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REVIEW ARTICLE

Vitamin D and Effective Mechanisms in the Control of Body Weight

Burçak TOK[1], Engin ŞAHİN[2], Esen TAŞĞIN[3,*]

[1] *Bayburt University, Faculty of Health Sciences, Department of Nutrition and Dietetics, Bayburt, Turkiye*
[2] *Bayburt University, Faculty of Health Sciences, Department of Nutrition and Dietetics, Bayburt, Turkiye*
[3] *Atatürk University, Faculty of Health Sciences, Department of Nutrition and Dietetics, Erzurum, Turkiye*

** Corresponding author E-mail: esent25@atauni.edu.tr*

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ABSTRACT

Recently, hypovitaminosis D and obesity have reached large masses worldwide simultaneously. The number of studies linking two public health problems is increasing day by day. Vitamin D deficiency and related disorders are among the leading problems. A stronger perspective is that vitamin D deficiency causes obesity. Obesity is becoming a rapidly increasing health problem today. Particularly, studies have shown that obese individuals are at risk for Vitamin D deficiency and that increasing Body Mass Index leads to a decrease in Vitamin D levels. It is known that adipocyte tissue stores soluble vitamin D. Vitamin D affects the growth and differentiation of adipose tissue through different mechanisms. It could lead to many factors such as changes in leptin-ghrelin levels, parathyroid hormone level, calcium level, vitamin D accumulation in adipose tissue to these mechanisms. Various studies have been conducted to understand the link between abdominal obesity and blood levels of vitamin D3. Waist circumference, which is an important indicator of fat accumulation in the abdominal area, is significantly affected by the level of vitamin D3. In addition, regular vitamin D intake also affects the release of Leptin and Ghrelin. This study aims to examine vitamin D and its effective mechanisms in body weight control, the roles of vitamin D on adipocyte cells, the relationship of hormones such as ghrelin and leptin with vitamin D and their relationship with fat oxidation.

Contents

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1. Introduction

Obesity (BMI - Body Mass Index >30) is a pathological disease marked by excessive body weight as a result of the buildup of fat mass brought on by genetic mutations, inactivity, endocrine problems, imbalance, and malnutrition. [1] The fact that obesity is linked to chronic disorders such the metabolic syndrome, diabetes, hypertension, renal diseases, cardiovascular diseases, and cancer makes it a global health concern. Over the past 50 years, obesity rates have shown an increasing prevalence. More than 650 million individuals were thought to have obesity in 2016, and further than 340 million children and adolescents were overweight or obese [2].

Several investigations have shown vitamin inadequacies in obese people, including deficiencies in vitamin B1, folic acid, and vitamin D [3–5]. Although vitamin D is primarily recognised for its effects on bone health and calcium balance, new research has revealed a biological role in immune modulation, inflammation and cell differentiation [6–8]. Although vitamin D is primarily recognized for its roles in calcium balance and bone health, new research has revealed that it also has a biological role in immune modulation, inflammation, and cell differentiation [9].

This study revealed the effect of vitamin D on adipocyte cells, the relationship between leptin and ghrelin hormones and vitamin D, and effective mechanisms in ß-oxidation and body weight control.

2. Vitamin D and Obesity

Several clinical and observational studies have shown that low levels of vitamin D in the blood are associated with the formation of belly fat and obesity [10, 11]. It has been discovered that circulating 25(OH)D3 levels decrease by 1.15 percent for every unit rise in body mass index [12]. The possibility of vitamin D3 deficiency in obese people increases with excess adiposity, according to certain research, which also shows that the link between high BMI and vitamin D3 insufficiency is independent of vitamin D supplementation and diet [13, 14].

Waist circumference is a key indicator of abdominal fat accumulation [15]. To comprehend the connection between abdominal obesity and blood vitamin D3 levels, several investigations have been carried out. In the meta-analysis by Hajhahemy et al., the response to vitamin D given at different doses was observed. This meta-analysis found that the risk of abdominal obesity decreased by 8% for every 25 nmol/L rise in vitamin D levels. Also, this research demonstrated a correlation between each 25 nmol/L rise in blood vitamin D levels with a 10% lower risk of central obesity in the study groups [16].

Rodríguez-Rodríguez et al. [14]demonstrated that waist circumference was importantly greater in women with low serum vitamin D3 than in women with higher serum vitamin D3.. 0.29 nmol/L decrease in vitamin D was found for each 1 cm increase in waist circumference [17].

3. Effect of Vitamin D on Adipose Cells

While researchs examining the relationship between vitamin D insufficiency and nutritional status have increased over the last decade, there has also been a large increase in meta-analyses examining how adding vitamin D to diets affects parameters related to adiposity, weight gain or weight loss [17–20]. Adipogenesis leads to the differentiation of mature adipocytes as a result of different events and causes adipocyte hypertrophy which causes obesity. Several studies have revealed that adipogenesis can be inhibited in preadipocytes exposed to 1,25(OH)2D, and 50% of triglyceride accumulation is not observed in exposed cells [21, 22].

Several ideas describe how vitamin D and adipogenesis are related. The first theory is that exposure to sunlight may decrease because obese individuals participate in fewer outdoor activities due to psychological reasons and use covering clothes compared to normal individuals, thus limiting the synthesis of vitamin D [23]. Nevertheless, multiple epidemiological studies have found that, when all factors are taken into account, this theory is insufficient to clarify the link between obesity and vitamin D insufficiency [24]. Another idea holds that some of the vitamin D and cholecalciferol metabolites are retained by excess body fat before they are transported to the liver and initially hydroxylated [6]. Also, the increased intake of 25(OH)D3 is supported by excess vitamin D activation enzyme alpha-1-hydroxylase in adipose cells. This theory contends that the quantity of subcutaneous body fat directly affects vitamin D stores [3, 25, 26].

According to some research, vitamin D deficiency or insufficiency can increase fat production. As vitamin D levels decrease, parathyroid hormone increases, and so being allowed calcium to enter adipocytes and trigger lipogenesis, supporting this theory [27].

The information acquired further showed that 1,25(OH)2D3 stimulates adipogenesis by blocking intracellular receptors of crucial adipogenesis molecular components that are reliant on vitamin D. As a result, increased preadipocyte development into adipocytes may result from low vitamin D reserves [28]. The enzyme that catalyzes the conversion of 25(OH)D to 1,25(OH)2D is encoded by the Cyp27b1 gene, and this gene has been identified in the adipose tissue of rats and humans [3]. Another study claims that vitamin D inhibits adipogenesis through a mechanism including peroxisome proliferator-activated receptor gamma (PPAR) and Vitamin D receptor [29]. Moreover, 1,25(OH)2D reduced cell development and the expression of PPAR and other adipocyte marker genes in a study using preadipocytes from guinea pigs (Lpl, Pck2, Scd) [30].

The connection between vitamin D metabolism and adipogenesis has been studied in various ways, including low sun exposure in obese people, vitamin D retention in adipose tissue, volumetric amount of vitamin D3 supplied on digestion or synthesized through the skin. Similarly, it is important in this connection enzymes of vitamin D3 metabolism in adipocytes, PTH, and calcium levels, and regulation of adiposity-related genes. Still, future studies are

demanded to understand the precise mechanisms responsible for this association and the effect of vitamin D addition on reducing obesity and abdominal fat (Table 1).

Table 1 Possible pathophysiological mechanisms; a) The effect of obesity on low vitamin D levels, b) The effect of low vitamin D levels on obesity

(a)	(b)
Volumetric dilution	Elevation of PTH levels
Retention of vitamin D in adipocytes	Decreased serum calcium level
Decreased expression of vitamin D	Regulation of leptin hormone
Decreased exposure to sunlight	Regulation of VDR gene

4. Vitamin D and Leptin/Ghrelin

4.1. Leptin and Vitamin D

Leptin called the satiety hormone, is produced by adipocytes. Leptin is involved in regulating energy homeostasis and is directly proportional to the proportion of adipose tissue [31]. The leptin interacts with vitamin D receptor (VDR), which has an autocrine-paracrine lipolytic effect, and so, effects adipocytes. In this metabolic process, lipid metabolism is regulated by blocking lipogenesis and inducing lipolysis [32].

In certain investigations on this subject, the impact of vitamin D supplementation on blood leptin levels has been investigated. The results of intervention studies showed that, in human adipose tissue culture, vitamin D directly decreases leptin release [33, 34]. Ghavamzadeh et al. [33] showed a significant increase in leptin levels ($p=0.046$) after 400 IU vitamin D supplementation for 14 weeks in individuals with Type 2 Diabetes. Ulutas et al. [35] reported that the use of 50,000 IU oral cholecalciferol once a week for 4-8 weeks significantly increased serum leptin levels in peritoneal dialysis patients with hypovitaminosis D ($p<0.05$) [36]. Contrary to these studies, some studies have shown different results. It was noted that leptin levels 12, 24, and 48 weeks after consuming 2000 IU of vitamin D did not significantly differ between HIV-1 infected individuals and those with hypovitaminosis D. ($p=0.609$) [37].

Adipocyte tissue stores vitamin D, which is soluble. The hypovitaminosis D observed in obese individuals may result from excess vitamin D trapped in adipocyte tissue [38]. As a result, vitamin D content in adipocyte tissue rises and so does its impact on adipocyte function and leptin expression. The inverse ratio of the reported vitamin D and serum leptin levels can be expressed by the high concentration of vitamin D in adipocyte tissue, which stimulates leptin secretion in obesity [39].

4.2. Ghrelin and Vitamin D

Previous studies have observed that serum ghrelin levels, which are mostly included in regulating food consumption and body weight, are reduced in individuals with high BMI and insulin resistance [40]. Cell culture studies have shown that there are specific receptors for vitamin D in stomach cells. Vitamin D supplementation effects the expression of many genes in the different parts of the stomach to control cell division and stomach hormone release. Though more studies are required to ensure a precise conclusion, a study observed that 1000 IU vitamin D supplementation daily for 12 weeks significantly increased ghrelin (71%) and leptin (84.1%) levels [41]. In conclusion, regular vitamin D intake can raise blood levels of ghrelin and leptin while lowering the ratio of leptin to ghrelin. The available data suggest that vitamin D addition may have a positive effect on appetite hormones and insulin sensitivity. Results from research on humans, however, are not conclusive.

5. The Effect of Vitamin D in ß-Oxidation

Cholecalciferol is a versatile hormone involved in different pathways that regulate gene expression and cause multiple effects on adipocytes. Vitamin D affects the growth and differentiation of adipose tissue by different mechanisms: (1) by inhibiting the expression of adipogenic transcription factor genes, preadipocyte differentiation is prevented; (2) Inhibition of fatty acid production by upregulating insulin-induced gene-2 expression; (3) lowering fatty acid synthase gene expression to reduce lipid buildup in vacuoles; and (4) apoptotic induction in mature preadipocytes [42–44]. Besides these findings, several studies claim that overexpression of VDR may inhibit preadipocyte differentiation [43].

Hence, it has been established that low blood vitamin D concentrations are effect growth of adipose tissue, which raises the risk of obesity. In contrast to these observations, some experimental research on animal and human adipose tissue suggests that vitamin D influences adipogenesis through transcriptional factors and the activation of gene expression in both an inhibitory and promoter manner [45]. As a result, research on the influence of vitamin D on adipogenesis has produced inconsistent results, and its pathophysiological significance in the differentiation and development of adipose tissue is still unknown. Increased PTH levels in vitamin D deficiency or insufficiency are other potential causes. PTH enhances lipogenesis via boosting calcium influx into adipocytes. Although, it also increases the synthesis of 1,25(OH)2D, the active vitamin D metabolite [45–47]. A crucial regulator of calcium metabolism is vitamin D, as well. Adipocyte fatty acid synthase expression has been demonstrated to be suppressed by increasing dietary calcium, which inhibits lipogenesis and promotes lipolysis [48].

In conclusion, vitamin D insufficiency may be linked to weight increase and excessive fat formation by its effects on PTH and calcium. However, the pathway by which vitamin D deficiency/insufficiency promotes obesity is not known exactly. More studies are needed to explain this relationship.

6. Vitamin D and Nutrition

Worldwide epidemiological studies have informed a widespread prevalence of vitamin D inadequate intakes [49]. In particular, vitamin D3 (cholecalciferol) is substantially more effective than vitamin D2 (ergocalciferol) for maintaining blood vitamin D levels and biological functions as well as raising serum 25(OH)D levels [50]. Therefore, vitamin D3 is the preferred form of an oral supplement to correct vitamin D deficiency [51]. Only a few foods contain vitamin D3. These are oily fish, mushrooms exposed to sunlight, milk, and eggs [52, 53]. Although being a natural source of vitamin D3, cod liver oil should not be consumed

in excessive amounts due to the vitamin A it contains and its possible interactions with heavy metals [54, 55].

According to previously released recommendations, vitamin D deficiency is defined as 25(OH)D levels below 20 ng/mL and vitamin D inadequacy as 20–30 ng/mL [56]. Values of Vitamin D meeting the requirements of ≥ 97.5 of the population for different age groups are shown in Table 2.

Table 2 The Recommended Amount of Nutrients (RDAs) [56]

Life Stage	RDA (IU/d) (Amount sufficient to meet the needs of 97.5% of the population)	Serum 25(OH) D3 Level (ng/ml) (corresponding to RDA)
Baby (1-12 months)	400	20
Age 1-70	600	20
Age +70	800	20
Pregnancy / Lactation Period	600	20

IU: International Unit, RDA: Recommended Food Consumption.

A recent publication, however, defines vitamin D deficiency as 25(OH)D values below 12 ng/mL and vitamin D inadequacy as 12–20 ng/mL. For the general population, concentrations between 20 and 50 ng/mL are regarded as safe and sufficient for bone health [56]. Although the US Institute of Medicine accepts these values, older people at risk of fractures and those with bone, renal, and digestive issues should have levels over 30 ng/mL [55, 57].

7. Conclusion

Serum vitamin D levels and obesity have a significant association, according to extensive epidemiological research. Up until now, research has concentrated on the pathophysiological reasons for the relationship between obesity and low vitamin D levels. Many factors such as gene polymorphisms, changes in leptin-ghrelin levels, volumetric dilution, increased parathyroid hormone level, decreased calcium level, vitamin D retention in adipose tissue, and decreased vitamin D expression have led to these mechanisms. More research is still needed to determine the specific processes behind the bidirectional association between blood vitamin D status and obesity as well as the therapeutic benefits of utilizing vitamin D supplements to decrease the percentage of fat tissue.

Healthcare professionals, such as physicians and Nutritionists, should assess low serum vitamin D status in obese individuals and properly address the requirement for addition and prohibition of vitamin D deficiency/insufficiency.

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Conflict of Interest

The authors declared no conflict of interest.

References

[1] Greco EA, Lenzi A, Migliaccio S. Role of hypovitaminosis D in the pathogenesis of obesity-induced insulin resistance. *Nutrients* **11**(7):1506.
[2] WHO. *Obesity and overweight* (2015) [cited 2019 Aug 11]. Available from: https://www.who.int/news-room/fact-sheets/detail/obesity-andoverweight.
[3] Wood RJ. Vitamin D and adipogenesis: new molecular insights. *Nutrition reviews* (2008) **66**(1):40–46.
[4] Kerns JC, Arundel C, Chawla LS. Thiamin deficiency in people with obesity. *Advances in nutrition* (2015) **6**(2):147–153.
[5] Kant AK. Interaction of body mass index and attempt to lose weight in a national sample of US adults: association with reported food and nutrient intake, and biomarkers. *European journal of clinical nutrition* (2003) **57**(2):249–259.
[6] Cheng S. Adiposity, cardiometabolic risk, and vitamin D status: the Framingham Heart Study. *Diabetes* (2010) **59**(1):242–248.
[7] Arabi A, Rassi R, Fuleihan G-H. Hypovitaminosis D in developing countries—prevalence, risk factors and outcomes. *Nature Reviews Endocrinology* (2010) **6**(10):550–561.
[8] Yetley EA. Assessing the vitamin D status of the US population. *The American journal of clinical nutrition* (2008) **88**(2):558–564.
[9] D'Aurizio F, Villalta D, Metus P, Doretto P, Tozzoli R. Is vitamin D a player or not in the pathophysiology of autoimmune thyroid diseases? *Autoimmunity reviews* (2015) **14**(5):363–369.
[10] Fornari R. Lean mass in obese adult subjects correlates with higher levels of vitamin D, insulin sensitivity and lower inflammation. *Journal of endocrinological investigation* (2015) **38**:367–372.
[11] Liu S, Song Y, Ford ES, Manson JE, Buring JE, Ridker PM. Dietary calcium, vitamin D, and the prevalence of metabolic syndrome in middle-aged and older US women. *Diabetes care* (2005) **28**(12):2926–2932.
[12] Vimaleswaran KS. Causal relationship between obesity and vitamin D status: bi-directional Mendelian randomization analysis of multiple cohorts. *PLoS medicine* (2013) **10**(2):1001383.
[13] Greene-Finestone LS, Garriguet D, Brooks S, Langlois K, Whiting SJ. Overweight and obesity are associated with lower vitamin D status in Canadian children and adolescents. *Paediatrics & child health* (2017) **22**(8):438–444.
[14] Rodríguez-Rodríguez E, Navia B, López-Sobaler AM, Ortega RM. Vitamin D in overweight/obese women and its relationship with dietetic and anthropometric variables. *Obesity* (2009) **17**(4):778–782.
[15] Després JP. Abdominal obesity and the metabolic syndrome: contribution to global cardiometabolic risk. *Arteriosclerosis, thrombosis, and vascular biology* (2008) **28**(6):1039–1049.
[16] Hajhashemy Z, Shahdadian F, Ziaei R, Saneei P. Serum vitamin D levels in relation to abdominal obesity: a systematic review and dose–response meta-analysis of epidemiologic studies. *Obesity Reviews* (2021) **22**(2):13134.
[17] McGill A-T, Stewart JM, Lithander FE, Strik CM, Poppitt SD. Relationships of low serum vitamin D3with anthropometry and markers of the metabolic syndrome and diabetes in overweight and obesity. *Nutrition journal* (2008) **7**(1):1–5.
[18] Pathak K, Soares MJ, Calton EK, Zhao Y, Hallett J. Vitamin D supplementation and body weight status: a systematic review and meta-analysis of randomized controlled trials. *Obesity Reviews* (2014) **15**(6):528–537.
[19] Lotito A, Teramoto M, Cheung M, Becker K, Sukumar D. Serum parathyroid hormone responses to vitamin D supplementation in overweight/obese adults: a systematic review and meta-analysis of randomized clinical trials. *Nutrients* (2017) **9**(3):241.

[20] Mallard SR, Howe AS, Houghton LA. Vitamin D status and weight loss: a systematic review and meta-analysis of randomized and nonrandomized controlled weight-loss trials. *The American journal of clinical nutrition* (2016) **104**(4):1151–1159.
[21] Ishida Y, Taniguchi H, Baba S. Possible involvement of 1α, 25-dihydroxyvitamine D3 in proliferation and differentiation of 3T3-L1 cells. *Biochemical and biophysical research communications* (1988) **151**(3):1122–1127.
[22] Pannu PK, Zhao Y, Soares MJ. Reductions in body weight and percent fat mass increase the vitamin D status of obese subjects: a systematic review and metaregression analysis. *Nutrition Research* (2016) **36**(3):201–213.
[23] Sato M, Hiragun A. Demonstration of 1α, 25-dihydroxyvitamin D3 receptor-like molecule in ST 13 and 3T3 L1 preadipocytes and its inhibitory effects on preadipocyte differentiation. *Journal of cellular physiology* (1988) **135**(3):545–550.
[24] Pereira-Santos M, F Costa PR, Assis A, S T Santos CA, Santos DB. Obesity and vitamin D deficiency: a systematic review and meta-analysis. *Obesity Reviews* (2015) **16**(4):341–349.
[25] Mosekilde L. Vitamin D and the elderly. *Clinical endocrinology* (2005) **62**(3):265–281.
[26] Clarke NM, Page JE. Vitamin D deficiency: a paediatric orthopaedic perspective. *Current opinion in pediatrics* (2012) **24**(1):46–49.
[27] Martini LA, Wood RJ. Vitamin D status and the metabolic syndrome. *Nutrition reviews* (2006) **64**(11):479–486.
[28] Li J, Byrne ME, Chang E, Jiang Y, Donkin SS, Buhman KK, et al. 1alpha,25-Dihydroxyvitamin D hydroxylase in adipocytes. *The Journal of steroid biochemistry and molecular biology* (2008) **112**(1-3):122–126. doi:10.1016/j.jsbmb.2008.09.006.
[29] Zhuang H, Lin Y, Yang G. Effects of 1, 25-dihydroxyvitamin D3 on proliferation and differentiation of porcine preadipocyte in vitro. *Chemico-biological interactions* (2007) **170**(2):114–123.
[30] Crujeiras AB, Carreira MC, Cabia B, Andrade S, Amil M, Casanueva FF. Leptin resistance in obesity: an epigenetic landscape. *Life sciences* (2015) **140**:57–63.
[31] Abbas MA. Physiological functions of Vitamin D in adipose tissue. *The Journal of steroid biochemistry and molecular biology* (2017) **165**:369–381.
[32] van Etten E, Mathieu C. Immunoregulation by 1,25-dihydroxyvitamin D3: basic concepts. *The Journal of steroid biochemistry and molecular biology* (2005) **97**(1-2):93–101. doi:10.1016/j.jsbmb.2005.06.002.
[33] Ghavamzadeh S, Mobasseri M, Mahdavi R. The effect of vitamin D supplementation on adiposity, blood glycated hemoglobin, serum leptin and tumor necrosis factor-α in type 2 diabetic patients. *International journal of preventive medicine* (2014) **5**(9):1091.
[34] Menendez C. Retinoic acid and vitamin D3 powerfully inhibit in vitro leptin secretion by human adipose tissue. *Journal of endocrinology* (2001) **170**(2):425–432.
[35] Ulutas O, Taskapan H, Taskapan MC, Temel I. Vitamin D deficiency, insulin resistance, serum adipokine, and leptin levels in peritoneal dialysis patients. *International urology and nephrology* (2013) **45**:879–884.
[36] van den Bout-van den Beukel CJP, van den Bos M, Oyen WJG, Hermus ARMM, Sweep FCGJ, Tack CJJ, et al. The effect of cholecalciferol supplementation on vitamin D levels and insulin sensitivity is dose related in vitamin D-deficient HIV-1-infected patients. *HIV medicine* (2008) **9**(9):771–779. doi:10.1111/j.1468-1293.2008.00630.x.
[37] Wortsman J, Matsuoka LY, Chen TC, Lu Z, Holick MF. Decreased bioavailability of vitamin D in obesity. *The American journal of clinical nutrition* (2000) **72**(3):690–693.
[38] Tschop M, Weyer C, Tataranni PA, Devanarayan V, Ravussin E, Heiman ML. Circulating ghrelin levels are decreased in human obesity. *Diabetes* (2001) **50**(4):707–709.
[39] St-Pierre DH. Association of acylated and nonacylated ghrelin with insulin sensitivity in overweight and obese postmenopausal women. *The Journal of Clinical Endocrinology & Metabolism* (2007) **92**(1):264–269.
[40] Matsuzawa Y, Funahashi T, Nakamura T. Molecular Mechanism of Metabolic Syndrome X: Contribution of Adipocytokines· Adipocyte-derived Bioactive Substances. *Annals of the New York Academy of Sciences* (1999) **892**(1):146–154.
[41] Kong J, Li YC. Molecular mechanism of 1, 25-dihydroxyvitamin D3 inhibition of adipogenesis in 3T3-L1 cells. *American Journal of Physiology-Endocrinology and Metabolism* (2006) **290**(5):916–924.
[42] Earthman CP, Beckman LM, Masodkar K, Sibley SD. The link between obesity and low circulating 25-hydroxyvitamin D concentrations: considerations and implications. *International journal of obesity* (2012) **36**(3):387–396.
[43] Rayalam S, Della-Fera MA, Ambati S, Yang JY, Park HJ, Baile CA. Enhanced effects of 1, 25 (OH) 2D3 plus genistein on adipogenesis and apoptosis in 3T3-L1 adipocytes. *Obesity* (2008) **16**(3):539–546.
[44] Mutt SJ, Hyppönen E, Saarnio J, Järvelin MR, Herzig KH. Vitamin D and adipose tissue—more than storage. *Frontiers in physiology* (2014) **5**:228.
[45] Parikh SJ. The relationship between obesity and serum 1, 25-dihydroxy vitamin D concentrations in healthy adults. *The Journal of Clinical Endocrinology & Metabolism* (2004) **89**(3):1196–1199.
[46] Querfeld U. Antagonistic effects of vitamin D and parathyroid hormone on lipoprotein lipase in cultured adipocytes. *Journal of the American Society of Nephrology* (1999) **10**(10):2158–2164.
[47] Zemel MB, Shi H, Greer B, Dirienzo D, Zemel PC. Regulation of adiposity by dietary calcium. *The FASEB Journal* (2000) **14**(9):1132–1138.
[48] Mensink G. Mapping low intake of micronutrients across Europe. *British journal of nutrition* (2013) **110**(4):755–773.
[49] Tripkovic L. Comparison of vitamin D2 and vitamin D3 supplementation in raising serum 25-hydroxyvitamin D status: a systematic review and meta-analysis. *The American journal of clinical nutrition* (2012) **95**(6):1357–1364.
[50] Belenchia AM, Tosh AK, Hillman LS, Peterson CA. Correcting vitamin D insufficiency improves insulin sensitivity in obese adolescents: a randomized controlled trial. *The American journal of clinical nutrition* (2013) **97**(4):774–781.
[51] Macdonald HM. Contributions of sunlight and diet to vitamin D status. *Calcified tissue international* (2013) **92**:163–176.
[52] Lentjes M, Mulligan AA, Welch AA, Bhaniani A, Luben RN, Khaw KT. Contribution of cod liver oil-related nutrients (vitamins A, D, E and eicosapentaenoic acid and docosahexaenoic acid) to daily nutrient intake and their associations with plasma concentrations in the EPIC-Norfolk cohort. *Journal of Human Nutrition and Dietetics* (2015) **28**(6):568–582.
[53] Muscogiuri G. Vitamin D and chronic diseases: the current state of the art. *Archives of toxicology* (2017) **91**:97–107.
[54] Smutna M, Kruzikova K, Marsalek P, Kopriva V, Svobodova Z. Fish oil and cod liver as safe and healthy food supplements. *Neuroendocrinology Letters* (2009) **30**(1):156.
[55] Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP. Endocrine Society. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* (2011) **96**:1911–1930.
[56] Ross AC, Taylor CL, Yaktine AL, Valle H. Committee to review dietary reference intakes for vitamin D and calcium. *Food and Nutrition Board* (2011).
[57] Giustina A. Consensus statement from 2 nd International Conference on Controversies in Vitamin D. *Reviews in Endocrine and Metabolic Disorders* (2020) **21**:89–116.