UDC: 616.391:615.356
Review article

HYPERVITAMINOSIS AS A PUBLIC HEALTH ISSUE IN THE ERA OF DIETARY SUPPLEMENTS

Gjylai ALIJA[1]*, Merita DAUTI[1], Drita HAVZIU[1], Arlinda HAXHIU-ZAJMI[1], Sihana AHMETI - LIKA[1], Meral FERATI[2], Driton SELMANI[2], Qail IBRAHIMI[1]

[1*,1] *Department of Pharmacy, Faculty of Medical Sciences, State University of Tetova, Tetova R. N. M.*
[,2] *Clinical Hospital Tetovo, Department of Gynecology and Obstetrics, University of Tetovo, Faculty of Medical Sciences, Tetovo, Republic of Macedonia*
[,2] *Faculty of Medical Sciences University of Tetovo, Tetovo, Republic of Macedonia*
[*] *Corresponding Author: e-mail: gjylai.alija@unite.edu.mk*

Abstract

The rise in global dietary supplement use has raised alarms about the risks of consuming too many vitamins. Excessive vitamin intake, often from supplements, can lead to hypervitaminosis, a state with considerable health dangers, despite their necessity for bodily processes.
Excessive vitamin intake, despite vitamins' essential role in bodily functions, can lead to toxicity and severe health issues. Vitamins fall into two categories: water-soluble (such as vitamin C and the B-complex) and fat-soluble (A, D, E, and K). Water-soluble vitamins are typically eliminated via urine when taken in excess, whereas fat-soluble vitamins tend to accumulate in adipose tissue and the liver, heightening the danger of toxicity.
To stay healthy, adhere to daily nutrient guidelines and consult a healthcare provider before taking any supplements.
Biochemical tests, like blood vitamin levels, and dietary assessments are used to confirm hypervitaminosis.
Treatment aims to cease the troublesome supplement and modify eating patterns, with medical supervision reserved for dire situations.
Electronic databases such as PubMed, Scopus, and Google Scholar were utilized for a narrative review. The study encompassed articles released concentrating on vitamin toxicity, the overuse of supplements, and their broader public health consequences.
Fat-soluble vitamins, are commonly linked to toxicity because they build up in the body. High-dose supplements are more readily obtainable, and the absence of medical supervision plays a major role in the heightened risk.
In summary, vitamins are essential for health, yet overconsumption carries notable dangers. A public health concern is hypervitaminosis. To reduce these hazards, improved regulatory frameworks, public education, and expert advice are required.

Keywords: Vitamins, Hypervitaminosis, Toxicity, Dietary supplements, Public health

Introduction

Maintaining bodily functions, growth, and overall well-being depends on proper nutrition. This requires a balanced intake of macronutrients (proteins, carbohydrates, fats, and water) as well as micronutrients (vitamins and minerals). These elements are essential for maintaining the body's structural integrity, generating energy, supporting the immune system, and regulating metabolic processes. The use of dietary supplements has grown considerably in recent decades, largely due to increased awareness of health, disease prevention, and wellness trends. Vitamins, as essential micronutrients, are commonly consumed through both diet and supplements. However, the belief that vitamins are always safe, irrespective of dosage, has led to their excessive and sometimes inappropriate use (Alex, 2020)
Vitamins are organic compounds that are essential nutrients typically obtained from food. They play a crucial role in the proper functioning of the human body. The human body utilizes vitamins for various important processes, including the synthesis of biochemicals such as

enzymes, hormones, and neurotransmitters, as well as metabolism, energy production, and antioxidant activities.

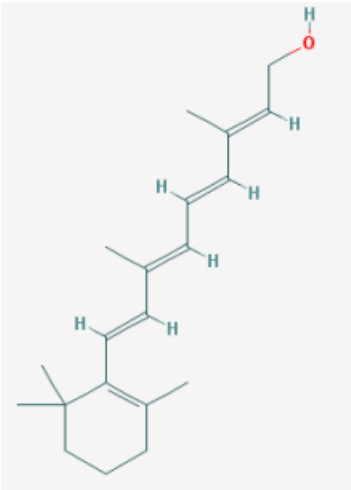
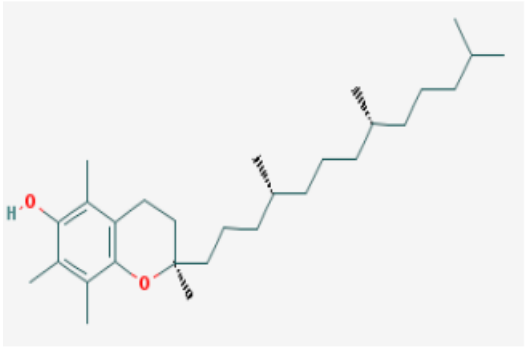
Vitamins are sorted into two primary classes by their solubility:

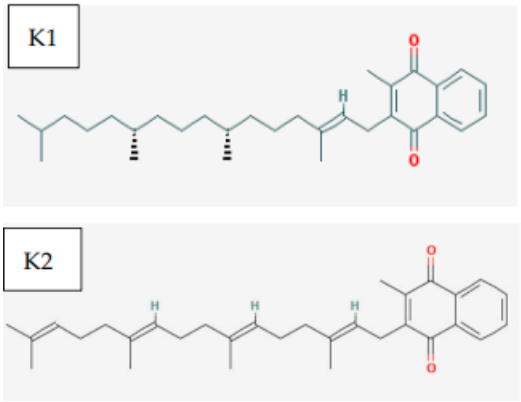
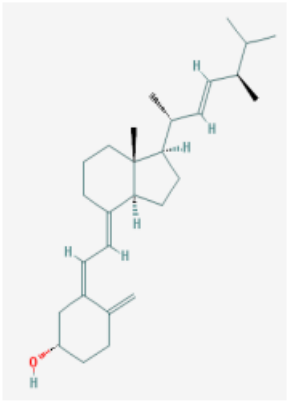
Fat-soluble vitamins: Comprising Vitamins A, D, E, and K, they are absorbed with dietary fats and accumulate in the body's fat stores and liver. While vital for numerous roles, surplus amounts can build up and may cause toxicity.

Water-soluble vitamins: This group includes Vitamin C and the B-complex family. In contrast to fat-soluble vitamins, they are not stored extensively in the body and are eliminated through urine, requiring regular dietary intake (Gropper, & Smith, 2020; Alija et al. 2024, Nicolov et al. 2021)

The 2D formulas and the main biological functions for all hydro- and lipo-soluble vitamins analyzed in the current study are presented in Table 1.

Table 1. 2D structural formulas and the main biological functions for lipo-soluble vitamins (Nicolov et al. 2021)

Vitamin A- Retinol- C20H28O2, MW = 233.43 g/mol, Carotenoide; beta carotene. - an essential substance that the hum an essential substance that the human body requires in small amounts for several processes, such as proper functioning of the visual system, reproduction, growth and development, immune system, cell structure, growth, differentiation, apoptosis and regeneration. It also regulates the metabolism of lipids, proteins and carbohydrates. 	**Vitamin E** α-tocoferol—$C_{28}H_{48}O_2$, MW = 416.68 g/m β-tocoferol—$C_{28}H_{48}O_2$, MW = 416.68 g/mol, γ-tocoferol—$C_{28}H_{48}O_2$, MW = 416.68 g/mol, δ-tocoferol—$C_{27}H_{45}O_2$, MW = 430.71 g/mol It protects several substances from oxidation by free radicals, having anti-ageing properties - involved in maintaining the normal morphology of erythrocytes; has anti-platelet, anti-inflammatory, and anti-proliferative properties and can induce a protective role for several pathologies such as cardiovascular, neurological and immunological diseases 
Vitamin K—includes 2 natural vitamins: vitamin K1 —phylloquinone —C31H46O2, MW = 450.7 g/mol and vitamin K2 — menaquinone-4 — C31H40O2, MW= 444.6 g/mol Plays a key role in the coagulation process; deficiency can induce bleeding problems, while when taken orally, natural sources of vitamin K1 seem without major side effects,	**Vitamin D**—Ergocalciferol (D2)—C28H44O, MW = 396.65 g/mol and cholecalciferol (D3)—C27H44O, MW = 348.648 g/mol. Vitamin D can either be synthesized from a cholesterol precursor in the skin (vitamin D3) after sunlight exposure (considered a prohormone) or it can be taken from dietary sources (vitamin D3 or D2);

although increased coagulation was observed in patients taking warfarin 	has an important role in maintaining the balance of calcium and phosphate circulating levels within the body, contributing to bone mineralization, muscle contraction and other functions 

Nevertheless, excessive or extended usage of vitamins—whether fat-soluble or water-soluble—can cause the body to accumulate and become poisonous, a disease called hypervitaminosis.
In instances of acute poisoning resulting from vitamin supplements or medications, prompt medical care is crucial to counteract the toxic effects and restore normal organ function. Timely and accurate diagnosis plays a vital role in effectively managing hypervitaminosis and aiding in the safe removal of excess vitamins from the body. Although dietary supplements are typically designed to promote health, they are not universally safe for all individuals. Like pharmaceutical medications, supplements containing active ingredients can have physiological effects that may lead to adverse reactions or harmful interactions, especially in sensitive individuals.
Careful monitoring of potential side effects and interactions is essential to prevent serious medical complications. Healthcare professionals recognize that many individuals use dietary supplements and regularly inquire about their usage during consultations. This knowledge is crucial for delivering safe, effective, and tailored medical treatment (Alie de Boer, 2022).
Vitamins come in a range of forms, from syrups and tablets to capsules and powder packets, offered by drug makers and supplement brands to suit personal health requirements. Consuming these vitamins correctly is key to avoiding deficiencies and supporting overall wellness.
Hypervitaminosis, or vitamin toxicity, happens when vitamins accumulate far beyond safe levels in the body, causing detrimental effects. This condition is commonly the outcome of taking too many vitamin supplements rather than from normal food consumption.
Clinical features of hypervitaminosis span from subtle complaints like nausea, headache, and fatigue to serious outcomes such as liver toxicity, kidney dysfunction, neurological issues, and heart-related problems. At-risk groups, notably children, expectant mothers, and older adults, are especially susceptible (Roop, 2018).
Data from the National Health and Nutrition Examination Survey (NHANES) conducted between 2003 and 2006 revealed that 33% of the U.S. population aged 1 year and older took a multivitamin supplement within a given month. Similarly, a 2009 survey indicated that 56% of U.S. consumers used vitamins or supplements, with 44% taking them daily. This widespread usage highlights the importance of understanding the potential risks associated with excessive vitamin intake (Elango et al. 2015)

The rapid growth of the dietary supplement market, along with assertive marketing techniques and easy availability over the counter, has led to concerns about unmanaged consumption. This trend emphasizes the importance of assessing hypervitaminosis not just as a clinical issue but also as an increasing public health concern (James 2014)
This review aims to analyze the current evidence on hypervitaminosis and evaluate its implications in light of the rising use of dietary supplements.

Methods

Electronic databases such as PubMed, Scopus, and Google Scholar were utilized for a narrative review. The study encompassed articles released concentrating on vitamin toxicity, the overuse of supplements, and their broader public health consequences.

Results

Vitamins Associated with Toxicity
Fat-soluble vitamins are frequently associated with hypervitaminosis because they can be stored in body fat and the liver.
Vitamin A: Long-term excessive intake can lead to liver damage, increased pressure in the skull, and birth defects.
Vitamin D: Intake beyond recommended levels can result in elevated calcium levels in the blood, kidney problems, and calcification of blood vessels.
Vitamin E: Large amounts may disrupt blood clotting and heighten the risk of bleeding.
Vitamin K: Although uncommon, toxicity can impact anticoagulant treatments.

Hypervitaminosis A- It denotes an excess amount of vitamin A in the body. Vitamin A is crucial to maintain strong vision health. Additionally, it acts as a potent antioxidant that preserves the health of our brain, heart, brain, and skin. Vitamin A toxicity can arise from overusing supplements. The toxicity can be acute or chronic. Acute toxicity may bring bone pain, diminished vision, and skin issues. But if it becomes chronic, it can harm the liver, kidneys, bones, and brain.
Thus, keeping vitamin A at healthy levels is important by eating vitamin-rich foods such as yellow and orange fruits and vegetables, dark green leafy greens, egg yolks, cheese, milk, and organ meats like liver.
Some signs of vitamin A toxicity include irritability, nausea, vomiting, abdominal cramps, blurred vision, reduced appetite, cracked and dry skin that itches, hair loss, weakened immunity, mouth ulcers, and bone swelling and discomfort.
The primary treatment for hypervitaminosis A involves immediately discontinuing vitamin A supplements and adhering strictly to prescribed doses. Early intervention can prevent further complications and facilitate recovery (Sarı, 2019).

Hypervitaminosis D- Vitamin D serves as another essential nutrient for preserving healthy bone density, robust renal immunity, cardiovascular health, and brain wellness. It participates in numerous biochemical processes occurring within the body. Vitamin D aids the uptake of calcium and phosphorus, which is necessary to keep bones and teeth strong. A deficiency of vitamin D links to a higher risk of infections and illnesses.
Vitamin D toxicity cannot arise from dietary sources. It is mostly observed in individuals who take large amounts of vitamin D supplements over an extended period. Toxicity is reached when blood levels exceed 150 ng/ml.
Elevated vitamin D in the body raises calcium levels as well. It can trigger nausea, vomiting, constipation, abdominal discomfort, and loss of appetite. High vitamin D increases calcium but

lowers vitamin K2 in the body, a player in bone metabolism. This can weaken bones, cause excessive calcium leakage from bone into the bloodstream, making bones porous, soft, and prone to osteoporosis. Since kidneys are crucial in vitamin D metabolism, high vitamin D levels may also lead to renal failure.
Therefore, vitamin D capsules should be taken with careful monitoring.
Earlier investigations in North Macedonia have chiefly examined vitamin status, especially vitamin D deficiency, rather than vitamin toxicity.

Hypervitaminosis E- Vitamin E is celebrated for its strong antioxidant function in the body. It helps lower the risk of numerous cancers, brain disorders, and heart diseases, while supporting healthy blood vessels and skin.
Vitamin E is plenty in nuts, olive oil, olives, seeds, seed oils, mango, spinach, and broccoli. People also commonly use Vitamin E to keep skin healthy, lessen signs of aging, reduce wrinkles, strengthen hair, and boost immunity.
However, excessive supplement use can lead to vitamin E toxicity. It may cause blood thinning and bleeding. Since it participates in the blood clotting action of vitamin K, high levels could raise the risk of heart issues, excessive bleeding, and hemorrhage (figure 6).

Hypervitaminosis K - Vitamin K plays a crucial role in the body's blood clotting process. It serves as a cofactor for numerous clotting factors and is necessary for the production of coagulation proteins. The body stores vitamin K in two active forms—K1 (phylloquinone) and K2 (menaquinone).
Vitamin K1 is produced in green leafy vegetables such as turnip, spinach, cauliflower, cabbage, broccoli and is also present in cow's milk, soy oil, canola oil, and olive oil. Vitamin K2 is created by intestinal bacteria within the body. Both forms are generally safe for most individuals when taken orally or injected into a vein. Side effects are minimal for most people who follow the physician's recommended daily amount. High doses of vitamin K can worsen clotting issues linked to severe liver disease. Vitamin K toxicity is possible only with vitamin K3, which can cause hemolytic anemia by inhibiting glutathione function and potentially leading to the buildup of reactive oxygen species.

Public health

The growing use of dietary supplements presents new challenges for public health systems globally. While vitamins are crucial for normal bodily functions, their excessive and uncontrolled intake has made hypervitaminosis an emerging public health issue. This concern is particularly relevant given the rapidly expanding supplement market, where high-dose formulations are readily available without stringent regulatory oversight (WHO, EFSA).
A major public health issue related to hypervitaminosis is the common misconception that vitamins are safe at any dosage. This belief is bolstered by marketing strategies that promote supplements as beneficial for health and disease prevention. Consequently, individuals often self-medicate and take multiple supplements at once without professional advice, which raises the risk of cumulative toxicity (Starr, 2015; Bailey et al. 2011).
One significant public health issue related to hypervitaminosis is the common belief that vitamins are safe in any quantity. This notion is supported by marketing tactics that promote supplements as essential for health and disease prevention. Consequently, many individuals self-medicate and take various supplements without consulting professionals, raising the risk of cumulative toxicity.
An additional concern is the increasing strain on healthcare systems. Although cases of vitamin toxicity are often underreported, they can result in severe health issues, such as liver damage,

kidney dysfunction, and metabolic problems. These complications may necessitate hospitalization and ongoing treatment, leading to higher healthcare costs and resource use. Moreover, the nonspecific symptoms of hypervitaminosis can cause delays in diagnosis and treatment (Marcinowska-Suchowierska et al. 2018; Dickinson et al. 2014).
Certain populations are especially vulnerable. Children may receive excessive doses due to improper supplementation practices, while older adults often take multiple supplements alongside prescribed medications, heightening the risk of negative interactions. Pregnant women are another high-risk group, as excessive intake of specific vitamins, particularly vitamin A, is linked to teratogenic effects (Manson et al. 2018).

Discussion

The results of this review highlight that hypervitaminosis is a growing yet often overlooked concern. While vitamins are vital for health, excessive intake—particularly through supplements—can lead to serious negative effects.
The increasing use of dietary supplements is a significant factor. Many people take supplements without professional consultation, frequently surpassing recommended upper intake levels. Furthermore, the belief that "natural" products are always safe compounds the issue.
Another key aspect is the lack of stringent regulation in the supplement industry in various areas. Unlike pharmaceutical drugs, dietary supplements typically do not undergo thorough pre-market assessment, resulting in the widespread availability of high-dose products.
Healthcare professionals have an important role in tackling this issue by educating patients, overseeing supplement consumption, and recognizing early signs of toxicity.

Table 2. General Overview of Fat-Soluble Vitamins and Potential Risks (Based on Selected Literature)

Vitamin	High dose	Main Physiological Role	Risk of Excess Intake	Notes from Literature	References
Vitamin A	>10,000 IU/day	Vision, immune function	Chronic toxicity (liver damage)	Vitamins are essential but require balanced intake	(Alex, 2020; Alie de Boer, 2022)
Vitamin D	>50,000 IU/day	Calcium metabolism, bone health	Hypercalcemia due to overdose	Uncontrolled supplementation increases risk	(Alex, 2020; Alie de Boer, 2022)
Vitamin E	>400 IU/day	Antioxidant, cellular protection	Impaired coagulation at high doses	Protective role but dose-dependent	(Alie de Boer, 2022)
Vitamin K	Very high doses	Blood clotting	Interactions with anticoagulants	Important for maintaining hemostasis	(Alie de Boer, 2022)

A study conducted by Penniston and colleagues in 2006 indicated that hypervitaminosis A is a recognized result of excessive intake of preformed vitamin A, mainly from supplements. Prolonged toxicity is linked to liver injury, bone demineralization, and neurological signs. The condition underscores the narrow therapeutic range of fat-soluble vitamins.
A study by Atanasova Boshku (2025) examined vitamin D levels and supplement usage among pregnant women, highlighting a high level of supplement intake despite a prevalent deficiency. Although hypervitaminosis was not specifically investigated, the findings underscore the

importance of careful monitoring of vitamin supplementation to prevent potential negative effects.

In 2005, Edgar et al. noted that hypervitaminosis E is rare but can occur due to extended high-dose supplementation. Excess vitamin E can interfere with vitamin K-dependent clotting factors, raising the risk of bleeding. The majority of reported adverse effects are associated with pharmacological doses rather than typical dietary intake.

In 2018, author Roop noted that hypervitaminosis K can occur with excessive use of the synthetic form, menadione. Clinical signs of this toxicity may include jaundice, elevated bilirubin levels, and hemolytic anemia.

Shearer, in 2012, indicated that hypervitaminosis K is uncommon in adults, although it can result from excessive intake of synthetic vitamin K (menaquinone or menadione). Elevated levels can affect anticoagulant therapy and disturb the body's normal coagulation balance. Natural dietary vitamin K seldom leads to toxicity.

Conclusion

In an effort to address poor diets or vitamin deficiencies, many individuals resort to excessive consumption of vitamin supplements without consulting medical professionals, nutritionists, or dieticians. While vitamin supplements can be beneficial, excessive intake, whether of fat-soluble or water-soluble vitamins, can lead to accumulation in body tissues and fluids, causing toxicity and hypervitaminosis.

Water-soluble vitamins usually carry a lower risk of toxicity because the body eliminates excess amounts in urine. In contrast, fat-soluble vitamins like A, D, E, and K can accumulate and cause intoxication syndrome, with more severe health consequences. Hypervitaminosis is frequently addressed by boosting urine production and cutting back on vitamin supplement intake.

Hypervitaminosis highlights the need for a balanced vitamin intake. Although vitamins are essential for well-being, overconsumption can trigger serious health problems. Guidance on prudent supplement use, knowledge of vitamin-rich dietary sources, and routine medical check-ups can avert this condition. By recognizing the dangers linked to hypervitaminosis and taking proactive steps, people can manage their nutritional needs safely and sustain peak health.

From a regulatory standpoint, dietary supplements are typically categorized as food products instead of pharmaceuticals, which restricts the level of pre-market safety assessment. This regulatory limitation permits high-dose products to be introduced to the market without adequate proof of safety and effectiveness. As a result, there is a need for enhanced regulatory frameworks and better labeling standards.

Education and awareness are important strategies for addressing this issue. Public health initiatives should highlight the potential harm of excessive vitamin consumption. Healthcare professionals are essential in advising on proper supplement usage and recognizing early signs of toxicity.

In conclusion, hypervitaminosis is a complex public health issue that necessitates coordinated efforts, which may include better regulation, increased public education, and heightened clinical awareness.

References

[1]. Alex M (2020) ‘Role of nutrition in maintaining health’ International Journal of Physical Education, Sports and Health; 7(4): 279-280 E-ISSN: 2394-1693

[2]. Alie de Boer (2022) ‘Nutrition and health’ Applied food science (pp.385-406), DOI:10.3920/978-90-8686-933-6_17

[3]. Alija Gj., Dauti M., Havziu D., Haxhiu-Zajmi A., Nuhii N., Ibrahimi Q. (2024) “Human Health and Importance of Nutrition” Acta Medica Balkanica International Journal of Medical Sciences Vol.9 / No.17-18 / ISSN: 2545 - 4110 UDC: 613.2:616-084 pp 147-155 Professional paper
[4]. Bailey RL, Gahche JJ, Lentino CV, (2011) “Dietary supplement use in the United States. J Nutr. ;141(2):261–266.
[5]. Boshku Aleksandra Atanasova 1, Vasko Aleksovski 2, Krstevska Slagana Simeonova 1, Nikolovska Elena Gjorgievska 1, Igor Samardjiski 1, Markova Ana Daneva 1, (2025) “Vitamin D status among pregnant women of North Macedonia: Assessing deficiency rates and associated risks factors” J Med Biochem Sep 5;44(6):1183-1190 doi: 10.5937/jomb0-55601.
[6]. Dickinson A, MacKay D. (2014) “Health habits and supplement use in older adults” Nutrients. ;6(10):4336–4352.
[7]. Edgar R Miller 3rd 1, Roberto Pastor-Barriuso, Darshan Dalal, Rudolph A Riemersma, Lawrence J Appel, Eliseo Guallar (2005) “Meta-analysis: high-dosage vitamin E supplementation may increase all-cause mortality” Ann Intern Med Jan 4;142(1):37-46. doi: 10.7326/0003-4819-142-1-200501040-00110. Epub 2004 Nov 10.
[8]. Elango G., Venkataraman D.D., Venkata Rao S. and Ravi Kiran V.S. (2015). Hypervitaminosis. International Journal of Biomedical Research ; 6(03): 151-154.
[9]. European Food Safety Authority. 2012 Tolerable upper intake levels for vitamins and minerals. EFSA Journal.
[10]. Ewa Marcinowska-Suchowierska 1, Małgorzata Kupisz-Urbańska 1, Jacek Łukaszkiewicz 2, Paweł Płudowski 3, Glenville Jones (2018) “Vitamin D toxicity – a clinical perspective” Front Endocrinol. 9:550.
[11]. Gropper, S. S., & Smith, J. L. (2020). Advanced Nutrition and Human Metabolism (7th ed.). Cengage Learning
[12]. James b. Mowry, pharmd, daniel a. Spyker (2015) Annual Report of the American Association of Poison Control Centers’ National Poison Data System (NPDS): 32nd Annual Report. Clinical Toxicology 53(10): 962–1146. DOI: 10.3109/15563650.2015.1102927
[13]. Kristina L Penniston 1, Sherry A Tanumihardjo (2006) “The acute and chronic toxic effects of vitamin A” Am J Clin Nutr . Feb;83(2):191-201. doi: 10.1093/ajcn/83.2.191.
[14]. M J Shearer 1 (2012) “Vitamin K metabolism and nutriture” Blood Rev Jun;6(2):92-104. doi: 10.1016/0268-960x (92)90011-e.
[15]. Manson JE, Bassuk SS. (2018) Vitamin and mineral supplements: what clinicians need to know. JAMA. ;319(9):859–860.
[16]. Nicolov, M.; Cocora, M.; Buda, V.; Danciu, C.; Duse, A.O.; Watz, C.; Borcan, F. (2021) Hydrosoluble and Liposoluble Vitamins: New Perspectives through ADMET Analysis. Medicina, 57, 1204. https://doi.org/10.3390/ medicina57111204
[17]. Roop JK. (2018) Hypervitaminosis—an emerging pathological condition. Int J Health Sci Res. ;8(10):280-288
[18]. Sarı HK. (2019) Hypervitaminosis A. Eurasian J Toxicol. 1(3):85-90.
[19]. Starr RR. (2015) Too little, too late: ineffective regulation of dietary supplements in the United States. Am J Public Health. ;105(3):478–485.
[20]. World Health Organization. 2006 Guidelines on food fortification with micronutrients. Geneva: WHO.