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The impact of food fortification on health and strategies to reduce micronutrient loss

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ABSTRACT

Functional and fortified foods have become increasingly important today due to their effective role in disease prevention and public health promotion. Food fortification is a process in which micronutrients such as vitamins, minerals, essential fatty acids, and bioactive compounds are added to food products to compensate for nutritional deficiencies and meet the physiological needs of the body. This approach is known as one of the most effective strategies for reducing the prevalence of diseases caused by micronutrient deficiencies, including beriberi, pellagra, and rickets. However, the direct addition of these compounds to food faces challenges such as low stability, limited solubility, low bioavailability, and high sensitivity to processing conditions. Encapsulation technology, as a new method, has been able to overcome many of these limitations. Encapsulation increases stability, protects against environmental factors, improves absorption, and allows for controlled release of micronutrients in the digestive tract. Common encapsulation methods include spray drying, freeze drying, emulsion, extrusion, and fluidized bed, each of which has its own advantages and applications. This review article aims to examine the importance of food fortification, the role of micronutrients in health, and the benefits of encapsulation technology. The results indicate that simultaneous use of fortification and encapsulation can be considered as an effective strategy in public health programs, and further research in this area is necessary.

1-Introduction

In recent years, natural bioactive compounds have received widespread attention due to their significant functional effects in the food industry and human health. These compounds, including antioxidants, antimicrobials, phytochemicals, and phenolic compounds, not only play a role in improving the sensory properties and stability of food products, but also have anti-inflammatory, anticancer, antidiabetic, and antimicrobial properties, which are effective in promoting consumer health. However, low stability, poor solubility, limited intestinal permeability, and low bioavailability in free form have posed challenges for the direct use of these compounds; especially since adverse environmental conditions such as heat, light, pH, and pressure can lead to their degradation. In this regard, microencapsulation, as a new and effective technology, is considered a suitable solution to maintain bioactivity and increase the efficiency of bioactive compounds in functional food products by providing structural protection, controlled release, and increased absorption in the gastrointestinal tract [1].

Research has focused on the relationship between health, the importance of a healthy lifestyle, and having a proper diet and regular physical activity. Because nutrient absorption decreases with age and the typical diet of people lacks the recommended amount of nutrients such as omega-3, the role of fortified foods and nutritional supplements in the health of society is becoming more prominent. Also, due to busy work or aging, people spend less time outside the workplace and home, which causes them to be less exposed to sunlight, which reduces the synthesis of vitamin D. Vitamins play an important role in growth, immune function, heart function, muscle function, vision, and blood clotting[2,3]. The 2022 World Health Report found that one in five children under the age of five is born stunted, and about 40% of adults are overweight or obese. Studies have shown that deaths from diet-related diseases have increased by 15% since 2010, accounting for a quarter of all deaths, which is linked to a decline in dietary quality and an increase in the consumption of ultra-processed foods (UPFs)[1][4].

Fortification increases nutrient intake without changing the nutritional behavior of the population and is one of the most cost-effective ways to improve the nutritional quality of foods. This process is carried out by modifying the original recipe and adding nutritional ingredients with the aim of improving the nutritional, sensory and functional properties of the product. According to the definition of the Food and Agriculture Organization of the United Nations (FAO)[2] fortification involves the targeted addition of one or more micronutrients to foods in order to improve nutritional quality [5,6].

Vitamins are organic compounds essential for normal body function, and thirteen vitamins have been identified, which are divided into two groups based on solubility: water-soluble (WSVs)[3] and fat-soluble (FSVs)[4]. Vitamins are classified based on their physicochemical properties, metabolic characteristics, and physiological roles[7]. Water-soluble vitamins are not stored in the body and must be supplied regularly through diet or supplements [8,9]. The fat-soluble vitamins A, D, E, and K are found in various forms in foods and their metabolism involves complex steps of absorption, transport, storage, and excretion. These vitamins are excreted primarily in the feces and, to a lesser extent, in the urine. Excess amounts of fat-soluble vitamins are stored in the liver to maintain homeostasis and prevent toxicity [7].

Fatty acids, especially polyunsaturated fatty acids (PUFAs)[5] are of great importance in nutrition due to their key roles in cell membrane structure, inflammation reduction, cell signaling, and prevention of chronic diseases. Since some fatty acids, such as EPA[6] and

1 -Ultra-processed foods
2 -Food and Agriculture Organization
3 -Water-soluble vitamins
4- Fat-soluble vitamins
5 -Polyunsaturated fatty acids
6- Eicosapentaenoic acid

DHA[7], are not synthesized in the body, they must be supplied through the diet. Due to reasons such as low stability, susceptibility to oxidation, off-flavor, and limited solubility in water, their direct application in food products is challenging. Coating technology, as an effective solution, improves the stability, bioavailability, sensory properties, and distributability of fatty acids in food matrices, which has attracted increasing attention from researchers and the food industry [10,11].

Probiotics are live microorganisms that, when consumed in adequate amounts, confer a health benefit on the host. These microorganisms are effective in preventing and treating disorders such as irritable bowel syndrome, obesity, type 2 diabetes, and some cancers by regulating the intestinal microbiota and inhibiting pathogens. The survival of probiotics depends on environmental factors, digestive conditions, and processing, and microencapsulation technology can help maintain their viability, improve their efficacy, and functional properties [12,13].

Minerals are essential micronutrients that play a vital role in biological functions, growth, metabolism, and immune system function. Deficiencies of these elements, especially iron, zinc, and calcium, are major public health challenges in many developing countries, leading to complications such as anemia, growth failure, thyroid problems, and immunodeficiency. The use of mineral supplements is associated with limitations such as low acceptance, limited availability, and gastrointestinal side effects. Fortification of foods with minerals has been considered as a cost-effective, safe, and sustainable approach. For reasons such as poor stability, metallic taste, and limited bioavailability, food fortification faces challenges that can be overcome by nutrient encapsulation [14,15].

Encapsulation is a new technique in the food industry that is used to protect active ingredients such as vitamins, antimicrobial compounds, and other substances sensitive to environmental conditions and the digestive tract. This technology increases the stability and controlled and targeted release of active ingredients and is a suitable method for the development of new and enriched food products. Bacterial encapsulation is carried out with the aim of producing functional products and also inhibiting the growth of unwanted microorganisms [16]. Food processing and fortification is a successful strategy to reduce nutrient deficiencies and improve community health. Mandatory food fortification is a common approach to compensate for nutrient deficiencies and prevent their complications, which is mostly implemented in low- and middle-income countries [17].

The aim of this article is to highlight the importance of bioactive compounds such as vitamins, minerals, fatty acids, and probiotics for improving health and preventing chronic diseases. This study also examines the role of coating technology in improving stability, bioavailability, preventing nutrient loss, targeted release, and increasing efficiency in the digestive tract of nutrients.

Vitamins

Vitamins are organic molecules and micronutrients essential for growth and maintenance that are not synthesized in the body of vertebrates (except K, D and B7) and must be supplied through the diet. In the early 20th century (1906), the British biochemist Sir Frederick Hopkins stated that food contains other cofactors in addition to carbohydrates, proteins, fats, water and minerals. The word vitamin was first discovered by Funk, which was formed from the two words vital and amine, and after it was discovered that not all of them are amines (they are nitrogenous or amine), the letter "e" was dropped in 1920. Later, it was found that vitamins have different benefits and different chemical properties. Vitamins are classified into two groups based on their solubility: fat-soluble (A, D, E, K) and water-soluble (C and group B) [18,19].

Water-soluble vitamins include thiamine (B1), riboflavin (B2), niacin (B3), pantothenic acid

7 -Docosahexaenoic acid

(B5), pyridoxine (B6), biotin (B7), folate (B9), cobalamin (B12), and ascorbic acid (vitamin C). These vitamins are not stored in the body and must be supplied regularly through diet or supplements [8,9].

Vitamin A is present in food as retinol or precursor carotenoids and after absorption in the intestine, it is converted to retinol and transported to the liver or tissues by the retinol-binding protein (RBP). Vitamin D3 is supplied to the skin by UV light or through the diet and after absorption, it is converted to the active form 1.25-dihydroxyD3 in the liver and kidneys. Vitamin E is present as tocopherols and tocotrienols and after absorption by specific carriers, it is distributed in the body via lipoproteins. Vitamin K also exists in two forms, K1 (vegetable) and K2 (animal and fermented), and after absorption, it plays a role in the synthesis of coagulation factors in the liver. Fat-soluble vitamins have a more diverse and complex physiological function. After entering the small intestine, fat-soluble vitamins cross the cell wall and enter the bloodstream, and are ultimately stored in the liver [3].

Whereas vitamin K2 is mainly absorbed in the large intestine. Vitamin D, unlike other fat-soluble vitamins, has a hormonal precursor role and its metabolism is subject to feedback regulation by blood calcium levels. The recommended intake of fat-soluble vitamins, including A, D, E, and K, varies based on age, gender, and physiological status such as pregnancy or lactation. Approximately, the recommended intakes for adults are 600 to 900 micrograms of retinol equivalents for vitamin A, 600 to 800 IU of vitamin D, 15 to 30 mg of vitamin E, and 70 to 120 micrograms of vitamin K per day [7].

Fat-soluble vitamins

Vitamin A

Vitamin A is found in the body in three forms, including retinol, retinal, and retinoic acid, together known as retinoids and found in animal sources. Carotenoids found in plant sources can also be converted to the vitamin [15]. Its structure is an unsaturated isoprenoid complex that has animal (such as retinol and derivatives) and plant (as provitamins such as carotenoids) origin. The human body cannot obtain the vitamin through diet. Its most important roles include growth, immune system enhancement, gene expression, reproduction, light transmission to the retina, and vision [19,20]. Its two main forms are retinoids (retinal, retinol, and retinoic acid) and carotenes (α, β, and γ) [18]. Animal foods such as liver and fortified milk contain retinoids, and plant foods such as carrots, squash, and spinach contain carotenoids. The recommended daily intake of this vitamin for women and men is 700 and 900 micrograms per day, respectively [15].

Vitamin A deficiency leads to decreased serum retinol levels, which are associated with a variety of physiological disorders. Reports indicate that between 44 and 50 percent of preschool children in South Asia are severely vitamin A deficient. Also, about one-third of global deaths in Bangladesh and India are related to malnutrition and vitamin A deficiency. Vitamin A deficiency has become a major public health issue, and one of its most important symptoms is dry eyes, which affects about 120 million children worldwide due to inadequate dietary intake of the vitamin. Studies have shown that about 6% of children under five in Africa die from vitamin A deficiency. Data from 2020 show that three out of five children need vitamin A supplementation, with the highest prevalence of deficiency in southern Africa and southern Asia. Obesity is a common non-communicable disease and is increasing, affecting about 13% of adults worldwide. In many societies, malnutrition and obesity coexist. Provitamin A carotenoids play a role in compensating for vitamin A deficiency, reducing weight, and improving blood lipid indices [6,21]. Fortification of foods is an effective way to combat vitamin A deficiency, reducing the causes of deficiency, including childhood blindness and mortality from severe infections. Due to the low stability of vitamin A during processing and storage, it can be prevented from being destroyed and wasted by coating it [22].

There are more than 50 provitamin A carotenoids, which are mostly found in cereals, vegetable oils, fruits and vegetables. They are yellow to orange organic pigments with antioxidant activity. The best known of them are α-carotene, β-carotene, γ-carotene, lycopene, lutein and cryptoxanthin. Beta-carotene is found in red, orange and green vegetables such as carrots, tomatoes and spinach. Beta-cryptoxanthin is found in citrus fruits, mangoes, persimmons, papaya and peppers. Carotenoids exist in free form or esterified with fatty acids (palmitic, lauric and myristic) [20]. The absorption of carotenoids depends on factors such as the type of carotenoid, the food matrix and the host [19].

Retinol is a hydrophobic form of vitamin A that is essential for growth, immune system enhancement, and epithelial tissue differentiation, and is also very effective in treating skin diseases. Due to its low solubility in water, crystallization at room temperature, and low stability to light, oxygen, and heat, its bioavailability and stability can be increased by encapsulation. Retinol is absorbed in the small intestine and is very high (absorption efficiency 70 to 90%) [19,23].

Retinoic acid (RA) or all-trans retinoic acid (ATRA)[8] is a vitamin A metabolite that plays an important role in growth and development, cell proliferation, embryonic development, apoptosis, nervous system function, skin aging prevention, allergy, treatment of myelocytic leukemia (APL)[9], prevention and treatment of metabolic disease and cancer, and chemotherapy prevention [24]. Studies have shown that ATRA has various antitumor and therapeutic effects such as Kaposi's sarcoma, boroblastoma, bladder cancer, ovarian cancer, and anti-vascular inflammation [25].

In a study by Yousefi *et al* (2023), sesamol and retinol were encapsulated using W/O/W emulsion and alginate and chitosan coating containing Tween 80 and Span 80. The results showed that the optimal sample had EE of 92.93% and particle size of 381.94 nm, which were expressed as 24.6, 84.10 and 70.37% for Tween 80, Span 80 and W/O. Regarding the release in simulated gastric fluid (SGF), 39% and 22% for sesamol and retinol were expressed as 56% and 22% for simulated intestinal fluid (SIF), respectively [23].

Vitamin D

Vitamin D exists in two forms, D2[10] (plant foods) and D3[11] (animal foods and skin), both of which are used in supplements and food fortification. Vitamin D3 is more efficiently absorbed in the human intestine[26].

It was previously believed that D2 and D3 were the same and could be used interchangeably, but scientific evidence now shows differences in their bioavailability (higher metabolism and clearance of D2 in the liver and D3 in the kidney)[27]. The vitamin is absorbed in the small intestine along with dietary fat. Lipid emulsification is then initiated by bile acids, and pancreatic lipase hydrolyzes triglycerides, and micelles containing lipid and vitamin D enter the enterocyte[19]. The most important biological function of this vitamin is to maintain blood calcium and phosphorus concentrations. Vitamin D strengthens bones, protects the skin, prevents aging, and prevents cancers such as colon, breast, prostate, and pancreas. Its antiproliferative mechanism, increased apoptosis, and enhanced immunity reduce cancer and mortality [28]. Due to deprivation and insufficient doses of ultraviolet radiation (for reasons such as geographical location, angle of radiation, duration of exposure, cultural and religious reasons) and the scarcity of natural sources rich in vitamin D (cod liver oil, salmon, eggs, several wild species of mushrooms and certain species of plant algae) as well as nutritional data from different countries, it can be concluded that there is a deficiency of this vitamin in the diet, and that by enriching products, the occurrence of diseases can be prevented [27]. The required dose for adults (19 to 70 years) is 15 micrograms per day or 600 IU per day, and for

8- All-trans retinoic acid
9 -Promyelocytic leukemia
10 -Its other name is ergocalciferol.
11- Its other name is cholecalciferol.

people over 70 years of age, 20 micrograms per day or 800 IU per day is recommended [15].

Groups at high risk of vitamin D deficiency include the elderly, hospitalized patients, obese patients, dark-skinned individuals, those living in areas with limited sunlight, and those with chronic diseases such as kidney failure [7]. Vitamin D deficiency causes immune disorders such as inflammatory bowel disease, multiple sclerosis, rheumatoid arthritis, sclerosis, hypertension, cardiovascular disease, diabetes, microbial infection, and acute respiratory syndrome [26]. Deficiency of this vitamin can also cause rickets[12], osteomalacia[13], osteoporosis[14], and rickets [15]. Since few foods contain vitamin D in small amounts, daily nutritional requirements can be met by fortification of foods. For reasons such as hydrophobicity, oxidation, low bioavailability, poor chemical stability, sensitivity to light, pressure, and processing conditions, fortification of products with vitamin D is challenging, which can be overcome by encapsulating it at the nano or micro scale. On the other hand, during fortification and storage of foods, problems such as homogeneity in the food matrix, reduction in quantity during processing and storage, physicochemical degradation, and interaction with other food components that change the taste, appearance, and texture of the food reduce its acceptability and marketability, which can be prevented by microencapsulation [27]. The most common products fortified with vitamin D include dairy products, breakfast cereals and bread. Studies have shown that fortification can significantly improve vitamin D intake. For example, in Finland, a mandatory policy of fortification of foods with vitamin D was implemented, which increased the serum concentration of 25-hydroxyvitamin D by 18 nmol/L in the population. Vitamin D fortification policies vary in different countries around the world, which can be divided into three groups: mandatory fortification (such as Canada and Finland), voluntary fortification (such as the United Kingdom and Ireland), and limited fortification (such as Asia and Europe). The implementation of a mandatory fortification policy has been considered for reasons such as limited natural sources of vitamin D in the diet, low use of supplements, and increasing vitamin D intake without changing dietary behavior. Evidence suggests that fortification increases this vitamin, with intakes averaging about 2 to 3 micrograms per day higher than in countries without such a policy [5].

In a study by Esmaeili *et al* (2021), vitamin D was nanoencapsulated. Due to limited natural sources of vitamin D, vitamin D deficiency has affected a large population worldwide. Encapsulation of vitamin D increases its bioavailability and stability during processing and storage. The results showed that encapsulation minimizes loss during processing, storage, and gastric transit, and factors affecting bioavailability were capsule size, wall-to-core ratio, carrier oil composition, and coating method [29].

In another study, Lips *et al* (2021) examined the status of vitamin D in people around the world. The results showed that in Australia and Latin America, vitamin D levels were sufficient, but people in Asia, the Middle East, and Europe were deficient in this vitamin. The results indicate that 58-62% of children, 44-60% of adults, and 41-62% of the elderly in the Middle East are deficient in this vitamin. Also, vitamin D deficiency in the sun-exposed population of Iran is 86%, India 61%, and Turkey 51%. Due to the type of clothing, lack of fortified foods, and reduced exposure to sunlight, vitamin D deficiency is more common in women than in men. The most important factors of vitamin D deficiency are low physical activity, increased body mass index (BMI), lack of fortified foods, reduced exposure to sunlight, increased use of sunscreen, and poor social activity, and the determining factors for increasing this vitamin are food fortification with vitamin D and vitamin D supplements. Results regarding food

12 -In this disease, bones cannot calcify normally, causing growth disorders and abnormal skeletal development, and it mostly affects black children and adolescents.

13 -It weakens the bones and causes soft, flexible, deformed, and brittle bones.

14 -It causes osteoporosis and bone fractures.

fortification, especially in milk, dairy products, and orange juice, showed that this problem can be solved by food fortification [30].

In a study by Lee and Duggan (2022), the efficacy and stability of vitamin D3 was investigated using whey protein isolate (WPI) microgels. Analyses were performed against factors such as temperature (72°C for 15 seconds and 63°C for 30 minutes), UV light (254 nm), and storage for four weeks at 4, 20, and -20°C. The results showed that the microgels were able to encapsulate 98% of vitamin D3 and significantly stabilized it against environmental stresses. The release in the mouth and stomach was negligible, and 97% was released in the intestine and at the end of digestion, indicating that the microgels can provide adequate protection against digestive and environmental conditions [31].

Vitamin E

Discovered in vegetables in 1922, this vitamin is a plant-derived, fat-soluble substance that has a chromanol ring with a side chain at the C2 position in its structure. Vitamin E is a natural antioxidant that protects cell membranes and lipids from oxidative damage. This vitamin plays a role in reducing the risk of cardiovascular diseases by reducing LDL oxidation and improving endothelial function. It is also effective in anti-inflammatory effects, accelerating wound healing, and protecting the skin from damage caused by UV rays and free radicals. Sources of this vitamin include vegetable oils, nuts, legumes, whole grains, vegetables, and fruits. This vitamin has positive effects on the intestinal epithelial barrier [3,7,19]. Studies have also shown that this vitamin is also useful in preventing breast cancer and reducing menopausal symptoms [32]. The recommended dose for adults is 15 mg per day. The most important symptoms of vitamin E deficiency include the breakdown of red blood cells (erythrocyte hemolysis), neuromuscular disorders, and impaired vision and speech [15].

In a study, Kiani *et al* (2021) investigated the production and evaluation of physicochemical properties of nanostructured lipid carriers (NLC) and lipid nanocapsules (LNC) of vitamin E for milk fortification. The optimal encapsulation efficiency of NLC and LNC was expressed as 95 and 99%, respectively. Spectroscopic results showed that no adverse reaction occurred between the vitamin and the nanocarrier. Regarding the release under similar gastric conditions, NLC and LNC were expressed as 29 and 4%, respectively. Also, in sensory evaluation, these nanocarriers were accepted by consumers[33].

Vitamin K

This vitamin takes its name from the Danish word Koagulation, meaning coagulation, and is known for its role in the synthesis of blood-clotting proteins and its anti-inflammatory effects. This vitamin is a family of fat-soluble compounds and its basic structure is 2-methyl-1,4-naphthoquinone and a variable aliphatic side chain. Vitamin K exists in the forms of phylloquinone (K), menaquinone (K_2) and menadione (K3), where phylloquinones are of plant origin, menaquinones are synthesized in the body and by bacteria, and menadione is produced industrially or synthetically and is considered a precursor to the vitamin. This vitamin acts as an essential cofactor in blood coagulation pathways and plays a vital role in the activation of vitamin K-dependent proteins that are essential for normal homeostasis. This vitamin plays a role in the metabolism of bone proteins, especially osteocalcin, and without it, osteocalcin cannot bind to the minerals that make up bone, causing a decrease in bone density. The recommended daily intake of this vitamin for women and men is 90 and 120 micrograms per day, respectively [15]. Vitamin K deficiency can cause hemorrhagic disease (uncontrollable bleeding), coagulation disorders, and an increased risk of bleeding. This vitamin also plays a role in preventing venous thrombosis, reducing vascular calcification, and maintaining bone health by activating proteins such as osteocalcin and MGP[15]. Studies have also shown that K1 and

[15] Matrix Gla Protein

K2 have important biological effects, such as antiproliferative activities, induction of proliferative processes, and stimulation of autophagy, which inhibit the growth of cancer cells. About 10 to 50 percent of the body's daily requirement for vitamin K is provided by the synthesis of beneficial intestinal bacteria, and the majority of the body's needs must be met through diet. The daily intake of this vitamin varies in different countries, for example, in the United States, the recommended daily intake for women is 90 micrograms and for men is 120 micrograms, and in the United Kingdom, the daily intake is based on body weight and is equivalent to 1 microgram per kilogram. Vitamin K, especially in supplement forms and processed foods, faces limitations such as instability to light, heat, and oxidation, as well as low bioavailability, which can be overcome by coating it [7,15,19].

Water-soluble vitamins

B vitamins

B vitamins are water-soluble and perform a variety of vital functions in the body. This group includes thiamine (B1), riboflavin (B2), niacin or niacinamide (B3), pantothenic acid (B5), pyridoxine (B6), biotin (B7), folate (B9), and cobalamin (B12). Their absorption occurs primarily in the small intestine and is concentration-dependent, with low levels of absorption occurring via active transport systems and higher levels of absorption occurring primarily via passive diffusion [8,9].

The recommended daily allowance (RDI)[16] for vitamin B1 is 1.1–1.2 mg, B2: 1.1–1.3 mg, B3: 14–16 mg, B5: 5 mg, B6: 1.3–1.7 mg, B7: 30 µg, B9: 400 µg, and B12: 2.4 µg, and higher amounts are recommended for vulnerable individuals, infants (for growth, development, metabolism, and nervous system development), and pregnant women (for fetal growth, cell division, blood production, energy and nutrient transport, maternal health, and breastfeeding) [8]. Encapsulation of B vitamins increases their stability against environmental factors, improves bioavailability, controlled release in the gastrointestinal tract, better absorption in the body, and increases shelf life in food products [1,34].

Vitamin B1

Vitamin B1, or thiamine, is a coenzyme of TPP (thiamine pyrophosphate) and plays an important role in energy metabolism. This vitamin plays a vital role in energy metabolism, nervous system function, heart health, and neurotransmitter synthesis. Thiamine acts as a coenzyme of thiamine pyrophosphate in glucose oxidation and has both direct and indirect effects on cellular metabolism. Thiamine acts as a coenzyme in the enzymatic decarboxylation of red tartaric acid. Accumulation of cornelian tartaric acid and tartaric acid can lead to neurological disorders, circulatory failure, heart failure, and anorexia [35]. The most important sources of this vitamin include dairy products, brown rice, whole grains, meat, legumes, and fortified breads, and since the body does not store it, daily consumption is essential. The recommended daily intake for women and men is 1.1 and 1.2 mg per day, respectively [15]. Thiamine deficiency occurs when the recommended daily intake (RDI) is not met, and impaired intestinal absorption with high excretion occurs in alcoholics, people with acquired immunodeficiency syndrome (AIDS), and people with malnutrition. Also, people with certain conditions such as the elderly, diabetes, gastrointestinal disease, obesity-related surgery, hyperthyroidism, kidney failure, unbalanced diet, fasting, prolonged starvation, pregnancy, and breastfeeding are more susceptible to deficiency. Vitamin B1 deficiency in the diet causes disruption of metabolic and biochemical processes such as mitochondrial dysfunction, neurotransmitter synthesis, glucose metabolism, and bioenergetic processes. Thiamine deficiency may also lead to diseases such as beriberi (dry type with neurological symptoms such as numbness, muscle weakness, and ataxia, and wet type with symptoms such as heart failure), Wernicke-Korsakoff syndrome (severe brain disorder with confusion, visual impairment,

16- Recommended daily intake

memory impairment, and Alzheimer's), Parkinson's, Huntington's disease, cardiomyopathy, general weakness, anorexia, chronic fatigue, and irritability [36]. Failure to recognize and treat vitamin B1 deficiency can lead to death, which in neonates can occur within hours of the onset of clinical symptoms. In the past, results of thiamine fortification in the Philippines showed that consumption of rice fortified with thiamine, niacin, and iron significantly reduced beriberi (the second leading cause of death after tuberculosis), and that mortality from beriberi in infants was reduced by 52% in the first year of intervention [17]. Vitamin B1 is inactivated by ultraviolet radiation, pH, and other environmental factors, and can be encapsulated using methods such as freeze-drying to improve stability, lipid solubility, and bioavailability [37].

In a study by Juhász *et al* (2021), vitamin B1 was encapsulated in asolectin-based liposomes for pH-dependent controlled release. The nanocarriers had an average hydrodynamic size of about 225 nm under physiological conditions and 245 nm under acidic conditions. Release studies under physiological conditions (pH=7.4) and gastric conditions (pH=1.5) showed that the liposomes had controlled release and were more persistent compared to the free form (about 4.5 times under physiological conditions and 1.5 times under gastric conditions) [35].

Vitamin B2

This substance was noticed by chemists in 1879, and in 1936 the American Chemical Society chose the term flavin, and finally riboflavin was accepted. Riboflavin is a naturally occurring yellow-green fluorescent pigment, also known as lactoflavin, and occurs as orange-yellow crystals [38]. Vitamin B2, or riboflavin, is produced by all plants and most microorganisms and plays a vital role in the growth and reproduction of humans and animals. This vitamin plays a role in energy metabolism, tissue growth and repair, red blood cell production, antioxidant function, and maintaining healthy skin and eyes. Vitamin B2 acts as a precursor of the coenzymes FAD[17] and FMN[18] and is involved in redox reactions as well as in the metabolism of carbohydrates, lipids, ketone bodies and proteins. Riboflavin is also effective in the conversion of tryptophan to niacin, the activation of vitamins B6 and B9 and the transport of iron. Its most important sources include dairy products, eggs, red meat, liver, fatty fish, nuts, green leafy vegetables, some fruits and fortified cereals. Riboflavin is absorbed from the small intestine and transported to the tissues, and its excess amount is excreted in the urine in the form of metabolites such as 7-hydroxymethylriboflavin and lumiflavin, due to its water solubility. Because the body does not store riboflavin, it must be consumed daily. The recommended daily allowance for this vitamin is 1.1 and 1.3 mg/day for women and men, respectively (Book). Riboflavin deficiency can lead to symptoms such as fatigue, inflammation of the tongue, cracks in the corners of the mouth, lip ulcers, sensitivity to light, vision problems, anemia, and neurological disorders. This vitamin is stable to heat, acid, and oxidation, but it is sensitive to light, especially ultraviolet (UV) radiation [38,39]. Industrial production of riboflavin is done through chemical synthesis or fermentation. Fermentation is economical because it is a single-step process, but chemical synthesis is a complex, multi-step, and expensive process. For this reason, fermentation production of riboflavin has completely replaced the chemical method and is more suitable economically and environmentally. This vitamin is extracted from microorganisms such as Ashbya gossypii, Candida famata, and Bacillus subtilis [39].

Vitamin B3

Vitamin B3 or niacin has two chemical structures, nicotinic acid and nicotinamide, and plays a vital role in energy metabolism, nervous system function, skin health, and blood cholesterol regulation. Niacin is a precursor to two important coenzymes, nicotinamide adenine dinucleotide NAD^+ (nicotinamide adenine dinucleotide) and $NADP^+$ (the phosphate form of NAD), which play a role in

17 -Flavin adenine dinucleotide

18 -Flavin mononucleotide

carbohydrate, lipid, and protein metabolism. This vitamin also plays a significant role in DNA synthesis, immune system function, and repair of genetic damage. Rich sources of niacin include red meat, poultry, fish, liver, peanuts, legumes, whole grains, and eggs. The human body can also synthesize a limited amount of niacin from the amino acid tryptophan, a process that depends on adequate vitamin B6 and iron. The recommended daily intake of this vitamin for women and men is 14 and 16 mg per day, respectively (Book). Mild niacin deficiency can cause decreased metabolism and headaches, and severe deficiency can lead to pellagra, a disease characterized by diarrhea, skin disorders, dermatitis, dementia, and even death [40].

Vitamin B5

In 1931, American biochemist Roger J. Williams identified pantothenic acid as a growth factor and named it from the Greek word “pantos” meaning “everywhere.” He and his colleagues observed that this acidic compound could stimulate the growth of the yeast Saccharomyces cerevisiae, so they introduced it as a “building block of living matter.” Vitamin B5, or D-pantothenic acid (D-PA), is an essential nutrient and a precursor of coenzyme A (CoA) and plays an important role in biological processes such as regulating the metabolism of carbohydrates, fats, proteins, and nucleic acids. In the brain, acetyl CoA is also essential for the production of myelin and the neurotransmitter acetylcholine. This vitamin is involved in energy metabolism, synthesis of coenzyme A (CoA), synthesis of hormones, production of red blood cells, immune system and maintenance of healthy skin, hair and nails. The most important sources of this vitamin include beef, poultry, liver, fish, eggs, dairy products, legumes, whole grains, green leafy vegetables, tomatoes and broccoli. The recommended daily dose of this vitamin is 5 micrograms [15]. Vitamin B5 deficiency can lead to symptoms such as fatigue, headaches, irritability, numbness or tingling in the hands and feet, impaired coordination and muscle cramps, sleep disorders, nausea, vomiting, and loss of appetite. Pantothenic acid is destroyed during freezing, canning, and related processing, and encapsulation can be used to prevent its destruction and loss [15,41].

Vitamin B6

This vitamin exists in three forms: pyridoxal, pyridoxine, and pyridoxamine, and can be converted to the coenzyme PLP (pyridoxal phosphate) and plays a role in carbohydrate, amino acid, and fatty acid metabolism. The most important sources of B6 include meat, poultry, fish, potatoes, and fruits (except citrus fruits). Unlike other water-soluble vitamins, vitamin B6 is stored in large quantities in muscle tissue. The recommended daily intake of this vitamin is 1.3 mg per day. Its deficiency is also known as pyridoxine and causes increased IL-4 levels and decreased antibody production. Vitamin B6 deficiency also causes decreased neurotransmitters, depression, confusion, and seizures[1,15]. Vitamin B6 is heat and acid resistant and sensitive to oxidation, ultraviolet light, and alkali, and about 50% is lost during processing and cooking[42].

Vitamin B7

Vitamin B7 or biotin is a water-soluble vitamin of the B group that plays an essential role in the metabolism of carbohydrates, fats and proteins, the synthesis of fatty acids, gluconeogenesis and the activity of carboxylase enzymes. Its deficiency plays an important role in the development of chronic inflammatory diseases and its use in the diet is essential for maintaining healthy skin, hair, nails and nervous system function. Biotin is found in various food sources such as liver, egg yolk, peanuts, sunflower seeds, salmon, avocado, sweet potatoes and green leafy vegetables. Biotin is also produced by bacteria in the digestive tract. The recommended daily intake of this vitamin for adults is 30 micrograms. Biotin deficiency is rare but can lead to symptoms such as hair loss, brittle nails, skin rashes around the eyes and mouth, inflammation of the tongue, itchy skin, nervous disorders, fatigue, nausea, depression, insomnia, and in severe cases hallucinations and numbness and tingling of the arms and legs. This deficiency often occurs in people with genetic disorders or with chronic consumption of raw egg whites (more than 2 servings per day for several months) due to the presence of avidin (cooking eggs denatures protein bonds) [15].

Vitamin B9

Folate was discovered in the 1930s during research on macrocytic anemia in pregnant women, and in 1941 folic acid was isolated from spinach leaves as a synthetic form of vitamin B9. The word folate is derived from the Latin word “Folium” meaning leaf. Folate is found in the glutamyl form (containing several glutamate residues), and folic acid (the synthetic form of vitamin B9) is in the monoglutamate form with one glutamate unit. Also, natural folates have a reduced structure, and folic acid is completely oxidized. Chemical differences have a direct impact on bioavailability, such that folate is absorbed more readily than folate at equivalent intake levels. The folic acid molecule is composed of three moieties: glutamic acid, p-aminobenzoic acid, and pterin, and its molecular formula is C19H19N7O6. This vitamin is also known as folic acid or folate and its chemical name is Pteroylglutamic acid (PGA). Vitamin B9 plays an important role in cell division, bone marrow formation, spinal cord formation and the fetal nervous system. It is also essential in energy production, nucleic and amino acid metabolism and maintaining cell activity. Folic acid is a yellow, odorless crystalline substance with limited solubility in water and insoluble in fatty solvents. It is stable to heat in neutral and alkaline environments and is sensitive to sunlight. Folate is present in food and the body, while folic acid is mostly found in supplements and fortified foods. The most important sources of folate include vegetables, fruits, legumes, and fortified cereal products. Because this vitamin plays an important role during pregnancy, the daily requirement of pregnant women is several times higher than the daily requirement of individuals, and given that the formation of the fetal neural tube usually occurs before the woman is aware of the pregnancy, daily supplementation with 400 micrograms of folic acid is recommended. Taking this dose of folic acid, along with folate-containing foods, plays a vital role in preventing birth defects and does not exceed the upper safe daily limit (1000 micrograms). B9 deficiency is rare and is most common in alcoholics (due to impaired metabolism and impaired folate absorption, as well as malnutrition), pregnant women (to prevent neural tube defects in the fetus and increase nucleic acid synthesis, it is necessary to consume enough folic acid before pregnancy), and people with digestive disorders (such as irritable bowel syndrome, celiac disease, dengue fever, and gastritis due to impaired folate absorption). The most important symptoms of this vitamin deficiency include anemia and neurological disorders such as weakness, fatigue, and irritability. Sources include legumes, vegetables, fruits, and whole grains. In general, vitamin B9 plays an important role in pregnancy health, depression prevention, heart health, skin health, acne treatment, and cancer reduction, and it also activates vitamin B12. Folate acts as a coenzyme in nucleic acid synthesis and amino acid metabolism. The coenzymes THF (tetrahydrofolate) and DHF (dihydrofolate) are used in DNA synthesis and new cell formation. Research has shown that vitamin C limits the degradation of the natural coenzyme folate and folic acid and improves bioavailability [43].

Vitamin B12

The molecular structure of vitamin B12, or cobalamin, consists of a core of cobalamin with a central cobalt ion and a dimethylbenzimidazole ring. Its active forms include methylcobalamin, adenosylcobalamin, hydroxycobalamin, and cyanocobalamin, the latter being the most stable and predominant form in supplements. Due to the sensitivity of this vitamin to environmental factors, nanoemulsion technology has improved its stability and bioavailability[8]. Vitamin B12 is a water-soluble vitamin that is essential for the metabolism of fatty acids and amino acids, DNA synthesis, and red blood cell formation. It plays an important role in the functioning of the nervous system and bone marrow health. Its absorption in the gastrointestinal tract requires the presence of hydrochloric acid, pepsin, and intrinsic factor (IF), which forms the IF–B12 complex [44].

This vitamin is found mainly in animal foods and is synthesized by intestinal bacteria, and endogenous production is insufficient to meet the body's needs. Rich sources of B12 include liver, red meat, eggs, and dairy products. The recommended daily intake is 2.4 µg for adults and 2.8 µg for pregnant and lactating women. Food fortification and supplementation are recommended in high-risk populations (such as the elderly and vegetarians) [45]. Vitamin B12 absorption is a complex process dependent on three key proteins: haptocorrin (HC), intrinsic factor (IF), and transcobalamin (TC). Cobalamin is first released from dietary proteins in the stomach and binds to HC. In the duodenum, HC is broken down by pancreatic enzymes, and B12 binds to IF. The IF-B12 complex is absorbed in the distal ileum with the help of calcium, then enters the bloodstream and binds to TC. Some of the vitamin B12 is secreted into the bile and reabsorbed. This vitamin is excreted in the urine in cases of excessive consumption or injection [45,46]. Factors such as temperature, pH, oxygen and light during processing and storage cause the vitamin to decrease. Decreased IF due to diseases such as atrophic gastritis or gastric antrum resection leads to B12 malabsorption. Also, drugs such as proton pump inhibitors, metformin, some antiepileptic drugs and colchicine interfere with the absorption or metabolism of B12 [9].

B12 deficiency may be due to inadequate intake (especially in vegetarians), malabsorption, genetic disorders, gastrointestinal diseases (e.g., Crohn's disease, bacterial overgrowth), or drug interactions. Symptoms of deficiency include megaloblastic anemia, neurological damage (anesthesia, depression, Alzheimer's, psychosis), and cognitive impairment. Pernicious anemia, as one of the main causes, is caused by a lack of IF in autoimmune gastritis. B12 deficiency is associated with neurological diseases, cognitive decline, and age-related macular degeneration (AMD). Taking B12 supplements helps reduce hospitalizations, improve muscle function, and reduce the risk of AMD [45,46]. Deficiency of this vitamin is common in vegetarians, with 25–86% of children, 21–41% of adolescents, 11–91% of adults, and 62% of pregnant women experiencing symptoms, and the rate of deficiency is higher in individuals who have been on a vegetarian diet for a longer period of time [47]. Studies have shown that older adults, especially those with atrophic gastritis, have reduced absorption of vitamin B12 due to decreased gastric acid secretion and intrinsic factor (IF). Accordingly, the US Institute of Medicine recommends increased intake of B12 through fortified food sources or supplements for individuals over 51 years of age. Consumption of fortified foods is an effective strategy to compensate for this reduced absorption and prevent nutritional deficiencies in this age group [46].

Karbalaei-saleh *et al* (2024) studied a low-cost method for preparing vitamin B12 nanoemulsion via spontaneous emulsification. In this study, the effects of sunflower oil (4–8%), Tween 80 (8–16%), and vitamin B12 (5–15%) concentrations on the physicochemical properties of vitamin B12 nanoemulsion were evaluated using response surface methodology (RSM). Data analysis showed that the quadratic model provided the best fit to the experimental data. The optimal conditions for the final formulation were determined to include 6.5% sunflower oil, 99.66% Tween 80 and 13% vitamin B12. Under these conditions, the parameters obtained were reported as pH 7, viscosity 24 cP, turbidity 17.0024, encapsulation efficiency 98.51%, vitamin B12 content 54.5 ppm, p-Anisidine content 2.19, dispersion index (PDI) 0.01 and particle size 322 nm, respectively. The results show the high efficiency of the designed nanoemulsion in improving the stability and bioavailability of vitamin B12[44].

Vitamin C

Vitamin C or ascorbic acid was discovered during research to identify the causative agent of the disease and death of scurvy and was initially called an antiscorbutic agent. Centuries later, it was discovered that this agent has a 6-carbon compound similar to glucose and was named ascorbic acid [15,48]. The chemical structure of vitamin C consists of six carbon atoms, eight hydrogen atoms, and six oxygen atoms ($C_6H_8O_6$). Vitamin C is effective in preventing cardiovascular diseases, cancer, and inflammatory diseases and has a protective role in skin health. It also increases the absorption of non-heme iron, strengthens the immune system, and reduces oxidative damage. Vitamin C is a cofactor for the enzyme hydroxylase for the synthesis of catecholamine hormones (such as norepinephrine) and peptide amide hormones (such as vasopressin). Recent research also suggests a role for this vitamin in regulating gene transcription and cell signaling pathways by regulating transcription factor activity and epigenetic marks [15,49]. Sources of vitamin C include citrus fruits, kiwi, strawberries, peppers, tomatoes, potatoes, and vegetables such as broccoli, cabbage, and spinach. This vitamin is destroyed by heat and oxygen [1,48]. Given that humans are unable to synthesize vitamin C internally, its daily intake through diet or supplements is essential for maintaining general health. The amount required to prevent scurvy is about 10 mg/day, and the recommended dietary allowances for women and men are 75 and 90 mg/day, respectively. This essential nutrient cannot be synthesized by humans due to the loss of a key enzyme in its biosynthesis. Scurvy causes weakened collagen structure, poor wound healing, bleeding gums, increased inflammation, and impaired immunity, making people susceptible to fatal infections such as pneumonia. This vitamin is a water-soluble antioxidant found in cells and plasma and plays an important role in metabolic functions and immunity [15,49].

Table 1. Vitamins and their role in the body

Vitamin	**Other names**	**Daily required dose**	**Performance**	**Deficiency symptoms**	**Food sources**	**Destructive factors**
A	Retinol, retinal, retinoic acid	700-900 µg	Vision, maintenance of the cornea, bone and tooth growth, skin, reproduction, immunity	Night blindness, corneal dryness, corneal softness, corneal destruction and blindness, immune system disorder, infectious disease	Orange fruits, vegetables, fish and liver	**Light, heat and oxygen**
D	Ergocalciferol, cholecalciferol	15 µg Or 600 IU	Bone growth, helping to absorb calcium and phosphorus, controlling Parkinson's, protecting nerve cells and the brain, reducing inflammation	Rickets, osteoporosis, osteomalacia, bowed and bow-legged legs	Sunlight, fortified milk, fatty fish, liver	**Light, heat, oxygen and pH**
E	Tocopherol	15 mg	Antioxidant and prevention of chronic diseases, prevention of oxidative stress, neutralization of free radicals	Neuromuscular disorder, visual impairment	Vegetable oils, seeds, and nuts	**Light, heat, and oxygen**
K	Phylloquinone, Menaquinone, Menadione	90-120 µg	Making blood clotting proteins and bone proteins	Hemorrhagic disease	Synthesis of digestive bacteria, vegetables, and vegetable oils	**Light, heat, oxygen, and pH**
B1	Thiamine	1.1-1.2 mg	Part of the TPP coenzyme and energy metabolism	Beriberi, nerve problems, heart failure and enlargement, muscle	Legumes, whole grains, and meat	**Light, heat, oxygen, and pH**

				weakness, anorexia, and weight loss		
B2	Riboflavin	1.1-1.3 mg	Part of the coenzyme FAD and FMN and energy metabolism	Inflammation of the mouth and skin, red tongue	Dairy, whole grains, liver	**Light, heat, oxygen, and pH**
B3	Niacin	14- 16 mg	Part of the coenzymes NAD and NADP and energy metabolism	Plagger	Milk, eggs, whole grains, meat, poultry, nuts	**Light, heat, oxygen, and pH**
B5	Pantothenic acid	5 mg	Part of coenzyme A and energy metabolism	Neurological disorders, depression, hypoglycemia, increased insulin sensitivity, nausea	Meat, whole grains, potatoes, tomatoes, broccoli	**Light, heat, oxygen, and pH**
B6	Pyridoxal, pyridoxine, and pyridoxamine	1.3-1.7 mg	Part of the coenzymes PLP and PMP, amino acid and fatty acid metabolism, red blood cell production, conversion of tryptophan to niacin, and serotonin	Depression, confusion, seizures	Meat, fish, vegetables, and fruits	**Oxidation, ultraviolet light, and alkali**
B7	Biotin	30 µg	Energy metabolism, amino acid metabolism, and gluconeogenesis	Numbness and tingling in the legs, hair loss, depression, weakness, and hallucinations	Egg yolk, liver, gastrointestinal bacteria	**Light, heat, oxygen, and pH**
B9	Folate, folic acid	400 µg	Part of the coenzyme THF and DHF, DNA synthesis, and new cell formation	Neural tube defects, neurological disorders, and anemia	Vegetables, legumes, and fruits	**Light, heat, oxygen, and pH**
B12	Cobalamin	2.4 µg	Part of the coenzyme methylcobalamin and deoxyadenosylcobalamin helps maintain nerve cells, builds new cells, and helps break down some fatty acids and amino acids	Anemia, nerve damage, cognitive and memory impairment, paralysis, constipation, tongue ulcers, fatigue	Animal foods such as dairy, meat, poultry, and eggs	**Light, heat, oxygen, and pH**
C	Ascorbic acid	75-90 mg	Antioxidant, cofactor in collagen synthesis, thyroxine, and neurotransmitter	Scurvy, inflammation and bleeding of the gums, red spots on the skin, non-healing wounds, abnormal bone growth, and joint pain	Citrus fruits, vegetables, tomatoes, potatoes	**Heat and oxygen**

Minerals

Minerals are inorganic elements and one of the seven major groups of nutrients required by the human body, which play a vital role in the formation of tissues, maintaining physiological and biochemical functions. Since the body is not able to synthesize minerals, their daily intake is essential [50]. There are 90 naturally occurring chemical elements in the earth's crust, of which about 25 are essential for life and are found in living cells and food sources. Minerals are divided into two categories: major and minor. Major elements include calcium, magnesium, phosphorus, sodium, potassium and chloride, and minor minerals include iron, iodine, zinc, selenium, copper, manganese, chromium and fluoride. Today, the development of advanced analytical technologies has enabled the identification and accurate measurement of the concentrations of most elements of the periodic table, which allows for a deeper understanding of their role in health and nutrition [14]. In terms of food safety, minerals are divided into essential elements (such as Ca, Mg, Fe, and Zn) and non-essential elements (such as Pb, Cd, and Hg). High doses of non-essential elements, which include heavy metals, are toxic and originate from pesticides, chemical fertilizers, domestic wastewater, garbage, industrial and automotive exhausts, and radioactive pollution [50].

The way minerals are handled and absorbed in the body is different from that of vitamins. For example, potassium is easily absorbed by the blood and then excreted through the kidneys (like water-soluble vitamins). Other minerals, such as calcium, require a carrier for absorption and transport, and excessive use can be harmful (like fat-soluble vitamins). Like vitamins, the presence or absence of minerals can affect the absorption, metabolism, and excretion of other nutrients. For example, increased sodium intake leads to increased excretion of sodium and calcium (due to interactions between sodium and calcium), or increased phosphorus intake leads to reduced absorption of magnesium (due to the binding of phosphorus to magnesium in the digestive tract) [15].

More than half of the world's population, especially in low- and middle-income countries, suffers from micronutrient deficiencies, especially minerals. Minerals play a role in numerous physiological processes, including bone formation, hormone synthesis, neurotransmission, and enzyme function. Iron (Fe) deficiency or iron deficiency anemia is one of the most common micronutrient deficiencies worldwide, affecting about 40% of the world's population. Its deficiency occurs due to poor absorption, inadequate consumption, or increased demand in certain conditions such as pregnancy and menstruation, and is most commonly seen in women, children, and infants (receiving a diet high in milk, also called milk anemia). Iron is involved in the structure of hemoglobin, myoglobin, and enzymes involved in various cellular reactions such as cellular respiration. The most important symptoms of iron deficiency include weakness, fatigue, impaired hearing and cognitive function, headache, paleness, and inability to regulate body temperature. The recommended intake is 8 mg per day for men and 18 mg per day for women aged 19 to 50 (8 mg for those over 50), and its main sources include red meat, fish, eggs, and legumes [1,15].

Calcium (Ca) is an essential nutrient and the most abundant mineral in the body, 99% of which is found in bones and teeth and 1% in extracellular serum. Calcium reduces the risks of osteoporosis and fractures, cancer, diabetes, obesity, cardiovascular disease, and metabolic syndrome. Calcium also plays a role in muscle contraction and relaxation, nerve function, blood pressure, blood clotting, and hormonal secretion. Its most important sources include dairy products, broccoli, kale, bean curd, bok choy, and legumes. The recommended daily intake is 1000 to 1200 mg per day, and people with lactose intolerance, adolescents, the elderly, and women are among the groups at risk of calcium deficiency [15,51].

Magnesium (Mg) is a divalent cation, more than half of which is in bones, the rest in muscles and soft tissues, and 1% in extracellular fluid. The most important roles of magnesium include energy production, protein, fat, nucleic acid synthesis, glycolysis, oxidative phosphorylation, immune system enhancement, blood pressure regulation, and lung function. Magnesium also plays a role as a catabolist in mitochondrial adenosine triphosphate (ATP) synthesis and the formation of MgATP. Magnesium ions, together with calcium, are effective in muscle contraction and blood clotting. Magnesium is a cofactor in over 600 enzyme reactions and is required for the activity of protein kinases, phosphorylation processes, glycolytic enzymes, and ATP-related reactions. The recommended daily intake of magnesium for women and men is 310 and 400 mg/day, respectively. The most important sources of magnesium include nuts, legumes, green leafy vegetables, whole grains, and some fish. Magnesium deficiency causes sleep disorders, weakness, cognitive impairment, increased free radicals, cardiovascular disease, diabetes, cancer, mental disorders, high blood pressure, stroke, muscle diseases, and bone fractures [15,52].

Zinc (Zn) deficiency also affects approximately 17% of the world's population and is seen in diets based on grains and low consumption of animal products. Osteoporosis, which is mainly caused by chronic calcium deficiency, is recognized as one of the most important global health problems after cardiovascular diseases. Zinc plays an important role in immune function and its deficiency leads to stunted growth, impaired immune function, hair loss and the development of infections such as malaria, HIV, pneumonia, tuberculosis and measles. Zinc plays an important role in the formation of genetic material and proteins, stabilization of cell membranes and DNA, growth and development, transport of vitamin A, wound healing, and function of hormones and enzymes. The recommended daily intake for women and men is 8 and 11 mg, respectively, and its main sources include whole grains, red meat, and shellfish [15,53,54].

Selenium (Se) is an essential micronutrient for health, playing a role in immunity, antioxidant and reproduction. Studies have shown that about 0.5 to 1 billion people worldwide lack selenium in their diets and many more do not consume the required daily amount. Selenium reduces the risk of cancer (such as breast, lung, esophageal and prostate), autoimmune diseases and neurodegenerative diseases, and its deficiency is associated with cognitive impairment, endothelial dysfunction and depression. The recommended daily intake of selenium for adults is 55 micrograms. The main sources of selenium include vegetables (depending on soil and region), fruits, wholemeal bread, seafood and meat. The amount of selenium is related to the region and soil conditions, and countries such as America, Europe, China and Oceania are deficient, and Brazil has the highest amount of selenium in its soil. Studies have shown that this deficiency is prevalent in agricultural areas and due to reasons such as climate change, the decrease in selenium in the soil will be up to 4.8% by 2080-2099 [15,54].

The bioavailability of minerals is influenced by both extrinsic and intrinsic factors such as age and nutritional status. Minerals are only obtained through the diet, and not all mineral elements in food are fully absorbed, and their bioavailability is limited due to complex interactions with other food components. For example, the absorption of iron and zinc is affected by inhibitors such as phytate, polyphenols, and fiber, and phytate prevents the absorption of iron and zinc by forming insoluble complexes. Compounds such as ascorbic acid, organic acids, and sulfur-containing amino acids can increase the bioavailability of iron and zinc [53].

Probiotics

In 1908, Nobel Prize winner Eli Metchnikoff attributed the long life of Bulgarian farmers to the consumption of fermented dairy products in his book "The Prolongation of Life". The term probiotic was first used by Lilly and Stillwell in 1965 to describe substances secreted by microorganisms that also stimulate growth [51,55]. The definition of probiotics has been revised many times and finally in 2002, WHO and FAO proposed a new definition, and probiotics were defined as live microorganisms which, when administered in adequate amounts, confer a health benefit on the host [55,56]. By competing with pathogens, regulating the composition of the intestinal microbiota, and inducing diverse biological effects, these microorganisms can be effective in managing diseases such as irritable bowel syndrome, digestive disorders, intestinal inflammation, diarrhea, obesity, insulin resistance syndrome, type 2 diabetes, nonalcoholic fatty liver disease, and some cancers [57].

Encapsulation of bacteria is done for reasons such as the production of functional products and the inhibition of the growth of unwanted microorganisms. For example, encapsulation of Bifidobacterium animalis and Lactobacillus acidophilus in sodium alginate inhibited the growth of fungi such as Aspergillus niger in feta cheese (during 45 days of storage). This process also increased the viable bacterial cell population by about 0.1 log CFU during storage [16].

The efficacy and survival of probiotics depend on environmental factors such as temperature, humidity, pH, and oxygen during processing, storage, and transportation. In addition, gastric acid and bile salts significantly reduce their viability in the gastrointestinal tract. One of the effective ways to maintain the survival and increase the effectiveness of probiotics is the use of microencapsulation technology [58,59]. Probiotics also have the ability to increase the absorption of B vitamins such as B1, B3, B5, and B12, and are able to produce enzymes such as esterase, lipase, and coenzymes such as CoA, Q, NAD, and NADP [60]. In selecting probiotic strains, it is essential to pay attention to their safety, functional efficiency, resistance to adverse environmental conditions, and beneficial potential [57]. Prebiotics are non-digestible compounds that stimulate the growth and activity of probiotics in the intestine. The simultaneous combination of prebiotics and probiotics in the form of synbiotics can create a synergistic effect and provide properties such as immune enhancement, anticancer and antibacterial effects [12]. For example, Lactobacillus plantarum is a gram-positive bacilli that enhances the immune system and digestive function, produces lactase and reduces symptoms of lactose intolerance. Several studies have confirmed the anticancer effects of this strain, especially in breast, cervical and colon cancers, which are associated with the activation of immune signaling pathways and the inhibition of tumor-related genes [61,62].

For optimal efficacy, probiotics must be resistant to gastric conditions, successfully reach and colonize the large intestine. Therefore, protection of probiotic bacteria during production, storage and handling plays an important role in maintaining their efficacy and stability. Consideration of particle size in microencapsulation is important, with particles smaller than 100 μm having better sensory properties and sizes in the range of 0.2–3 mm providing high protection against gastrointestinal conditions [13,63]. The addition of natural compounds such as moringa extract, green tea and prebiotics such as inulin and fructo-oligosaccharides increase the stability and viability of probiotics in the acidic environment of juices and yogurts [16].

Vaziri *et al* (2018) studied the simultaneous microencapsulation of Lactobacillus plantarum and DHA fatty acid in an alginate-pectin-gelatin biocomposite matrix. The results showed that this formulation was able to significantly maintain the survival of L. plantarum under simulated digestive conditions (4 hours in a simulated gastric environment and 2 hours in an intestinal environment). The survival of free cells was reported in the range of 88.06–78.87% and that of encapsulated cells in the range of 80.53–90.02%. A significant difference in the survival of free bacteria was observed compared to encapsulated bacteria (37.7–28.53%). The highest stability was reported for the alginate capsule at 1.576% and the lowest for the 2% alginate. The encapsulation efficiency ranged from 97.5% to 99.9%. The optimized formulation, consisting of 1.06% alginate, 0.55% pectin, and 0.39% gelatin, was able to maintain the survival rate up to 66.88% for microencapsulated cells, while this value was only 50.36% for free cells. These results demonstrate the high efficiency of the biocomposite system in simultaneously protecting probiotics and bioactive compounds[64].

Fatty acids

Fatty acids are organic compounds with a long hydrocarbon chain and a carboxyl group. In recent decades, fatty acids, especially polyunsaturated fatty acids (PUFAs), have received widespread attention due to their vital role in human health and prevention of chronic diseases. The most important roles of fatty acids include the formation of cell membrane structure, energy production, cell signaling, and regulation of inflammatory processes. Fatty acids (FAs) are the main components of lipids, including phospholipids, cholesterol esters, and triglycerides. These acids, which are classified into saturated and unsaturated, are found in different forms, such as conjugated linoleic acid (CLA), conjugated linolenic acid (CLNA), and CEPA, depending on their chemical structure and type of double bonds. Since some of these fatty acids are not synthesized in the human body, they are known as essential fatty acids and must be supplied through the diet. Important sources of these compounds include vegetable and marine oils, which have been widely used in the food and pharmaceutical industries. However, unsaturated fatty acids face challenges in processing and application due to their high sensitivity to oxidation, low chemical stability, off-flavors, and limited solubility in water. Microencapsulation or encapsulation technology, as a novel solution, has attracted the attention of researchers and food industries with the aim of maintaining stability, increasing bioavailability, improving sensory properties, and better distribution of these acids in the food matrix [65-67].

Regular and adequate intake of polyunsaturated fatty acids (PUFAs) reduces the risk of chronic diseases such as cancer, mental disorders, rheumatoid arthritis, psoriasis, respiratory diseases, obesity, diabetes, osteoporosis and cardiovascular diseases. The main sources of these acids are fish oil, which contains eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)[65].

A balanced diet, especially a balanced ratio between omega-6 and omega-3 fatty acids, is very important for maintaining health and preventing diseases. One of the major challenges in the application of unsaturated fatty acids is their susceptibility to oxidation, which can produce compounds with undesirable odors that negatively affect the shelf life and sensory properties of the product. Also, some oxidation products are toxic and their long-term consumption endangers the health of the consumer. Another challenge in enriching foods with fatty acids is their low solubility in water, for which encapsulation is a suitable method to improve dispersibility in aqueous environments, increase chemical and thermal stability, improve sensory properties and bioavailability [66]. Appropriate selection of the encapsulation method results in better compatibility in the food matrix and prevents changes in the texture, taste, odor and appearance of the product [67].

Polyunsaturated fatty acids (PUFAs), especially conjugated linoleic acid (CLA), have attracted much attention in the fields of nutrition and pharmaceutical sciences as bioactive compounds with broad health-promoting properties. First discovered in 1932 and investigated in the 1980s as a compound with anticancer effects, CLA is one of the conjugated isomers of linoleic acid, which has two double bonds in a conjugated arrangement (without a separating methylene group). The most important biologically active isomers of CLA include c9,t11 and t10,c12, which are naturally found in animal products, plants, and seafood, and can also be produced by some probiotic bacteria. Research has shown that CLA has numerous physiological effects, including anticancer activity, immune system regulation, reduction of body fat mass, improvement of body composition, anti-inflammatory, antidiabetic, antihypertensive, and cardiovascular disease prevention effects. Also, CLA's ability to cross the blood-brain barrier and its effect on brain tumors such as glioblastoma have added to its therapeutic importance. However, low chemical stability and sensitivity to thermal conditions have made the direct use of CLA challenging, and approaches such as microencapsulation and nanoencapsulation can be effective in improving its stability and bioavailability. The use of this compound in diet, especially in the field of obesity prevention and control, through mechanisms such as improving gut microbiota, increasing lipolysis, and activating molecular pathways of energy metabolism, are other prominent aspects of this functional fatty acid [68-70].

Microencapsulation of fatty acids increases the nutritional value of dairy products. For example, adding 1.3% omega-3 microcapsules to whole milk powder increases the stability of the product. Nowadays, the use of encapsulation techniques and enrichment of products such as fruit juices with fatty acids and probiotic microorganisms has received much attention. Research has shown that adding fish oil to fruit juices through microcapsules obtained from complex coagulase increases turbidity but does not affect the sensory acceptance of the product. The low pH of fruit juices poses challenges in the stability of microcapsules and the survival of microorganisms, especially in fruit juices such as raspberry, pineapple and orange, which causes further degradation of the capsules [16].

Encapsulation of Nutrients Microencapsulation is an emerging and advanced technology for food processing that can protect sensitive and valuable materials from environmental and digestive conditions by encapsulating them in a special material. Encapsulating materials inside a polymer improves the quality of food, protects them, and releases them in a targeted manner. The active ingredients or substances that are encapsulated are called the core, and the capsule walls are polymeric or non-polymeric materials. Different techniques are used for microencapsulation, including emulsion, spray drying, freeze drying, extrusion, fluid bed coating, and coacervation. The choice of microencapsulation technique depends on properties such as core material, capsule wall and morphology. Spray drying and extrusion methods are not suitable for probiotics due to the high temperature and large particle size, and methods such as emulsion, extrusion and spray drying are used [71-75]. Microcapsules are used in a wide range of food matrices including dairy products, cereals, meat, fruits and their derivatives and play an effective role in improving sensory quality, reducing fat, improving shelf life and developing functional products [16].

Encapsulated functional components such as vitamins, minerals and fatty acids are incorporated into the food matrix and must be released at a specific location and time depending on their type and application. For targeted protection and release, the type of shell material is of great importance. There are various mechanisms for targeted release, such as the explosive release mechanism (for encapsulated probiotics) and thermal degradation, in which the coating material is degraded at a specific temperature and the core is released [73]. Also, by coating multiple layers, microcapsules with thicker interface properties, increased phytothermal efficiency, antimicrobial power and stability against environmental stresses such as oxidation and thermal changes can be increased. Since coating materials have unique and limited functions, more effective and efficient capsules can be created by mixing and combining different materials. [76,77]. Coating protects materials from harsh environmental conditions such as oxygen, temperature, light and moisture and provides controlled and targeted release, which are used in various industries such as food, agriculture, pharmaceuticals, cosmetics and hygiene. [78].

Spray drying is one of the most common and oldest methods, which is widely used due to its economy and ability to produce on an industrial scale, and produces efficient and high-quality capsules. In this process, the active compound is mixed with a carrier material (usually polysaccharides or proteins) and a stable emulsion or suspension is formed. The emulsion is homogenized by an atomizer and the converted droplets are dried in a stream of hot air. One of the disadvantages of this method is the destruction of some materials due to thermal stability and lack of control over particle size [71,79].

In freeze drying, the coating is based on rapid formation, in which the core and wall mixture are atomized into cold air. The reduction in temperature causes the lipid coating to solidify rapidly, resulting in spherical particles with a uniform coating. Unlike spray drying, this method is solvent-free and more energy efficient. The coatings used include vegetable oils or their derivatives and fats with melting points between 32 and 72 °C, as well as solid mono- and diacylglycerols with melting points between 45 and 65 °C. In this process, a molten lipid is sprayed onto a core material at a temperature above its melting point, and contact with cold air causes the lipid to solidify rapidly, forming a uniform and stable coating. Rapid solidification results in the production of spherical, hydrophobic, and flowable microcapsules. These coatings are insoluble in water, making them very useful for water-soluble compounds such as vitamins, flavors, enzymes, and drugs [71,79].

Fluidized bed coating involves preparing a coating solution, fluidizing the core particles, and then coating the core particles at a specific temperature. The materials used in this method include water-soluble and water-insoluble polymers, waxes, and lipids. The absence of high temperatures in this method saves energy and time. This method is mainly used for secondary coating of pre-encapsulated products to increase stability [79].

Extrusion coating is an efficient method for producing dense, stable hard capsules. This method is based on liquid coextrusion, in which the core and the coating are pumped separately through concentric orifices in a rotating cylinder. The active ingredient passes through the core and the coating passes through the peripheral path of the nozzle and exits simultaneously. During rotation, centrifugal force drives the particles outward, and they form into fine spherical particles. The surface properties of the coating material cause them to spread rapidly around the core and completely cover it. This method is used to encapsulate sensitive compounds such as vitamins, flavors, and other bioactive substances. Common techniques in this method include jet cutting, resonant cutting, and electrostatic droplet generation [79].

Electrospinning is an advanced and efficient method for producing nanocapsules and polymer structures at the nanoscale. In this method, a strong electric field causes the separation of small droplets of polymer solution from the nozzle tip and their deposition on the collector surface. The electric charge of the droplets increases their uniformity and elongation, and nanoparticles with small size and high specific surface area are produced. Electrospinning allows the encapsulation of sensitive biological and pharmaceutical compounds without thermal degradation, and by adjusting the voltage, nozzle distance and viscosity, a stable flow and uniform particles can be created. Electrospinning is of particular importance in the food, pharmaceutical and biotechnology industries due to its precision, controllability and wide applicability [80].

An emulsion is a mixture of two immiscible liquids and is a convenient and inexpensive way to protect and confine materials [81,82]. Emulsion is a chemical separation method in which wall and core materials (dispersed phase) are added to oil (continuous phase) [96]. Emulsions are thermodynamically unstable and separate from each other through processes such as sedimentation, coalescence and flocculation. Surfactants, emulsifiers are used to stabilize the emulsion and thickening agents such as gums are used to modify the viscosity. Studies have shown that some synthetic surfactants with low molecular weight have harmful effects on humans and the environment [81]. Nowadays, Pickering emulsions have attracted much attention due to their higher oxidative stability than traditional emulsions. Unlike conventional emulsions, Pickering emulsions do not contain low molecular weight surfactants, and the irreversible adsorption of solid particles at the oil-water interface creates a stable, safe, and environmentally friendly system [96,97]. Pickering emulsions are suitable for multiphase reactions, significantly increase the surface area, and improve mass transfer. The stability of Pickering emulsions depends on the appropriate partial wettability of the particles, size, shape, concentration, surface charge, and contact angle [85,86].

In a study by De Melo *et al* (2021), vitamin D was nanoencapsulated with Acca sellowiana and its stability in a simulated gastrointestinal tract was investigated. The results showed that the produced nanoparticles were less than 200 nm in size, spherical in shape, had a homogeneous structure, and a smooth surface, and the encapsulation efficiency was 97.21%. The resulting nanoformulation (NP-D3) had good physicochemical and thermal stability and high amounts of bioactive compounds such as phenolic and flavonoid compounds with significant antioxidant capacity. Under simulated digestive conditions, approximately 80% of vitamin D3 was released in a controlled manner. Microbiological and stability evaluations also showed that the nanoformulation maintained good stability and efficacy after 90 days. The results indicate that Acca sellowiana-based nanoparticles are a promising approach to enhance the stability and bioavailability of vitamin D3 in food processing and the digestive environment [87].

2-Conclusion

The results of this study indicate that food fortification, as a simple, accessible, and low-cost strategy, can play an important role in reducing micronutrient deficiencies and improving community health. Given that individuals are exposed to varying degrees of nutritional deficiencies based on age, gender, genetic characteristics, and dietary patterns, the use of functional foods and mandatory fortification can prevent the occurrence of many diseases associated with these deficiencies. However, the high sensitivity of bioactive compounds, including vitamins, essential fatty acids, minerals, and probiotics, to heat, oxidation, and industrial processes limits their effectiveness. Encapsulation technology has been able to overcome many of these challenges by providing a protective coating, increasing stability, improving bioavailability, resolving solubility problems, and providing controlled release, and has enabled the production of food products with higher sensory quality and nutritional value. Accordingly, the combination of the two approaches of fortification and encapsulation can be considered as an effective strategy in improving public health. Furthermore, prospective studies on long-term effectiveness, cost-benefit, and consumer acceptance are essential to pave the way for the development of sustainable nutrition policies globally.

Conflict of Interest

There are none to declare.

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All authors have contributed to the design, analysis, writing, and approval of the final manuscript in this manner

3-References

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مقاله علمی_پژوهشی

تأثیر غنی‌سازی مواد غذایی بر سلامت و راهکارهای کاهش اتلاف ریزمغذی‌ها

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چکیده

غذاهای کاربردی و غنی‌شده امروزه به دلیل نقش موثر در پیشگیری از بیماری‌ها و ارتقای سلامت عمومی، اهمیت روزافزونی یافته‌اند. غنی‌سازی مواد غذایی فرآیندی است که طی آن ریزمغذی‌هایی مانند ویتامین‌ها، مواد معدنی، اسیدهای چرب ضروری و ترکیبات فعال زیستی به محصولات غذایی افزوده می‌شوند تا کمبودهای تغذیه‌ای جبران و نیازهای فیزیولوژیک بدن تأمین گردد. این رویکرد به‌عنوان یکی از مؤثرترین راهکارها برای کاهش شیوع بیماری‌های ناشی از کمبود ریزمغذی‌ها از جمله بری بری، پلاگر و راشیتیسم شناخته می‌شود. با این حال، افزودن مستقیم این ترکیبات به مواد غذایی با چالش‌هایی مانند پایداری کم، حلالیت محدود، فراهمی زیستی پایین و حساسیت بالا به شرایط فرآوری مواجه است. فناوری درون پوشانی به‌عنوان روشی نوین توانسته است بسیاری از این محدودیت‌ها را برطرف کند. درون پوشانی موجب افزایش پایداری، محافظت در برابر عوامل محیطی، بهبود جذب و امکان رهاسازی کنترل‌شده ریزمغذی‌ها در دستگاه گوارش می‌شود. روش‌های متداول درون پوشانی شامل خشک‌کن پاششی، خشک‌کن انجمادی، امولسیون، اکستروژن و بستر سیال است که هرکدام مزایا و کاربردهای خاصی دارند. این مقاله مروری با هدف بررسی اهمیت غنی‌سازی مواد غذایی، نقش ریزمغذی‌ها در سلامت بدن و مزایای فناوری درون پوشانی تهیه شده است. نتایج نشان می‌دهد که به‌کارگیری هم‌زمان غنی‌سازی و درون پوشانی می‌تواند به‌عنوان یک استراتژی موثر در برنامه‌های سلامت عمومی مورد توجه قرار گیرد و توسعه پژوهش‌های بیشتر در این حوزه ضروری است.