

DOI: <https://doi.org/10.56936/18290825-18.2024-4>**DIET THERAPY FOR TYPE 2 DIABETES: THE ROLE OF SPECIFIC NUTRIENTS AND DIETARY PRINCIPLES****NOSIĆ M.^{1,2}, BANJARI I.^{1*}, JURIŠIĆ-ERŽEN D.^{3,4}**¹ Department of Food and Nutrition Research, Faculty of Food Technology, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia² Department of Nursing, Faculty of Health Studies, University of Rijeka, Rijeka, Croatia³ Department of Internal Medicine, Faculty of Medicine, University of Rijeka, Rijeka, Croatia⁴ Department of Endocrinology and Diabetology, University Hospital Centre, Rijeka, Croatia*Received 14.11.2023; Accepted for printing 15.12.2023***ABSTRACT**

Due to the increase of diabetic patients, especially type 2, we are now facing a global pandemic. Diet control is the first line of treatment, and if planned well, can delay or alleviate its complications, both micro- and macrovascular.

One of the main postulates in diabetes mellitus type 2 treatment is nutrition education, glycaemic self-control and eventual adjustment of drug dosage. When making suggestions to individuals about diet therapy it is very important to consider various individual, social and economic characteristics.

There is no perfect diet for diabetics, or a dietary regime, which would properly reflect a person's individual needs, from clinical presentation to everyday life. There is no perfect diet therapy suitable for every type 2 diabetic. However, the so-called diabetic diet, avoiding the consumption of simple carbohydrates and refined starches, is recommended to the majority of patients.

Therefore, anyone planning a diet for a type 2 diabetic should familiarize themselves with the effects of macro- and/or micro-nutrients which have a clinical impact on type 2 diabetes.

Dietary therapy for patients with type 2 diabetes offers special dietary regimens such as the Mediterranean diet, low-fat diet, vegetarian and vegan diets.

This review provides insights into particular nutrients and some dietary regimens, including the Mediterranean diet, intermittent fasting and the Dietary Approach to Stop Hypertension diet.

INTRODUCTION

Diabetes is one of the most serious and the most common endocrine conditions with life-long consequences [Heald AH et al., 2020]. Diabetes is a general term for heterogenic metabolic disorders which consequently cause chronic hyperglycaemia. Diabetes is mainly caused by insulin excretion disorder or by insulin action disorder, al-

though, in most cases a combination of both factors prevail [Petersmann A et al., 2019]. According to the World Health Organization (WHO) there are several types of diabetes. Besides the most common type 2 diabetes (DMT2) and type 1 (DMT1) there are hyperglycaemia first detected in pregnancy, hybrid forms of diabetes and other specific

CITE THIS ARTICLE AS:

NOSIĆ M., BANJARI I., JURIŠIĆ-ERŽEN D. (2024). Diet therapy for type 2 diabetes: The role of specific nutrients and dietary principles; The New Armenian Medical Journal, vol.18(1), 4-17;

DOI: <https://doi.org/10.56936/18290825-18.2024-4>

ADDRESS FOR CORRESPONDENCE:

Ines Banjari, PhD, Assoc. Prof.

Department of Food and Nutrition Research, Faculty of Food Technology, Josip Juraj Strossmayer University of Osijek
18 Franje Kuhača Street, Osijek 31000, Croatia

Tel. (+385 31) 224 339

E-mail: ibanjari@ptfos.hr

TABLE 1

Types and subtypes of diabetes mellitus [WHO, 2019]

Main Types	Subtypes
Type 1	
Type 2	
Hyperglycaemia first detected in pregnancy	- diabetes in pregnancy - gestational diabetes
Hybrid forms	- slowly developing immuno-intermediated diabetes of adults - Type 2 prone to ketosis
Other specific types	- monogenic diabetes - diabetes caused by drugs or chemical reagents - exocrine pancreas diseases - diabetes related to infections - endocrine disorders - forms associated with specific immunological diseases - other genetic syndromes associated with diabetes

types of diabetes (e.g. monogenic diabetes, diabetes caused by drugs or chemical reagents) (Table 1) [WHO, 2019]. Additionally, the so-called non-classified diabetes and is used only temporarily if there is no clear diagnostic presentation.

EPIDEMIOLOGY: One among ten adult individuals has diabetes which amounts to approximately 61 million people. Amazingly, one among three diabetics is not aware of their disease. Every 8 seconds one person dies from diabetes in the age range of 20-79 years. It has been reported that 4.2 million people in the world die from consequences of diabetes [IDF, 2021]. It is estimated that by the year 2045, the number of diabetics will increase by 46%. At the moment, 10.5% of the adult population in the world suffer from diabetes. The International Diabetes Federation predicted an increase of diabetics from 536.6 million (2021) to 783.2 million (2045) [IDF, 2021].

METABOLIC CHANGES AND COMPLICATIONS OF DMT2: Various microvascular and macrovascular complications are characteristic of diabetes. Microvascular complications are diabetic nephropathy, retinopathy and diabetic polyneuropathy. Macrovascular complications include myocardial infarction, stroke and peripheral arterial disease. Diabetics are at two to ten times higher risk for developing macrovascular complications. Damage to coronary and cerebral arteries are considered as the leading causes of mortality among diabetic pa-

tients. Damage of the kidneys, eyes and nerves are far more frequent than the previously mentioned macrovascular complications, with a more significant influence on mortality among diabetics [Cole JB, Florez JC, 2020; Russel WR et al., 2016; Lazarou C et al., 2012]. According to one study, around 50% of people are either diagnosed with diabetes or have a positive family history for diabetes [Banjari I et al., 2023]. Non-alcoholic fatty disease and DMT2 share some pathophysiology processes, so it should be no surprise that almost 60% of patients with non-alcoholic fatty disease patients are also diagnosed with DMT2 [Smuglov EP et al., 2023].

PRINCIPLES OF DIET THERAPY USED IN DMT2

TREATMENT: One of the main postulates in DMT2 treatment is nutrition education, glycaemic self-control and eventual adjustment of drug dosage. In the last 40 years, a positive influence has been shown of structured nutritional therapy education on metabolic control and acute complications in type 1 and type 2 diabetics. To ensure successful implementation of nutrition education, additional factors need to be considered such as where diabetics live, work, gain new knowledge and spend free time. The right diet is an integral part of diabetic care, which can be considered as the core of diabetes treatment. Over time, it has become obvious that diabetics who implement rules of proper nutrition in daily life have improved outcomes of their diabetic treatment as well as quality of life [Powers MA et al., 2021]. When making suggestions to individuals about diet therapy it is very important to consider various individual, social and economic characteristics. There is no perfect diet therapy suitable for every type 2 diabetic [Evert AB et al., 2019]. However, the so-called diabetic diet, avoiding the consumption of simple carbohydrates and refined starches, is recommended to the majority of patients.

ROLE OF PARTICULAR NUTRIENTS IN DMT2 MANAGEMENT

Carbohydrates: Monosaccharides have a rapid blood entry, e.g. glucose, fructose and galactose, but disaccharides (e.g. sucrose and lactose) and polysaccharides (e.g. starch), first need to degrade, primarily to glucose, to enter the blood. The total daily amount of energy, 45-60% originates from

carbohydrates. Fruits, vegetables, legumes and whole grains, due to high content of complex carbohydrates, should be prioritized in a daily diet. Another favourable feature of these foods is high content of dietary fiber. Recommended daily intake of fiber should range between 25 and 30 g/day, but can be higher for men or specific cases, like in weight reduction diets. Daily recommendations of dietary fiber are 25 to 30 grams daily. Half of the dietary fiber needs to be in the soluble form (e.g. pectin, inulin) from fruit and vegetable sources. A ratio of 15 grams of carbohydrates to 3 grams of dietary fiber can be used as a feasible guide. Soluble dietary fiber and resistant starch give more energy in comparison to insoluble dietary fiber. Around 50% of dietary fiber in daily meals needs to originate from cereals, 30-40% from vegetables, and around 16% from fruits [Malkki Y, 2004]. Type 2 diabetics had their blood glucose level reduced by 1.2, 2.2 and 2.3 mmol/L as a result of β -glucans consumption in the amount of 4.0, 6.0 and 8.4 grams [Dungan KM et al., 2009]. During stress situations, hormones are synthesized in the liver, such as cortisol and catecholamine as well as cytokines which consequently increase blood glucose [ADA, 2021]. There is empirical evidence that obesity leads to insulin resistance which is a characteristic of DMT2. Therefore, it is very important that all meals are rich in dietary fiber in diabetic therapy. Decrease in blood glucose level leads to decrease of insulin resistance. That way, blood pressure as well as lipid levels can be made to decrease. Nutritional therapy of patients should be rich in dietary fiber, low in fat amounts and have a limited amount of protein. The diet must be adapted to medication or insulin therapy as well as to organ damage, if present.

Every diabetic should follow a daily dietary plan (dietary pattern) and go through dietary counselling and fundamental education about nutrition basics. Body mass should be measured approximately once a week. Self-measurement of blood glucose concentration in serum with glucose home monitors provide patients with knowledge on how to adjust food choices to expected range of blood glucose concentrations. That way, patients can avoid undesirable changes in blood glucose concentration due to changes in meal

times, physical activity or medication. There is also an alternative way of measuring glucose concentration by patient's urine. If the glucose concentration is more than 10 mmol/L, kidneys excrete glucose in urine. Research shows that regular measuring of blood glucose level on daily basis is in positive correlation to HbA_{1c} value in DMT1 and DMT2. It is still not clear what the optimal level of blood glucose is for diabetics. For type 2 diabetics who are on insulin, ADA recommends daily measuring of blood glucose concentration. Diabetics who regulate blood glucose concentration just by medication should measure blood glucose concentrations before breakfast and two hours postprandial one or two times a week. Diabetics treated with medication and insulin therapy should measure blood glucose before every meal and before bedtime one or two days a week. As an alternative, patients using medication and insulin, can measure once daily but in different times of the day. Despite various recommendations, it is obvious that insulin dependent patients should measure blood insulin concentration far more frequently than those who are non-insulin dependent. Diabetes monitoring is an important part of therapy; it provides information on blood glucose concentration before and after meals throughout the day and about foods in meals, their quantities and frequency of consumption (e.g. stress conditions, physical activities or some acute illnesses) [Chiu S et al., 2014; ADA, 2022; Sanchez J et al., 2023]. Replacing carbohydrates by the same quantity of fructose resulted in a significant decrease (0.53%) in HbA_{1c} concentration. Fructose intake should be supervised because an increase of fructose intake leads to the increase of hepatic lipids as well as Glutamate – Pyruvate Transaminase [St-Onge MP, 2005].

Fats: Daily consumption of fats should not exceed 35% of the total energy intake for diabetics. Saturated fats (e.g. from animal foods) or unsaturated fats (from e.g. plant foods), have an upper limit of 10% of the whole energy intake. Possible risk factors for development of DMT2 are saturated fats and high total fat intake. Possible protective factors are ω -3 fatty acids. Fatty acids with a higher number of double bonds (e.g. ω -fatty acids) are more susceptible to oxidation and have a negative impact on body cells causing oxidative stress. Therefore recommendations for

omega-3 fatty acids are lower than for simple unsaturated fatty acids. ω -3 fatty acids (e.g. arachidonic acid) are named essential fatty acids because our organism is not able to synthesise them, so it is totally dependent on the daily food intake [Meikle PJ, Summers SA, 2017]. Saturation and fatty acid chain length are the “biosignature” of insulin resistance, together with pro-inflammatory cytokines [Evans RM et al., 2004]. PPARs (Peroxisome Proliferator-Activated Receptors) are initiated through the presence of fatty acids and influence the glucose level in plasma because they regulate gene expression associated with glucose metabolism [Villarreal-Renteria AI et al., 2022]. Short chain fatty acids are absorbed in blood in an easier way than long chain fatty acids. Trans-fatty acids have a negative effect on human health and their origin is in industrial processes of fat hydrogenization. These types of acids have to be less than 1% of daily energy intake. Medium Chain Fatty Acids (e.g. in milk, fat, coconut oil) come into the liver through portal vein in comparison to Long Chain Fatty Acids (e.g. olive oil, fish, nuts, avocado) which first undergo esterification and after it incorporate in chylomicrons. The liver is the site of Medium Chain Fatty Acid oxidation, where it will be used as a source of glucose. Diabetics usually have a low level of HDL and a high level of LDL and atypical level of triglycerides. Supplementation of ω -3-fatty acids (e.g. in soya oil, salmon) lower the level of triglycerides [Barre DE et al., 2008; Koloveryou E et al., 2014; Roopashree PG et al., 2021]. If ω -3-fatty acids are taken at meal times, it lowers the blood lipid levels in DMT2. It is a lot easier to substitute saturated fatty acids with polyunsaturated fatty acids in daily dietary habits in comparison to introducing of low fat food. Eating habits can influence the structure of the lipids cell-membrane and consequently have a positive influence on insulin action especially taking Mediterranean diet into consideration [Schröder H, 2007; Ooi E et al., 2015]. If saturated fatty acids are more often replaced with unsaturated fatty acids, insulin sensitivity is improved. ω -6 fatty acids (e.g. in sunflower oil) are able to decrease levels of LDL cholesterol in comparison to mono-saturated fatty acids (e.g. in olive oil) [Kratz M et al., 2002; Guadarrama-López AL et

al., 2014]. Daily meals abundant in Eicosapentaenoic acid (EPA) and Docosahexaenoic acid (DHA) is recommended for type 2 diabetics, which can decrease postprandial insulin action. During diet, rich in mono-unsaturated fatty acids (e.g. in avocados and olives) HDL cholesterol is significantly increased [Liu G et al., 2019]. Stone fruit has a very low concentration of saturated fatty acids a lot of monounsaturated fatty acids (e.g. oleic acid) and polyunsaturated fatty acids, so stone fruit is able to decrease LDL-concentration and reduce cholesterol absorption. Stone fruit has a positive impact on inflammation factors in the human organism (e.g. CRP, IL-6). There are a lot of inflammation inhibitors in stone fruit such as ω -3-fatty acids, dietary fiber magnesium and arginine. Arginine is a substrate for enzyme NO-Synthase (Nitric Oxide Synthase) because it produces Nitric Oxides (NO) which is very important in vascular motility [Gannon MC, Nuttall FQ, 2006; Salas-Salvadó J et al., 2006].

Proteins: Although proteins are not capable of increasing blood glucose level, they can provoke insulin excretion. It is well known from the 1920's, that after the ingestion of 50 grams of animal protein, glucose was stable for the next 5 hours. This can be explained by the fact that synthesis of glucose from proteins via gluconeogenesis, is a very slow process [Zhao WT et al., 2018]. The amount of energy obtained from low protein or high protein diet has no effect on glycaemic variability of type 2 diabetics [Virtanen HEK et al., 2017]. High protein intake through prolonged period of time, unfortunately, leads to insulin resistance but low protein intake has the opposite effect. Animal proteins which originate from meat (e.g. fabricated red meat) are in correlation with an increase in DMT2 and inversely animal proteins from dairy products (e.g. yoghurt) are in correlation with the decrease. Plant proteins (e.g. legumes) always have the opposite effect than animal proteins which originate from red meat, which could be to some extent explained through the fact that plant proteins are usually surrounded by some important bioactive compounds (e.g. polyphenols). Egg proteins significantly correlated with lower risk for the development of DMT2 [Potier M et al., 2009]. Branched-chain amino acids (BCAA) of plasma (e.g. valine, leucine and isoleucine) are increased

with food intake and have positive effects on glucose control in type 2 diabetics, influencing discharge of ghrelin, leptin and GLP-1 [Chen Z et al., 2020]. Residents of some sea boarding countries (e.g. Greenland) have a lower number of DMT2 cases due to frequent fish intake. Proteins should be reduced in relation to kidneys impairment. Necessary reduction of body weight can be obtained by the increase of protein content in daily energy intake from 15-20% to 25-32% if kidneys are functioning properly [Koppes LLJ et al., 2005].

Alcohol: There is a U-shaped relationship between high alcohol consumption (>48 g/day) and insulin resistance which is crucial for the metabolic syndrome and diabetes [Ajani UA et al., 2000]. Daily recommendation of alcohol intake for persons living with DMT2 is 20 g/day (e.g. two glasses of wine) for men and 10 g/day for women at least 3-4 days per week [Hendriks HFJ. 2007]. This protective effect of alcohol, when consumed according to daily recommendations, is probably caused by high excretion of adiponectin and by anti-inflammatory effects in various organs [Shai I et al., 2007]. In a research conducted on type 2 diabetics, the recommended amount of wine (150 ml/day through 3 months) resulted in a significant decrease of fasting blood glucose level (9.2%) as well as HbA_{1c} concentration and LDL-cholesterol concentration. When choosing wine it is important to choose “dry wines” because their sugar content is very low in comparison to “sweet wines” because the majority of sugar is fermented into alcohol. When drinking “dry wines”, according to recommendations, there is a negligible risk of excessive sugar consumption [Knott C et al., 2015]. Reasonable consumption of alcoholic beverages, as part of the Mediterranean diet is related to lower risk of DMT2 [Pedersen-Bjergaard U et al., 2005]. Large consumption of alcohol can decrease blood glucose, especially during the night, so a meal is recommended prior drinking alcohol [Poudel RR et al., 2017].

Minerals: Zinc has a role in synthesis and excretion of insulin. Zinc-Insulin complexes are present in the pancreas cells (both α and β) and after insulin excretion, zinc is in the free form and incorporates again in the pancreatic tissue. Zinc protects pancreatic β -cells from oxidative stress and inflammation and reduces lipid peroxi-

dation because it protects thiol (-SH) groups [Maret W, 2008; Wang Y et al., 2020]. Selenium is able to simulate insulin functioning and get involved in metabolic pathways like glycolysis, glycogenesis, fatty acid synthesis and pentose phosphate pathway. It is suggested that selenium has a preventive influence on DMT2 through its antioxidative potential. When selenium is used as a food supplement, it has become obvious that levels of oxidative stress (and NF- κ B) decreases [Campbell SC et al., 2008; Mokgalaboni K, Phoswa WN, 2022]. Iron can catalyse hydroxyl radicals and impair lipids in the cell membrane, proteins and nucleic acids thus causing insulin resistance. Glucose production in the liver can be suppressed through iron (ferritin), accumulation in the liver, consequently leading to insulin resistance [Forouhi NG et al., 2007; Hajhashemy Z et al., 2022]. Patients with low blood concentrations of calcium have different concentrations of intracellular calcium concentration in pancreatic β -cells, which also consequently leads to insulin resistance [Pittas AG et al., 2007; Ekinçi EI et al., 2011]. Daily intake of sodium in type 2 diabetics should not be below 1,500 mg/day because of sodium excretion in the urine and increased registered number of deaths [Li L et al., 2022]. Lower sodium consumption has beneficial effects on HbA_{1c} regulation in type 2 diabetics [Chagas CEA et al., 2012].

Vitamins: Vitamin D controls calcium flow through the pancreatic β -cell membrane, and peripheral insulin cells [Chagas CEA et al., 2012]. There is a significant correlation between vitamin D deficiency and DMT2. Type 2 diabetics have lower concentrations of vitamin D in blood as compared to healthy individuals [Li L et al., 2022; Pittas AG et al., 2007]. *In vitro* studies showed that disturbances in insulin secretion correlate to decreased level of vitamin D in blood which can be corrected with vitamin D supplementation [Giulietti A et al., 2004], probably via vitamin D Receptors (VDR) present in pancreatic β -cells [Ortlepp JR et al., 2003; Zeitz U et al., 2003]. Vitamin D Receptors regulates up to 3% of the human genome which includes genes responsible for glucose and lipid metabolism as well as for blood pressure regulation [Freundlich M et al., 2008]. Vitamin D Receptors can be present in 38 various

types of tissue (e.g. intestine, kidneys, parathyroid glands) where it controls genes related to oxidative damage, chronic diseases and inflammation processes [Haussler MR et al., 2008]. Vitamin D Receptors gene mutations showed a strong correlation to insulin resistance in animal and human models [Ortlepp JR et al., 2003; Zeitz U et al., 2003]. Vitamin D deficiency elevates parathyroid hormone level and consequently elevates calcium level. The elevated calcium level hinders insulin binding on Glucose Transporter Type 4, but disables their ingestion in cells [Alvarez JA, Ashraf A, 2010]. Vitamin D has a negative correlation to cytokines (e.g. TNF- α , IL-6) which are associated with insulin sensitivity through Peroxisome Proliferator-Activated Receptor [Galmés S et al., 2018]. Vitamin E, in comparison to other fat soluble vitamins (D, K and A), is relatively non-toxic. Vitamin E taken regularly as a supplement, showed a significant decrease of fasting glucose and HbA_{1C} concentrations after a three month intake. The most important role of vitamin E is accumulation of Reactive Oxygen Species which consequently inhibit peroxidation of polyunsaturated fatty acids integrated in membrane lipids [Shinde SN et al., 2011]. Vitamin E also has a role in insulin sensitivity and decreases blood glucose and HbA_{1C} [Landrier JF et al., 2009].

Probiotics: There are certain anomalies in the intestinal microbiome of type 2 diabetics. A few microorganisms, among which is bacteria *Akkermansia muciniphila*, which are capable of dietary fiber fermentation into short-chain fatty acids, primarily butyrate as well as [McFarland LV et al., 2018]. Butyrate has a property of a signalling molecule which regulates excretion of pro-inflammatory cytokines (e.g. interleukin-18), satiety through glucagon-like peptide 1 and histone acetylase inhibitor. If probiotics, with similar composition of intestinal anaerobic bacteria as in healthy individuals, were taken by type 2 diabetics, butyrate production and glycaemic control can be improved. Probiotics can serve as a good alternative instead of microbiome transplantation since it appears to have promising effects [Koh A et al., 2016; Kolodziejczyk AA et al., 2019]. An increased number of *Akkermansia muciniphila* correlates significantly with the usage of the antidiabetic drug metformin, and it is considered to serve as a good sup-

port for this drug [Shin NR et al., 2013]. Research from 2020 showed that a probiotic formulation WBF-011 (containing dietary fiber inulin, *Akkermansia muciniphila*, *Clostridium beijerinckii*, *Clostridium butyricum*, *Bifidobacterium infantis* and *Anaerobutyricum hallii*) showed a significant decrease in postprandial glucose concentration [Kasińska M, Drzewoski J, 2015; Zhang Q et al., 2016; Yao K et al., 2017; Tao Y et al., 2020]. Probiotics (containing genera *Lactobacillus* and *Bifidobacterium*) showed a decrease in fasting glucose in type 2 diabetics [Bock PM et al., 2021; Rittipahiroj T et al., 2021]. That could be explained by the fact that short chain fatty acids (e.g. propionate, acetate and butyrate) in the gut microbiota, bind on GPR-43 (G-Protein-Coupled Receptor 43) and induce excretion of the hormone GLP-1, which stimulates insulin production in type 2 diabetics [Tilg H, Moschen AR, 2014].

SPECIFIC DIETARY REGIMENTS AND DMT2 MANAGEMENT

Mediterranean Diet: The main characteristic of this type of diet is the consumption of unprocessed foods such as cereal, legumes, vegetables, nuts, fruits and fish. It is an eating pattern rich in fats mainly from simple unsaturated fatty acids from olive oil. Red meat is consumed in low amounts. Milk and dairy products can be consumed in low to moderate amounts. Alcohol (e.g. red wine) can be consumed during the main meals in moderate amounts. In order to emphasize the multicultural importance of the Mediterranean diet, we can name the Mediterranean cuisine of Croatia, Morocco, Cyprus, Spain, Greece, Italy and Portugal which have become a non-material cultural heritage of the United Nations Educational, Scientific and Cultural Organization (UNESCO) since the year 2013. Regarding fats, olive oil has a special place in this diet and minimum of four spoons are recommended daily. Saturated fatty acids are in disproportion to unsaturated fatty acids which represent the main fat sources. Fats should represent 30% of total energy intake. When it comes to fruits and vegetables, a minimum of 5 portions of fruit and vegetables are required daily. Seasonal fruits and vegetables should be eaten in raw form if possible. Vegetables should be included in almost every meal of the day. A maximum of tree portions of nuts (e.g. walnuts, hazel-

nuts, almonds and peanuts) are recommended. Regarding dairy products, maximum two portions are required daily and low fat dairy products should be given preferential treatment (e.g. low fat cheese). Regarding cereal products, 1-2 portions are required in the main meal and whole grain cereals are recommended. Some cereal products (e.g. rice, couscous, pasta without eggs) should be consumed interchangeably. Considering legumes (e.g. kidney beans, green peas, soybeans), the recommendation is to consume them 3 times per week. In the category of "fish, meat and eggs", fish should be eaten more frequently (minimum 3 portions per week) in comparison to meat (2-3 portions per week). Poultry (2-3 portions per week), should be consumed more, in comparison to red meat. Processed meat products (e.g. ham, sausages, salami) should be consumed less than 70 g/day. Eggs can be used as an alternative to fish and meat, and recommendations are 2-4 eggs per week. Sweets should be consumed to a maximum of 3 portions per week and should be replaced by fresh fruit if possible. Alcoholic beverages (e.g. wine) should be consumed daily, two glasses for men and one glass for women. Non-alcoholic, sweet beverages should be avoided [Bach-Faig A et al., 2011; Banjari I et al., 2013; Mattioli AV et al., 2017]. Mediterranean diet showed positive correlation to glycaemic variability [Wheeler ML et al., 2012], and it is considered as a Low Carb Diet. This principle was shown to be the best method to decrease fasting blood glucose, consequently reducing HbA_{1c} concentration [Schwingshackl L et al., 2018a; Neuenschwander M et al., 2019]. Close monitoring of metabolic indicators (e.g. glucose, lipids, uric acid) in diabetics practicing the Mediterranean diet is recommended [Schwingshackl L et al., 2018b]. Decreased consumption of carbohydrates resulted in lower HbA_{1c} concentration during 12 months or longer adherence to this principle [Snorgaard O et al., 2017].

Low Fat Diet: The goal of a low fat diet is to restrict fat consumption to 60g/day or 500kcal/day. At the beginning of this type of diet, low fat sweets are not averted, but if individuals have a problem with losing weight, low fat sweets should be restricted. The basic requirement for weight loss is a daily intake of water or another energy free beverage in the amount of 2-3 litres daily. Even high fat foods (e.g. cheese, chips, sausages)

can be consumed if the initial requirement for the total fat consumption is satisfied. Regardless of this, the consumption of saturated fats will decrease. Since carbohydrates carry majority of the energy, consumption of dietary fiber, folic acid, vitamin C, magnesium and potassium is achieved. To ensure sufficient vitamin E intake, olive oil is recommended [Jéquier E, Bray GA, 2002]. All foods that have 3 g of fat per 100 kcal are considered as low-fat foods (e.g. legumes, fruits vegetables, chicken breasts without skin, seafood) [Roust LR et al., 1994; Bhandari P, Sapra A, 2023]. Recommended foods include low fat milk and dairy, lean meat, starchy vegetables (e.g. potatoes, beans, sweet potatoes) and whole grain cereals (e.g. whole grain oats, wheat, rice) [Van Zuuren EJ et al., 2018; Goldenberg JZ et al., 2021]. This type of diet does not show such successful results in comparison to Low Carb Diet [Ge L et al., 2020].

Vegetarian and Vegan Diets: A vegetarian diet has a decreased level of total fats, saturated fatty acids and cholesterol. This type of diet is abundant in dietary fiber, magnesium, potassium, vitamins C and E, folic acid and flavonoids. On the other hand, it has a low content of proteins, saturated fats, ω -3-fatty acids, vitamin A, vitamin B12, zinc, iron and iodine [Craig WJ, 2009]. Various forms of vegetarian diet exist, with lacto-ovo vegetarian diet being the most frequent. In lacto-ovo vegetarian diet, animal foods such as milk (lacto) and eggs (ovo) are frequently eaten but meat, fish and related products are avoided. A lower intake of saturated fats and cholesterol and an increased intake of dietary fiber and phytochemicals is highly recommended [Craig WJ, Mangels AR, 2009]. Lacto-vegetarians generally avoid eating meat, fish and eggs. Ovo-vegetarians avoid eating meat, fish and milk. Pudding vegetarians frequently eat processed meat substitutes which have negative consequences to their health. Pesco-vegetarians are considered to eat more than 50 grams of fish daily. They eat milk, dairy products, eggs, fish and seafood. Vegans avoid consuming all animal products such as meat, fish, milk, honey and eggs. The vegan diet, in comparison to a vegetarian diet, has an increased daily intake of magnesium, folic acid, vitamin C, vitamin E, iron and phytochemicals. Compared to a vegetarian diet, it has a lower total daily energy intake, less saturated fats, cholesterol, ω -3-fatty acids, vitamin D,

calcium, zinc and vitamin B12. It is well known that vegetarians have a lower concentration of lipids in plasma compared to omnivores [Craig WJ, 2009; Chiu THT et al., 2018]. Vegetarian and Low Fat Vegan Diet positively correlate with glycaemic variability in type 2 diabetics only when reduction in body weight is achieved, which is the usual outcome of these diets [Kahleova H et al., 2011]. Vegetarian and Vegan Diet were able to decrease HbA_{1c} concentration from 0.3 to 0.4% in type 2 diabetics [Viguiliouk E et al., 2019].

THE DIETARY APPROACH TO STOP HYPERTENSION (DASH) REGIME

The DASH diet is a combination of low fat and high fruit and vegetable consumption. The daily intake of saturated fatty acids should be < 7%. The DASH diet reduces the total daily intake of sodium (no more than 2.3 mg of sodium) and consequently leads to a decrease in blood pressure [Sacks FM et al., 2001]. This type of diet encourages consumption of fruit, vegetables and low fat or fat free milk and dairy, as well as whole grain cereals, poultry, lean fish and nuts. Red meat, confectionary products and sweet drinks are not recommended. Therefore, the DASH diet is poor in saturated fatty acids, total fats and cholesterol, while at the same time being rich in potassium, magnesium, proteins and dietary fiber [Siervo M et al., 2015]. Because it is based on plant foods, it is generally accepted by vegetarians and vegans [Ha SK, 2014]. Besides drop in blood pressure, decrease of adipose tissue is expected due to high consumption of foods rich in dietary fiber [Sacks FM et al., 2001]. The DASH diet showed an improved HbA_{1c} concentration in type 2 diabetics [Azadbakht L et al., 2011; Jacobs S et al., 2015].

INTERMITTENT FASTING

Although intermittent fasting cannot be classified as an eating pattern, it should be mentioned in this review, because there has been a rising attention towards this matter among diabetics since the last few years [Evert AB et al., 2019]. Intermittent fasting is a wilful avoidance of food during a certain period of time. If this fasting is conducted well, there is no feeling of hunger [Longo VD, Mattson MP, 2014]. The breaks between meals can last from 16 to 48 hours. The most well-known intermittent fasting method is “alternative day fast-

ing” when in a period of two days per week which follow one another and only 20%-25% of energy requirement is consumed. The use of the Mediterranean diet eating pattern is recommended during the intermittent fasting. On fasting days it is recommended to drink a lot of beverages (at least 2 litres per day) without sugar (e.g. water, tea, coffee, instant hot chocolate, low in energy value) as well as eating small meals rich in nutrients and low in carbohydrates (e.g. dairy products with low fat content, unpeeled apples, nuts). There is also the “eat-stop-eat-method” where there is fasting two times per week between two lunch meals or between two dinners. Another method implies fasting from 10 to 20 hours, and breakfast is usually consumed. If breaks between meals are longer, the concentration of an enzyme, protein-kinase A, decreases which leads to effective cell recovery [Patterson RE et al., 2015]. Intermittent fasting decreases the glucose level in blood and improves insulin sensitivity as well as lipids profile. If there is a low energy intake in the morning, it consequently reduces the total energy intake for the whole day and there is no hunger in the afternoon because of the changes in the metabolic reactions. At the same time, an empty stomach stimulates autophagy [Barnosky AR et al., 2014].

CONCLUSION

There is no perfect diet therapy suitable for each type 2 diabetic. Dietary regimens should focus on providing appropriate ratios of macronutrients, including important micronutrients (vitamins and minerals), but more importantly be in line with person's clinical presentation of DMT2 and lifestyle. Accumulating evidence from nutrition interventions and observational studies provide important insights on how diet and particular nutrients affect clinical presentation of DMT2, not only blood glucose but also lipid status, body weight, and overall quality of life. Diet seems to be even more important in diabetes treatment than we thought so far. While previous recommendations for diet therapy of DMT2 focused primarily on carbohydrates (its dietary sources, composition and dietary fiber content), accumulating evidence in recent years show promising results with diets like low-fat or intermittent fasting; diets previously considered as irreconcilable with DMT2.

REFERENCES

1. Ajani UA, Gaziano JM, Lotufo PA, Hennekens CH, Buring JE, Manson JE, (2000). Alcohol consumption and risk of coronary heart disease by diabetes status. *Circ J.* 2000;102(5):500-505. doi: 10.1161/01.CIR.102.5.500.
2. Alvarez JA, Ashraf A, (2010). Role of vitamin D in insulin secretion and insulin sensitivity for glucose homeostasis. *Int J Endocrinol.* 2010;2010:351385. doi: 10.1155/2010/351385.
3. American Diabetes Association. *Standards of Medical Care in Diabetes-2021 Abridged for Primary Care Providers.* *Clin Diabetes.* 2021;39(1):14-43. doi: 10.2337/cd21-as01.
4. American Diabetes Association. *Standards of Medical Care in Diabetes-2022 Abridged for Primary Care Providers.* *Clin Diabetes.* 2022;40(1):10-38. doi: 10.2337/cd22-as01.
5. Azadbakht L, Pour Fard NR, Karimi M, Baghaei MH, Surkan PJ, Rahimi M, et al, (2011). Effects of dietary approaches to stop hypertension (DASH) eating plan on cardiovascular risks among type 2 diabetic patients: A randomized crossover clinical trial. *Diabetes Care.* 2011;34(1):55-57. doi: 10.2337/2Fdc10-0676.
6. Bach-Faig A, Berry EM, Lairon D, Reguant J, Trichopoulou A, Dernini S, et al, (2011). Mediterranean diet foundation expert group, Mediterranean pyramid today. *Science and cultural updates.* *Public Health Nutr.* 2011;14(12A):2274-2284. doi: 10.1017/s1368980011002515.
7. Banjari I, Bajraktarović-Labović S, Misir A, Huzjak B, (2013). Mediterranean diet and cardiovascular diseases. *Timoč Med Glas.* 2013;38(4):196-202.
8. Banjari I, Han S, Al-Tawil N, Ćorić N, Balkić Widmann J, (2023). Stroke risk assessment and idet-related risk factors – comparison of two cities from Bosnia and Herzegovina. *New Armen. Med.* 2023;17(3):31-39. doi: .56936/18290825-2023.17.3-31.
9. Barnosky AR, Hoddy KK, Unterman TG, Varady KA, (2014). Intermittent fasting vs daily calorie restriction for type 2 diabetes prevention. A review of human findings. *Transl Res.* 2014;164(4):302-311. doi: 10.1016/j.trsl.2014.05.013.
10. Barre DE, Mizier-Barre KA, Griscti O, Hafez K, (2008). High dose flaxseed oil supplementation may affect fasting blood serum glucose management in human type 2 diabetics. *J Oleo Sci.* 2008;57(5):269-273. doi: 10.5650/jos.57.269.
11. Bhandari P, Sapra A, (2023). Low Fat Diet. [Updated 2023 Feb 6]. In: *StatPearls [Internet].* Treasure Island (FL): StatPearls Publishing; 2023. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK553097/>
12. Bock PM, Telo GH, Ramalho R, Sbaraini M, Leivas G, Martins AF, Schaan BD, (2021). The effect of probiotics, prebiotics or synbiotics on metabolic outcomes in individuals with diabetes: a systematic review and meta-analysis. *Diabetologia.* 2021;64(1):26-41. doi: 10.1007/s00125-020-05295-1.
13. Campbell SC, Aldibbiat A, Marriott CE, Landy C, Ali T, Ferris WF, et al, (2008). Selenium stimulates pancreatic beta-cell gene expression and enhances islet function. *FEBS Lett.* 2008;582(15):2333-2337. doi: 10.1016/j.febslet.2008.05.038.
14. Chagas CEA, Borges MC, Martini LA, Rogero MM, (2012). Focus on vitamin D, inflammation and type 2 diabetes. *Nutrients.* 2012;4(1):52-67. doi: 10.3390/nu4010052.
15. Chen Z, Franco OH, Lamballais S, Ikram MA, Schoufour JD, Muka T, Voortman T, (2020). Associations of specific dietary protein with longitudinal insulin resistance, prediabetes and type 2 diabetes: The Rotterdam Study. *Clin Nutr.* 2020;39(1):242-249. doi: 10.1016/j.clnu.2019.01.021.
16. Chiu S, Sievenpiper JL, de Souza RJ, Cozma AI, Mirrahimi A, Carleton AJ, et al, (2014). Effect of fructose on markers of non-alcoholic fatty liver disease (NAFLD): a systematic review and meta-analysis of controlled feeding trials. *Eur Clin Nutr.* 2014;68(4):416-423. doi: 10.1038/ejcn.2014.8.
17. Chiu THT, Pan WH, Lin MN, Lin CL, (2018). Vegetarian diet, change in dietary patterns, and diabetes risk: a prospective study. *Nutr*

- Diabetes*. 2018;8(1):12. doi: 10.1038/s41387-018-0022-4.
18. Cole JB, Florez JC, (2020). *Genetics of Diabetes Mellitus and Diabetes Complications*. *Nat Rev Nephrol*. 2020;16(7):377-390. doi: 10.1038/s41581-020-0278-5.
 19. Craig WJ, (2009). *Health effects of vegan diet*. *Am J Clin Nutr*. 2009;89(5):1627-1633. doi: 10.3945/ajcn.2009.26736N.
 20. Craig WJ, Mangels AR, (2009). *Position of the American Dietetic Association. Vegetarian diets*. *J Am Diet Assoc*. 2009;109(7):1266-1282. doi: 10.1016/j.jada.2009.05.027.
 21. Dungan KM, Braithwaite SS, Preiser JC, (2009). *Stress hyperglycaemia*. *Lancet*. 2009;373(9677):1798-1807. doi: 10.1016/S0140-6736(09)60553-5.
 22. Ekinçi EI, Clarke S, Thomas MC, Moran JL, Cheong K, MacIsaac RJ, Jerums G, (2011). *Dietary salt intake and mortality in patients with type 2 diabetes*. *Diabetes Care*. 2011;34(3):703-709. doi: 10.14341/2071-8713-4842.
 23. Evans RM, Barish GD, Wang YX, (2004). *PPARs and the complex journey to obesity*. *Nat Med*. 2004;10(4):355-361. doi: 10.1038/nm1025
 24. Evert AB, Dennison M, Gardner CD, Garvey WT, Lau KHK, MacLeod J, et al., (2019). *Nutrition therapy for adults with diabetes or pre-diabetes: A consensus report*. *Diabetes Care*. 2019;42(5):731-754. doi: 10.2337/dci19-0014.
 25. Forouhi NG, Harding AH, Allison M, Sandhu MS, Welch A, Luben R, et al, (2007). *Elevated serum ferritin levels predict new-onset type 2 diabetes: results from the EPIC-Norfolk prospective study*. *Diabetologia*. 2007;50(5):949-956. doi: 10.1007/s00125-007-0604-5.
 26. Freundlich M, Quiroz Y, Zhang Z, Zhang Y, Bravo Y, Weisinger JR, et al, (2008). *Suppression of renin-angiotensin gene expression in the kidney by paricalcitol*. *Kidney Int*. 2008;74(11):1394-1402. doi: 10.1038/ki.2008.408.
 27. Galmés S, Serra F, Palou A, (2018). *Vitamin E metabolic effects and genetic variants. A challenge for precision nutrition in obesity and associated disturbances*. *Nutrients*. 2018;10(12):1919. doi: 10.3390/nu10121919.
 28. Gannon MC, Nuttall FQ, (2006). *Control of blood glucose in type 2 diabetes without weight loss by modification of diet composition*. *Nutr Metab (Lond)*. 2006;3:16. doi: 10.1186/1743-7075-3-16.
 29. Ge L, Sadeghirad B, Ball GDC, da Costa BR, Hitchcock CL, Svendrovski A, et al, (2020). *Comparison of dietary macronutrient patterns of 14 popular named dietary programmes for weight and cardiovascular risk factor reduction in adults: systematic review and network meta-analysis of randomised trials*. *BMJ*. 2020;369:m696. doi: 10.1136/bmj.m696.
 30. Giulietti A, Gysemans C, Stoffels K, van Etten E, Decallonne B, Overbergh L, et al, (2004). *Vitamin D deficiency in early life accelerates type 1 diabetes in non-obese diabetic mice*. *Diabetologia*. 2004;47(3):451-462. doi: 10.1007/s00125-004-1329-3.
 31. Goldenberg JZ, Day A, Brinkworth GD, Sato J, Yamada S, Jönsson T, et al, (2021). *Efficacy and safety of low and very low carbohydrate diets for type 2 diabetes remission: systematic review and meta-analysis of published and unpublished randomized trial data*. *BMJ*. 2021;372:m4743. doi: 10.1136/bmj.m4743.
 32. Guadarrama-López AL, Valdés-Ramos R, Martínez-Carrillo BE, (2014). *Type 2 diabetes, PUFAs, and vitamin D: Their relation to inflammation*. *J Immunol Res*. 2014;2014:860703. doi: 10.1155/2014/860703.
 33. Ha SK, (2014). *Dietary salt intake and hypertension*. *Electrolyte Blood Press*. 2014;12(1):7-18. doi: 10.5049/ebp.2014.12.1.7.
 34. Hajhashemy Z, Rouhani P, Saneei P, (2022). *Dietary calcium intake in relation to type 2 diabetes and hyperglycaemia in adults: A systematic review and dose-response meta-analysis of epidemiologic studies*. *Sci Rep* 2022;12:1050. doi: 10.1038/s41598-022-05144-8.
 35. Haussler MR, Haussler CA, Bartik L, Whitfield GK, Hsieh JC, Slater S, Jurutka PW, (2008). *Vitamin D receptor: molecular signaling and actions of nutritional ligands in disease prevention*. *Nutr Rev*. 2008;66(10):98-112. doi: 10.1111/j.1753-4887.2008.00093.x.
 36. Heald AH, Stedman M, Davies M, Livingston M, Alshames R, Lunt M, et al, (2020). *Estimating life years lost to diabetes: outcomes from analysis of National Diabetes Audit and Office of National Statistics data*. *Cardiovasc*

- Endocrinol Metab.* 2020;9(4):183-185. doi: 10.1097/XCE.0000000000000210.
37. Hendriks HFJ, (2007). Moderate alcohol consumption and insulin sensitivity: observations and possible mechanisms. *Ann Epidemiol.* 2007;17(5):40-42. doi: 10.1016/j.annepidem.2007.01.009.
 38. Jacobs S, Harmon BE, Boushey CJ, Morimoto Y, Wilkens LR, Marchand LL, et al, (2015). A priori-defined diet quality indexes and risk of type 2 diabetes: the multiethnic cohort. *Diabetologia.* 2015;58(1):98-112. doi: 10.1007/s00125-014-3404-8.
 39. Jéquier E, Bray GA, (2002). Low-fat diets are preferred. *Am J Med.* 2002;113(9):41-46. doi: 10.1016/S0002-9343(01)00991-3.
 40. Kahleova H, Matoulek M, Malinska H, Oliyarnik O, Kazdova L, Neskudla T, et al, (2011). Vegetarian diet improves insulin resistance and oxidative stress markers more than conventional diet in subjects with type 2 diabetes. *Diabet Med.* 2011;28(5):549-559. doi: 10.1111/j.1464-5491.2010.03209.x.
 41. Kasińska MA, Drzewoski J, (2015). Effectiveness of probiotics in type 2 diabetes: A meta-analysis. *Pol Arch Med Wewn.* 2015;125(11):803-813. doi: 10.20452/pamw.3156.
 42. Knott C, Bell S, Britton A, (2015). Alcohol consumption and the risk of type 2 diabetes: a systematic review and dose-response meta-analysis of more than 1.9 million individuals from 38 observational studies. *Diabetes Care.* 2015;38(9):1804-1812. doi: 10.2337/dc15-0710.
 43. Koh A, Vadder FD, Kovatcheva-Datchary P, Bäckhed F, (2016). From dietary fiber to host physiology: Short-chain fatty acids as key bacterial metabolites. *Cell.* 2016;165(6):1332-1345. doi: 10.1016/j.cell.2016.05.041.
 44. Kolodziejczyk AA, Zheng D, Elinav E, (2019). Diet-microbiota interactions and personalized nutrition. *Nat Rev Microbiol.* 2019;17(12):742-753. doi: 10.1038/s41579-019-0256-8.
 45. Koloverou E, Esposito K, Giugliano D, Panagiotakos D, (2014). The effect of Mediterranean diet on the development of type 2 diabetes mellitus: a meta-analysis of 10 prospective studies and 136,846 participants. *Metabolism.* 2014;63(7):903-911. doi: 10.1016/j.metabol.2014.04.010.
 46. Koppes LLJ, Dekker JM, Hendriks HF, Bouter LM, Heine RJ, (2005). Moderate alcohol consumption lowers the risk of type 2 diabetes: a meta-analysis of prospective observational studies. *Diabetes Care.* 2005;28(3):719-725. doi: 10.2337/diacare.28.3.719.
 47. Kratz M, Kennenberg F, Kassner A, Fobker M, Abuja PM, Assmann G, Wahrburg U, (2002). Effects of dietary fatty acids on the composition and oxidizability of low-density lipoprotein. *Eur J Clin Nutr.* 2002;56(1):72-81. doi: 10.1038/sj.ejcn.1601288.
 48. Landrier JF, Gouranton E, El Yazidi C, Malezet C, Balaguer P, Borel P, Amiot MJ, (2009). Adiponectin expression is induced by vitamin E via a peroxisome proliferator-activated receptor gamma-dependent mechanism. *Endocrinology.* 2009;150(12):5318-5325. doi: 10.1210/en.2009-0506
 49. Lazarou C, Panagiotakos D, Matalas AL, (2012). The role of diet in prevention and management of type 2 diabetes: Implications for Public Health. *Crit Rev Food Sci Nutr.* 2012;52(5):382-389. doi: 10.1080/10408398.2010.500258.
 50. Li L, Mi Y, Xu M, Ruan L, Sun J, Song Q, (2022). Influence of Dietary Salt Intake on T2D Treatment. *Front Endocrinol (Lausanne).* 2022;13:926143. doi: 10.3389/fendo.2022.926143.
 51. Liu G, Guasch-Ferré M, Hu Y, Li Y, Hu FB, Rimm EB, et al, (2019). Nut consumption in relation to cardiovascular disease incidence and mortality among patients with Diabetes Mellitus. *Circ Res.* 2019;124(6):920-929. doi: 10.1161/CIRCRESAHA.118.314316.
 52. Longo VD, Mattson MP, (2014). Fasting molecular mechanisms and clinical applications. *Cell Metab.* 2014;19(2):181-192. doi: 10.1016/j.cmet.2013.12.008.
 53. Malkki Y, (2004). Trends in dietary fiber research and development. *Acta Aliment.* 2004;33(1):39-62. <http://dx.doi.org/10.1556/AAlim.33.2004.1.5>.
 54. Maret W, (2008). A role for metallothionein in the pathogenesis of diabetes and its cardiovascular complications. *Mol Genet Metab.* 2008;94(1):1-3. doi: 10.1016/j.ymgme.2008.01.010.

55. Mattioli AV, Palmiero P, Manfrini O, Puddu PE, Nodari S, Cas AD, et al, (2017). Mediterranean diet impact on cardiovascular diseases: A narrative review. *J Cardiovasc Med.* 2017;18(12):925-935. doi: 10.2459/JCM.0000000000000573.
56. McFarland LV, Evans CT, Goldstein EJC, (2018). Strain-specificity and disease specificity of probiotic efficacy: A systematic review and meta-analysis. *Front Med (Lausanne).* 2018;5:124. doi: 10.3389/fmed.2018.00124
57. Meikle PJ, Summers SA, (2017). Sphingolipids and phospholipids in insulin resistance and related metabolic disorders. *Nat Rev Endocrinol.* 2017;13(2):79-91. doi: 10.1038/nrendo.2016.169.
58. Mokgalaboni K, Phoswa WN, (2022). Cross-link between type 2 diabetes mellitus and iron deficiency anemia. A mini-review. *Clinical Nutrition Open Science.* 2022;45:57-71. doi: 10.1016/j.nutos.2022.08.006.
59. Neuenschwander M, Ballon A, Weber KS, Norat T, Aune D, Schwingshackl L, Schlesinger S, (2019). Role of diet in type 2 diabetes incidence: umbrella review of meta-analyses of prospective observational studies. *BMJ.* 2019;366:12368. doi: 10.1136/bmj.12368.
60. Ooi EMM, Watts GF, Ng TWK, Barrett PHR, (2005). Effects of dietary fatty acids on human lipoprotein metabolism: a comprehensive update. *Nutrients.* 2105;7(6):4416-4425. doi: 10.3390/nu7064416.
61. Orllepp JR, Metrikat J, Albrecht M, von Korff, Hanrath P, Hoffmann R, (2003). The vitamin D receptor gene variant and physical activity predicts fasting glucose levels in healthy young men. *Diabet Med.* 2003;20(6):451-454. doi: 10.1046/j.1464-5491.2003.00971.x.
62. Patterson RE, Laughlin GA, Sears DD, LaCroix AZ, Marinac C, Gallo LC, et al, (2015). Intermittent fasting and human metabolic health. *J Acad Nutr Diet.* 2015;115(8):1203-1212. doi : 10.1016/j.jand.2015.02.018.
63. Pedersen-Bjergaard U, Reubsæet JLE, Nielsen SL, Pedersen-Bjergaard S, Perrild H, Pramming S, Thorsteinsson B, (2005). Psychoactive drugs, alcohol, and severe hypoglycemia in insulin-treated diabetes: Analysis of 141 cases. *Am J Med.* 2005;118(3):307-310. doi: 10.1016/j.amjmed.2004.07.054.
64. Perraudeau F, McMurdie P, Bullard J, Cheng A, Cutcliffe C, Deo A, et al, (2020). Improvements to postprandial glucose control in subjects with type 2 diabetes: a multicenter, double blind, randomized placebo-controlled trial of a novel probiotic formulation. *BMJ Open Diabetes Research and Care* 2020;8:e001319. doi: 10.1136/bmjdr-2020-001319
65. Petersmann A, Mueller-Wieland D, Mueller UA, Landgraf R, Nauck M, Freckmann G, et al, (2019). Definition, Classification and Diagnosis of Diabetes Mellitus. *Exp Clin Endocrinol Diabetes.* 2019;127(1):1-7. doi: 10.1515/labmed-2018-0016.
66. Pittas AG, Lau J, Hu F, Dawson-Hughes B, (2007). The role of vitamin D and calcium in type 2 diabetes. A systematic review and meta-analysis. *J Clin Endocrinol Metab.* 2007;92(6):2017-2029. doi: 10.1210/jc.2007-0298.
67. Potier M, Darcel N, Tomé D, (2009). Protein, amino acids and the control of food intake. *Curr Opin Clin Nutr Metab Care.* 2009;12(1):54-58. doi: 10.1079/BJN20041138.
68. Poudel RR, Bhusal Y, Tharu B, Kafle NK, (2017). Role of zinc in insulin regulation and diabetes. *J Soc Health Diabetes.* 2017;5(2):83-87. doi: 10.1055/s-0038-1676241.
69. Powers MA, Bardsley JK, Cypress M, Funnell MM, Harms D, Hess-Fischl A, et al, (2021). Diabetes Self-Management Education and Support in Adults with Type 2 Diabetes; A Consensus Report of the American Diabetes Association, the Association of Diabetes Care and Education Specialists, the Academy of Nutrition and Dietetics, the American Academy of Family Physicians, the American Academy of PAs, the American Association of Nurse Practitioners, and the American Pharmacists Association. *J Acad Nutr Diet.* 2021;121(4):773-788. doi: 10.2337/dci20-0023.
70. Rittipahiroj T, Pongpirul K, Janchot K, Mueller NT, Li T, (2021). Probiotics contribute to glycaemic control in patients with type 2 diabetes mellitus: A systematic review and meta-analysis. *Adv Nutr.* 2021;12(3):722-734. doi: 10.1093/advances/nmaa133.
71. Roopashree PG, Shetty SS, Kumari NS, (2021). Effect of medium chain fatty acid in human health and disease. *J Funct Foods.* 2021;87:104724. doi: 10.1016/j.jff.2021.104724.

72. Roust LR, Hammel KD, Jensen MD, (1994). Effects of isoenergetic, low-fat diets on energy metabolism in lean and obese women. *Am J Clin Nutr.* 1994; 60(4):470-475. doi: 10.1093/ajcn/60.4.470.
73. Russel WR, Baka A, Bjorck I, Delzenne N, Gao D, Griffiths HR, et al, (2016). Impact of diet composition on blood glucose regulation. *Crit Rev Food Sci Nutr.* 2016;56(4):541-590. doi: 10.1080/10408398.2013.792772.
74. Sacks FM, Svetkey LP, Vollmer WM, Appel LJ, Bray GA, Harsha D, et al, (2001). Effects of blood pressure of reduced dietary sodium and the dietary approaches to stop hypertension (DASH) diet. *N Engl J Med.* 2001;344(1):3-10. doi: 10.1056/NEJM200101043440101.
75. Salas-Salvadó J, Bulló M, Pérez-Heras A, Ros E, (2006). Dietary fiber, nuts and cardiovascular diseases. *Br J Nutr.* 2006;99(2):46-51. doi: 10.1017/BJN20061863.
76. Sanchez JM, Zhao LN, Salehi A, Wollheim CB, Kaldis P, (2023). Pathophysiology of type 2 diabetes and the impact of altered metabolic interorgan crosstalk. *FEBS J.* 2023;290(3):620-648. doi: 10.1111/febs.16306.
77. Schröder H, (2007). Protective mechanisms of the Mediterranean diet in obesity and type 2 diabetes. *J Nutr Biochem.* 2007;18(3):149-160. doi: 10.1016/j.jnutbio.2006.05.006.
78. Schwingshackl L, Chaimani A, Hoffmann G, Schwedhelm C, Boeing H, (2018a). A network meta-analysis on the comparative efficacy of different dietary approaches on glycaemic control in patients with type 2 diabetes mellitus. *Eur J Epidemiol.* 2018a;33(2):157-170. doi: 10.1007/s10654-017-0352-x.
79. Schwingshackl L, Hoffmann G, Iqbal K, Schwedhelm C, Boeing H, (2018b). Food groups and intermediate disease markers: a systematic review and network meta-analysis of randomized trials. *Am J Clin Nutr.* 2018b;108(3):576-586. doi: 10.1093/ajcn/nqy151.
80. Shai I, Wainstein J, Harman-Boehm I, Raz I, Fraser D, Rudich A, Stampfer MJ, (2007). Glycaemic effects of moderate alcohol intake among patients with type 2 diabetes: a multi-center, randomized, clinical intervention trial. *Diabetes Care.* 2007;30(12):3011-3016. doi: 10.2337/dc07-1103.
81. Shin NR, Lee JC, Lee HY, Kim MS, Whon TW, Lee MS, Bae JW, (2013). An increase in the *Akkermansia* spp. population induced by metformin treatment improves glucose homeostasis in diet-induced obese mice. *Gut.* 2013;63(5):727-735. doi: 10.1136/gutjnl-2012-303839.
82. Shinde SN, Dhadke VN, Suryakar AN, (2011). Evaluation of oxidative stress in type 2 diabetes mellitus and follow-up along with vitamin E supplementation. *Indian J Clin Biochem.* 2011;26(1):74-77. doi: 10.1007/s12291-010-0041-y.
83. Siervo M, Lara J, Chowdhury S, Ashor A, Oggioni C, Mathers JC, (2015). Effects of the dietary approach to stop hypertension (DASH) diet on cardiovascular risk factors: A systematic review and meta-analysis. *Br J Nutr.* 2015;113(1):1-15. doi: 10.1017/S0007114514003341.
84. Smuglov EP, Maksimova EV, Pashkovsky DG, (2023). Features of the management of coronary heart disease in patients with metabolically associated fatty liver disease. *New Armen. Med.* 2023;17(2):28-34. doi: 10.56936/18290825-2023.17.2-28.
85. Snorgaard O, Poulsen GM, Andersen HK, Astrup A, (2017). Systematic review and meta-analysis of dietary carbohydrate restriction in patients with type 2 diabetes. *BMJ Open Diabetes Res Care.* 2017;5(1):e000354. doi: 10.1136/bmjdr-2016-000354.
86. St-Onge MP, (2005). Dietary fats, teas, dairy, and nuts: potential functional foods for weight control. *Am J Clin Nutr.* 2005;81(1):7-15. doi: 10.1093/ajcn/81.1.7.
87. Tao YW, Gu YL, Mao XQ, Zhang L, Pei YF, (2020). Effects of probiotics on type II diabetes mellitus: a meta-analysis. *J Transl Med.* 2020;18(1):30. doi: 10.1186/s12967-020-02213-2.
88. Tilg H, Moschen AR, (2014). Microbiota and diabetes: an evolving relationship. *Gut.* 2014;63(9):1513-1521. doi: 10.1136/gutjnl-2014-306928.
89. Van Zuuren EJ, Fedorowicz Z, Kuijpers T, Pijl H, (2018). Effects of low-carbohydrate- compared with low-fat-diet interventions on metabolic control in people with type 2 diabetes: a systematic review including GRADE assess-

- ments. *Am J Clin Nutr.* 2018;108(2):300-331. doi: 10.1093/ajcn/nqy096.
90. Vigiouliouk E, Kendall CW, Kahleová H, Rehelić D, Salas-Salvadó, Choo VL, et al, (2019). Effect of vegetarian dietary patterns on cardio-metabolic risk factors in diabetes: A systematic review and meta-analysis of randomized controlled trials. *Clin Nutr.* 2019;38(3):1133-1145. doi: 10.1016/j.clnu.2018.05.032.
 91. Villarreal-Renteria AI, Herrera-Echauri DD, Rodriguez-Rocha NP, Zuñiga LY, Muñoz-Valle JF, García-Arellano S, et al, (2022). Effect of flaxseed (*Linum usitatissimum*) supplementation on glycaemic control and insulin resistance in prediabetes and type 2 diabetes: A systematic review and meta-analysis of randomized controlled trials. *Complement Ther Med.* 2022;70:102852. doi: 10.1016/j.ctim.2022.102852.
 92. Virtanen HEK, Koskinen TT, Voutilainen S, Mursu J, Tuomainen TP, Kokko P, Virtanen JK, (2017). Intake of different dietary proteins and risk of type 2 diabetes in men: the Kuopio Ischaemic Heart Disease Risk Factor Study. *Br J Nutr.* 2017;117(6):882-893. doi: 10.1017/S0007114517000745.
 93. Wang Y, Rijntjes E, Wu Q, Lv H, Gao C, Shi B, Schomburg L, (2020). Selenium deficiency is linearly associated with hypoglycaemia in healthy adults. *Redox Biol.* 2020;37:101709. doi: 10.1016/j.redox.2020.101709.
 94. Wheeler ML, Dunbar SA, Jaacks LM, Karmally W, Mayer-Davis EJ, Wylie-Rosett J, Yancy WS, (2012). Macronutrients, food groups, and eating patterns in the management of diabetes. *Diabetes Care.* 2012;35(2):434-445. doi: 10.2337/dc11-2216.
 95. WHO-2019 World Health Organization. Classification of Diabetes Mellitus. Geneva, Switzerland: WHO, 2019. Available from: <https://apps.who.int/iris/handle/10665/325182>
 96. Yao K, Zeng L, He Q, Wang W, Lei J, Zou X, (2017). Effect of probiotics on glucose and lipid metabolism in type 2 diabetes mellitus: A meta-analysis of 12 randomized controlled trials. *Med Sci Monit.* 2017;23:3044-3053. doi: 10.12659/msm.902600.
 97. Zeitz U, Weber K, Soegiarto DW, Wolf E, Balling R, Erben RG, (2003). Impaired insulin secretory capacity in mice lacking a functional vitamin D receptor. *FASEB J.* 2003;17(3):509-511. doi: 10.1096/fj.02-0424fje.
 98. Zhang Q, Wu Y, Fei X, (2016). Effect of probiotics on glucose metabolism in patients with type 2 diabetes mellitus: A meta-analysis of randomized controlled trials. *Medicina.* 2016;52(1):28-34. doi: 10.1016/j.medic.2015.11.008.
 99. Zhao WT, Luo Y, Zhang Y, Zhou Y, Zhao TT, (2018). High protein diet is of benefit for patients with type 2 diabetes. *Medicine (Baltimore).* 2018;97(46):e13149. doi: 10.1097/MD.00000000000013149.



CONTENTS

4. **NOSIĆ M., BANJARI I., JURIŠIĆ-ERŽEN D.**
DIET THERAPY FOR TYPE 2 DIABETES: THE ROLE OF SPECIFIC NUTRIENTS AND DIETARY PRINCIPLES
18. **LIU X., PENG Y., LIU Q., CAI S., XIE F.**
THE CLINICAL RELATIONSHIP BETWEEN HLA-B27 AND JUVENILE SPONDYLOARTHRITIS
30. **LIU X., PENG Y., LIU Q., CAI S., XIE F.**
THE IMPACT OF HUANG QI GRANULES ON THE INTERLEUKINS, TUMOR NECROSIS FACTOR A AND CELLULAR IMMUNE FUNCTION IN PATIENTS DIAGNOSED WITH ACUTE KAWASAKI DISEASE
38. **AL-ALLAK H.M.A., AL-ABOODI A.H.N**
ASSESSMENT OF LEFT ATRIAL PHASIC VOLUMES AND FUNCTIONS DURING THIRD TRIMESTER OF HEALTHY PREGNANCY
46. **AKINLOLU A., AMEEN M., EBITO G., ASOGWA N., AKINDELE R. FAGBOHUNKA B.**
MO11 AND MS06 AMELIORATED CADMIUM CHLORIDE-INDUCED NEURO-DEGENERATION AND ALTERATIONS OF DOPAMINE, GLUTAMATE AND MYELIN BASIC PROTEIN EXPRESSIONS IN RATS
54. **FAGBOHUNKA B., AKINLOLU A., AMEEN M. KADIR R., OYEWOPO A., AHIALAKA O., DARE F., FAMOSE K., SULEIMAN K., ALIM B., LAWAL A., ADEMILOYE J.**
MORINGA OLEIFERA (MOF6) AND MUSA SAPIENTUM (MSF1) AMELIORATED 7,12-DIMETHYLBENZ[A]ANTHRACENE-INDUCED SKIN HISTO-PATHOLOGY, INFLAMMATION, HEPATIC OXIDATIVE STRESS AND MUTAGENESIS IN RATS
65. **GAVANJI S., BAGHSHAHI H., CHAMGORDANI H., KHANDAN M.**
HEPATOTOXICITY EFFECTS OF MEDICINAL PLANTS
80. **SONG Z.**
CURRENT VIEWS OF PSYCHEDELICS AND THEIR CONNECTION TO WELL-BEING
89. **VARZHAPETYAN A.M., CHITCHYAN A.A., SHAHBAZYAN S.S.**
ORGAN OF ZUCKERKANDL AS A SOURCE OF PARANGANGLIOMA PHEOCHROMOCYTOMA
98. **TAHANE B.M.A., POYIL M.M.**
REPURPOSING PAROXETINE: INVESTIGATION OF ANTIBACTERIAL AND ANTI-ADHESIVE PROPERTIES OF THE ANTI-DEPRESSION DRUG AGAINST MAJOR PATHOGENS CAUSING CATHETER-ASSOCIATED URINARY TRACT INFECTIONS
106. **HOKMABADI ME., AFSHARI SALEH L., TALAEI A**
PREDICTING JOB BURNOUT AND CAREER LIFE QUALITY OF NURSES BASED ON THE HEALTH BELIEF MODEL AND MEDIATING ROLE OF PSYCHOSOMATIC SYMPTOMS
113. **SHARIF M.R., SAFARI A., BAGHSHAHI H., AKBARI H., MEMARZADEH M.R., REZAI HAJIABAD H., MEHRAN M., KIANIPOUR P.**
THE EFFECT OF A THYME-IVY FLUID EXTRACT COMBINATION ON THE SEVERITY OF COUGH IN CHILDREN: RANDOMIZED CONTROLLED TRIAL
- 121 **BAGHERI A.R., AKBARI H., JAFARI M.M., RAHMATPANAH K., JAMSHIDI S, MOMENZADEH F**
COMPARISON OF THE EFFECT OF LIPEXAN HERBAL MEDICINE PRODUCT WITH PLACEBO AND GEMFIBROZIL ON BLOOD LIPID INDICES



The Journal is founded by
Yerevan State Medical
University after M. Heratsi.



Rector of YSMU

Armen A. Muradyan

Address for correspondence:

Yerevan State Medical University
2 Koryun Street, Yerevan 0025,
Republic of Armenia

Phones:

(+37410) 582532 YSMU

(+37493 588697 Editor-in-Chief

Fax: (+37410) 582532

E-mail: namj.ysmu@gmail.com, ysmiu@mail.ru

URL: <http://www.ysmu.am>

*Our journal is registered in the databases of Scopus,
EBSCO and Thomson Reuters (in the registration process)*



SCOPUS



EBSCO

REUTERS

Copy editor: Tatevik R. Movsisyan

Printed in "LAS Print" LLC
Director: Suren A. Simonyan
Armenia, 0023, Yerevan,
Acharyan St. 44 Bulding,
Phone: (+374 10) 62 76 12,
E-mail: las.print@yahoo.com

Editor-in-Chief

Arto V. Zilfyan (Yerevan, Armenia)

Deputy Editors

Hovhannes M. Manvelyan (Yerevan, Armenia)

Hamayak S. Sisakyan (Yerevan, Armenia)

Executive Secretary

Stepan A. Avagyan (Yerevan, Armenia)

Editorial Board

Armen A. Muradyan (Yerevan, Armenia)

Drastamat N. Khudaverdyan (Yerevan, Armenia)

Levon M. Mkrtchyan (Yerevan, Armenia)

Foregin Members of the Editorial Board

Carsten N. GUTT (Memmingen, Germany)

Muhammad MIFTAHUSSURUR (Indonesia)

Alexander WOODMAN (Dharhan, Saudi Arabia)

Hesam Adin Atashi (Tehran, Iran)

Coordinating Editor (for this number)

Mahdi Esmaeilzadeh (Mashhad, Iran)

Editorial Advisory Council

Ara S. Babloyan (Yerevan, Armenia)

Aram Chobanian (Boston, USA)

Luciana Dini (Lecce, Italy)

Azat A. Engibaryan (Yerevan, Armenia)

Ruben V. Fanarjyan (Yerevan, Armenia)

Gerasimos Filippatos (Athens, Greece)

Gabriele Fragasso (Milan, Italy)

Samvel G. Galstyan (Yerevan, Armenia)

Arthur A. Grigorian (Macon, Georgia, USA)

Armen Dz. Hambardzumyan (Yerevan, Armenia)

Seyran P. Kocharyan (Yerevan, Armenia)

Aleksandr S. Malayan (Yerevan, Armenia)

Mikhail Z. Narimanyan (Yerevan, Armenia)

Levon N. Nazarian (Philadelphia, USA)

Yumei Niu (Harbin, China)

Linda F. Noble-Haeusslein (San Francisco, USA)

Arthur K. Shukuryan (Yerevan, Armenia)

Suren A. Stepanyan (Yerevan, Armenia)

Gevorg N. Tamamyanyan (Yerevan, Armenia)

Hakob V. Topchyan (Yerevan, Armenia)

Alexander Tsiskaridze (Tbilisi, Georgia)

Konstantin B. Yenkovyan (Yerevan, Armenia)

Peijun Wang (Harbin, China)