>5</sup>. Adverse effects were observed at the intake of more than 240-280 mg of vitamin E per day. Symptoms include the digestive tract (i.a. nausea, diarrhea), muscle weakening or skin inflammations. In case of more severe forms, double vision, liver enlargement, sexual dysfunctions, hyperglycemia and hyperlipidemia occur. Symptoms usually subside after the dose is reduced<sup>10</sup>.

Vitamin C is practically non-toxic and a dose which causes acute poisoning has not been established. However, its consumption in high doses (2 g/day and more) may lead to the disorders of the digestive tract (i.a. nausea, diarrhea). In particularly sensitive persons (patients with chronic renal failure), an overdose of vitamin C may cause the crystallization of urates, which favors the formation of kidney stones<sup>6</sup>. Vitamin C hypervitaminosis is associated with the occurrence of skin rashes. Moreover, it can increase the sodium concentration in the blood and reduce the concentration of potassium, which can lead to a shortage of potassium. Besides this, it should not be taken together with vitamin B12, because the latter is then broken down. Taking high doses of vitamin C can lead to the distorting of results of examinations based on redox reactions, such as determining the level of glucose, bilirubin, creatinine or the AspAT liver enzyme<sup>10</sup>. Studies have shown that adverse prooxidative effects may even occur if vitamin C, copper and iron are taken at the same time for a longer period of time. Ascorbic acid causes the reduction of metals with the production of reactive oxygen species, which are very dangerous for cells because they show mutagenic and neurotoxic activity<sup>11</sup>. It is surprising that high doses of vitamin C can lead to addiction! Sudden discontinuation of taking high doses may cause withdrawal symptoms resembling scurvy<sup>10</sup>.

## Minerals

Excessive mineral supplementation may also be associated with the risk of complications. Although calcium is an indispensable macroelement, its high doses can promote atherosclerosis and other problems associated with the circulatory system. Moreover, its excess is often the cause of the formation of kidney stones and of the reduction of the absorption of zinc and iron. High doses of iron, in turn, can lead to memory problems in people with hemochromatosis, which is a genetically determined disorder associated with excessive absorption of iron. Chronic intake of high doses of iron (higher than the recommended daily intake) in genetically predisposed individuals may cause it to accumulate in various internal organs. Other symptoms of poisoning with this element include liver enlargement, skin discoloration, joint diseases and drowsiness<sup>11</sup>. Many studies have shown a close metabolic relationship between zinc and copper. Excessive amounts of copper in the diet cause disturbances in the intracellular balance of zinc. On the other hand, an excessive amount of zinc in the diet can lead to disturbances in copper absorption. Such a dependency may result in the impairment of iron metabolism and heme synthesis, which leads to anemia<sup>3</sup>. Copper is essential for the proper functioning of the enzyme ceruloplasmin, which oxidizes divalent iron to assimilable trivalent iron. Moreover, it facilitates the absorption of this element in the small intestine.

## Medication – Supplement Interactions

A danger resulting from improper use of dietary supplements are also interactions between medications and nutrients; therefore, people with chronic health problems should be particularly careful when using supplements. It turned out that ordinary grapefruit juice, commonly considered healthy, may inhibit the metabolism of many substances, reducing

the effectiveness of medications or exposing the patient to an increased risk of the occurrence of adverse effects. Some vitamins, minerals and plant supplements may have similar effects. By acting on the enzymatic system of the liver they can delay the metabolism of xenobiotics, and thus increase the concentration of the medication in the organism. Such a situation may result in dangerous complications. Another possible interaction is the acceleration of the metabolism of xenobiotics, which weakens their therapeutic effect because they are broken down and eliminated from the organism too quickly.

Many mood-enhancing preparations contain the popular herb – hypericum (*Hyperici herba*). Hyperforin, which is the active substance, interacts with some antipsychotics, antidepressants and hypnotics by stimulating certain liver isoenzymes and the protein involved in the transport of medications (P-glycoproteins). They are substrates for the mentioned enzymes, which may lead to the acceleration of their metabolism and the reduction of their effectiveness<sup>13</sup>. Large intake of folic acid (a vitamin from the B-group) may interfere with the action of anticonvulsant medications, which poses a threat to people with epilepsy<sup>5</sup>. Ginkgo biloba, known mainly for its properties improving memory and concentration, inhibits platelet aggregation, which – in combination with medications with a similar effect (acetylsalicylic acid, warfarin) – causes the occurrence of life-threatening hemorrhages. Moreover, if preparations made of ginkgo biloba are taken simultaneously with medications from the non-steroidal anti-inflammatory medications group, there is an increased risk of gastric mucosa irritation. Due to the possible presence of ginkgotoxins in products made of ginkgo biloba, there is a risk of the occurrence of adverse effects in the form of e.g. seizures<sup>1</sup>. As a result of the antagonistic action on GABA receptors, one can also expect interaction with benzodiazepines, which have a broad spectrum of pharmacological action (they have anti-anxiety, sedative, hypnotic (pro-sleep), anticonvulsant and myorelaxant effects), hence they are quite common in therapy of especially the elderly<sup>13</sup>. The very popular ginseng root is also potentially dangerous when combined with other medications. Like ginkgo biloba, it intensifies the effect of anticoagulants. Moreover, it can lead to a dangerous reduction of the blood sugar level in patients taking anti-diabetes mellitus medications (insulin), intensifying their effect. It also weakens the effect of hypotensive medications (amlodipine, diltiazem), increases the influence of monoamine oxidase inhibitors (used to treat depression) or haloperidol and increases the risk of adverse effects associated with these xenobiotics<sup>5,13</sup>. *Althaea officinalis*, in turn, known for its antitussive effect, as a mucilage raw material, may reduce the absorption of certain medications<sup>5</sup>. The action of the popular dietary fiber is similar – it absorbs nutrients and makes their absorption more difficult<sup>13</sup>. Excessive amounts of dietary fiber can reduce the absorption of fats and thus the absorption of fat-soluble vitamins such as vitamin A, D, E and K<sup>1</sup>.

In accordance with the law, a dietary supplement must be introduced to the market in a form allowing for its dosing. For this reason, it has a form associated mainly with medications – these are usually capsules, tablets, and also bottles with a dropper<sup>12</sup>. The mentioned forms resemble medicinal products, i.e. ones from which we expect a guarantee of the highest microbiological purity or quality of composition. Actually, a simple procedure of introducing to the market, low costs of development research, the possibility of manufacturing not only in pharmaceutical, but also in food and chemical production plants, result in the fact that manufacturers are highly interested in dietary supplements<sup>5</sup>. We observe situations where, next to medicines on the shelf there are products that are not so meticulously controlled and in fact may not meet sufficient quality criteria<sup>8</sup>.

The common use of multivitamin supplements or those containing minerals has not been proven to be significant for disease prevention. We can only talk about particular situations, groups of people, where supplementation is recommended. This refers, for example, to pregnant women, who should take folic acid and iron, and to elderly people, in case of whom we know for sure that they have deficiencies of many components in their diet. In our latitude, vitamin D supplementation<sup>16</sup> is also recommended. On the one hand, dietary supplements are a way to quickly supplement deficiencies in dietary components, but, on the other hand, if used improperly or in excess, they may

expose us to various dangerous complications. The risk of overdose increases in case of people who take particular care of their health and diet, and do not need an additional source of nutrients<sup>2</sup>. It is also worth to be skeptical about marketing messages and not to diagnose your health condition on your own, on the basis of the knowledge gained from advertisements. Taking dietary supplements should be consulted with a physician, pharmacist or nutritionist, and it would be best if it is preceded by appropriate examinations in order to be able to determine whether it is actually advisable to supplement deficiencies.

The author is a graduate of Biotechnology at the Faculty of Biochemistry, Biophysics and Biotechnology of the Jagiellonian University and a graduate of Pharmacy at the Faculty of Pharmacy of the Jagiellonian University Medical College UJ CM.

Review: Professor Iwona Wawer, Medical University of Warsaw, Faculty of Pharmacy, Department of Physical Chemistry (retired).

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