Chapter

Magnesium Intake in the Mediterranean Diet

Pierre-Anne Robbin Laird, Noah Stallard, Yasmin Momenian, Katherine Oshirak and Stella Lucia Volpe

Abstract

The Mediterranean Diet (MedDiet) is a nutritional pattern native to many cultures within the Mediterranean Basin. The diet is composed of fruits, vegetables, fish, eggs, fermented dairy, grains, poultry, and minimal consumption of red meats such as lamb and beef. The diet encourages the consumption of extra virgin olive oil and moderate red wine for those who consume alcohol. The diet does not incorporate processed foods and sugary beverages. The MedDiet is rich in many micronutrients and has a healthful fatty acid profile (primarily mono- and polyunsaturated fats, with low amounts of saturated fats). The diet is rich in foods with high magnesium content, such as leafy green vegetables, nuts, seeds, and some lesser magnesium-rich foods (e.g., fish). The MedDiet is associated with reduced incidence of several diseases such as cardiovascular disease, cerebrovascular disease, neurodegenerative disease, metabolic syndrome, and type 2 diabetes mellitus. Magnesium intake has been shown to play a prominent role in the prevention and management of many of these diseases, with some of the disease-preventing capacity of the MedDiet likely caused by its high magnesium content. Those making nutritional recommendations in line with the concepts of MedDiet should particularly encourage the consumption of foods high in magnesium.

Keywords: Mediterranean diet, magnesium, cardiovascular disease, Type 2 diabetes mellitus, neurodegenerative disease

1. Introduction

The Mediterranean diet (MedDiet) was a term coined by Dr. Ancel Keys following his "Seven Countries Study" in the 1960s [1]. The MedDiet is an eating pattern classically associated with the populations habituating the region of the Mediterranean Basin in the 1950s and 1960s, but less so in the present day [2, 3]. The MedDiet is the result of several millennia of cultural and culinary developments, nutritionally founded on the food cultivated in Mediterranean agriculture [4]. Unfortunately, due to the increased urbanization of the region and increasingly globalized food production, the consumption of foods traditionally associated with the MedDiet has significantly decreased [4].

The MedDiet emphasizes consumption of traditional foods and local seasonal produce, helping ensure a solid variety of fruits and vegetables [5]. Cultural vitality, vivacious and amicable culinary settings, adequate physical activity, and appropriate periods of rest are several lifestyle elements related to the MedDiet [4, 6]. Nutritionally, the diet incorporates seasonal fruits and vegetables, fresh seafood, bread, some dairy products, monounsaturated fats from olives (the fruit and the oil) and nuts, and moderate wine intake [4]. The consumption of red and processed meats, as well as sugary and fatty foods, is discouraged [4].

One of the potential benefits of MedDiet is its magnesium content. Magnesium is one of the most productive minerals in the body (second most prominent intracellular cation), implicated as a cofactor in more than 300 enzymatic processes in the body [7–9]. The most prominent sources of magnesium in the MedDiet are generally nuts, seeds, and leafy green vegetables (e.g., spinach). Magnesium consumption is implicated in the prevention of several chronic conditions. The MedDiet provides adequate amounts of magnesium, resulting in more favorable health outcomes. In the following chapter, we will explore the benefits of the MedDiet, potentially explained by its magnesium content.

2. The composition of the Mediterranean Diet

The MedDiet encourages significant consumption of locally grown and minimally processed fruits and vegetables, with sustainability and seasonality highly emphasized [6]. Furthermore, significant consumption of nuts, legumes, and unrefined grains (e.g., unprocessed cereals) is emphasized in the MedDiet [10]. The MedDiet is also characterized by minimal consumption of red and processed meats [2, 3]. This dietary pattern also excludes some dairy products, such as butter and ice cream, while including the consumption of fermented dairy products (e.g., yogurt and cheese) [2, 3, 10]. The primary sources of protein in the diet come from fish and shellfish, moderate poultry consumption, and occasional inclusion of beef, pork, and lamb (in traditional Mediterranean settings these meats are saved for celebrations) [2, 10]. Inconsistencies exist with egg consumption; some regard moderate egg consumption as a reasonable inclusion in the diet, while others do not include them in the MedDiet [4, 11]. Desserts consist of fresh fruit consumption, and not sugary cakes, pies, etc. [11]. Furthermore, beverage consumption is usually limited to water and red wine for those of age, avoiding sugar-sweetened beverages [11].

The MedDiet is extremely abundant in the consumption of extra virgin olive oil (EVOO), the recommended primary culinary oil and source of dietary fat (besides nuts and fish) [4]. Extra virgin olive oil is the oil produced from the first pressing of olives, which contains several antioxidants and bioactive polyphenols that do not present in more processed olive oil [2, 12, 13]. It has been postulated that EVOO may have antiatherogenic properties due to high concentrations of monounsaturated fatty acid and oleic acid [2, 14]. However, EVOO's high concentration of bioactive polyphenols is likely important in EVOO's cardioprotective and anti-inflammatory effects [2, 12, 15]. One specific polyphenol, oleocanthal, has been shown to have mechanistic effects similar to the non-steroidal anti-inflammatory medication ibuprofen, inhibiting the same cyclooxygenase enzymes in the prostaglandin-biosynthesis pathway [12]. Oleocanthal has been reported to stimulate a tingling sensation in the throat [13], thus it may be possible that this sensation could be a simple method to confirm the polyphenol content of EVOO.

The MedDiet is known to traditionally include moderate consumption of red wine with meals [10]. Red wine also contains bioactive polyphenols that may have antiatherogenic and cardioprotective properties [2, 12]. There are several polyphenols present in red wine including resveratrol, catechin, epicatechin, and anthocyanin, with resveratrol considered the most prominent polyphenol in red wine [16]. Resveratrol may be the main reason for many of the potential benefits of red wine, potentially leading to improved blood lipid concentrations, reduced insulin resistance, and attenuated oxidative stress of low-density lipoprotein cholesterol (LDL-C) [16]. Furthermore, red wine consumption has been associated with increased concentrations of high-density lipoprotein cholesterol (HDL-C) [16]. Thus, moderate red wine consumption may provide some health benefits when consumed in moderation. However, it is not recommended that individuals who do not drink, or those who are not of proper age, begin drinking red wine or other alcoholic beverages, despite its prevalence in the traditional MedDiet [2].

The MedDiet boasts an impressive nutritional profile with a higher monounsaturated fatty acid to saturated fatty acid ratio than other diets [6, 17, 18]. The MedDiet provides foods with high amounts of fiber, antioxidants, and anti-inflammatory compounds [6, 19–22]. Castiglione et al. evaluated the dietary habits and nutritional adequacy of a Sicilian cohort and reported that their dietary pattern allowed for adequate thiamine and biotin intake in the entire sample. Furthermore, greater than 50% of the participants consumed adequate iron, magnesium, selenium, zinc, and vitamins A, B_2, B_6, B_9, B_{12}, and C [23]. With respect to magnesium specifically, 66.9% and 90.4% of the study population met the European and Italian recommendations for magnesium of 363 mg/day and 240 mg/day, respectively [23–25].

A number of researchers have demonstrated the capacity of the MedDiet to reduce the incidence of cardiovascular disease, type 2 diabetes mellitus (T2DM), peripheral artery disease, atrial fibrillation, breast cancer, neurodegenerative disease, cerebrovascular disease, and cognitive decline [2, 6, 26–29]. Furthermore, the MedDiet has been implicated in reducing the risk of metabolic syndrome by targeting risk factors and aspects of the syndrome such as reducing waist circumference, blood pressure, and glucose concentrations, while subsequently increasing HDL-C concentrations [30]. Andreoli et al. implemented the MedDiet with a moderate energy deficit and exercise, which resulted in significant reductions in body weight, body mass index (BMI), fat mass, diastolic blood pressure, and total serum cholesterol, LDL-C, triglyceride, and fasting blood glucose concentrations, while simultaneously increasing HDL-C concentrations in women who were obese [31]. The MedDiet has also been found to reduce all-cause mortality [6, 28, 29, 32]. Thus, significant evidence demonstrates the potential for MedDiet to be a reasonable lifestyle intervention for disease prevention and management.

The MedDiet has potential for adoption in non-Mediterranean settings, providing that some flexibility is allotted and that the foods that are the central elements of the MedDiet are maintained [11]. The MedDiet has historically been a nutritional pattern shared among various cultural, religious, and ethnic groups, indicating a reasonable capacity for adoption among differing populations [11]. However, education regarding the many aspects of the MedDiet likely would be required [11]. This could be a potential barrier to the widespread adaptation of the diet.

As previously mentioned, some of the health benefits of the MedDiet may be due to the high prevalence of EVOO and red wine consumption, because the bioactive polyphenols present in these foods may have anti-inflammatory properties [12]. Furthermore, the potential benefits of MedDiet may be explained by the micronutrient density of the foods. Specifically, the MedDiet provides substantial magnesium, a crucial mineral (the fourth most abundant in the body), functioning in a large variety of metabolic processes [9]. Some foods in the MedDiet that may provide the greatest quantity of magnesium are nuts, seeds, chickpeas, and spinach [33].

3. Magnesium and health outcomes

The vast majority of magnesium in the human body is located within the mineral structures of the osseous tissues, with some residing intracellularly [23]. An extreme deficiency in magnesium can manifest as hypomagnesemia, defined as when the concentration of serum magnesium is less than 0.75 mmol/L. Symptoms associated with hypomagnesemia include tremors, spasms, muscle cramps, or general weakness [34]. Chronic low concentrations of magnesium have been implicated in the development of diseases with an inflammatory element such as Alzheimer's disease, asthma, attention deficit hyperactivity disorder, insulin resistance, T2DM, hypertension, cardiovascular disease, cerebrovascular disease, migraine headaches, and osteoporosis [8, 34, 35].

Magnesium functions primarily as a structural or enzymatic cofactor, helping to maintain protein structure and/or enzyme function. The presence of this mineral in the diet is crucial for normal biological functions because magnesium is required for adenosine triphosphate (ATP) metabolism, overall cellular energy production and storage, reproductive functions, stabilization of mitochondrial membranes, and the synthesis of deoxyribonucleic acid (DNA), ribonucleic acid (RNA), and proteins [8, 34, 36–39]. Magnesium is implicated in protein, nucleotide, and mitochondrial structure [34]. Via maintenance of this protein structure and function, magnesium aids in the formation of enzyme complexes, mitochondria, nucleic acids, bone, and polyribosomes [34]. Approximately 50% to 60% of magnesium in the body serves a structural role as hydroxyapatite within bone [34].

Magnesium also plays an integral role in oxidative phosphorylation and glycolysis, either via its role in the ATP complex (the principal form of biochemical energy in the body) or as a fundamental cofactor of key enzymes [34]. Magnesium is also involved in normal membrane functioning, assisting in the active processes required for potassium and calcium ion transport across the membrane. Proper ion transport is imperative for muscle contraction, nerve impulse transmission, normal cardiac rhythm, and vasomotor tone [34].

Magnesium is crucial for the proper absorption and utilization of certain vitamins such as cholecalciferol (vitamin D) and thiamine [34]. Magnesium is necessary for the binding of vitamin D to its binding protein, which is essential for proper transport of the vitamin throughout the body [34]. In addition, magnesium is necessary for the proper functioning of hepatic 25-hydroxylase and renal 1-alpha hydroxylase, the enzymes necessary for the conversion of cholecalciferol to 25-hydroxyvitamin D (calcidiol) in the liver, and then to 1,25-dihydroxyvitamin D_3 (1,25-$(OH)_2$ vitamin D_3 or calcitriol) in the kidneys, respectively [34]. Calcitriol or 1,25-$(OH)_2$ vitamin D_3 is the most active form of vitamin D, necessary for the proper exertion of vitamin D's effects on gene expression [34]. A magnesium deficiency could result in reduced calcitriol and parathyroid hormone response, implicating it in the development of osteomalacia (magnesium-dependent vitamin-D-resistant rickets) [34].

In addition, magnesium may have an important function in blocking calcium binding to the N-methyl D-aspartate (NMDA) receptor [34]. The NMDA receptor binds glutamate primarily (an excitatory neurotransmitter) and is ubiquitous throughout the central nervous system (CNS), with approximately 80% of cortical neurons having NMDA receptors [40]. The NMDA receptor plays an important role in neural plasticity and memory formation and may be implicated in a process called excitotoxicity, a potential element of pathologies in epilepsy and Alzheimer's disease [40]. Specifically, during states of epilepsy, stroke, or traumatic brain injury, damage to the brain may occur via calcium-mediated excitotoxicity [40]. In fact, magnesium's ability to prevent migraines, preeclamptic seizures, and protect against premature neonatal neural injury is mediated via the ability of magnesium to bind to the NMDA receptor and block calcium's entry into the neuron and cause depolarization [40, 41]. Thus, it is possible that by blocking calcium binding, magnesium reduces the excitability of the NMDA receptor, indicating a role of magnesium in altering CNS function, and perhaps even reducing disease risk.

Magnesium supplementation has the potential to be an effective and affordable therapy for migraine headaches, demonstrating a high safety profile [42]. In addition to its possible role in mitigating migraine headaches, magnesium may play a role in individuals with Alzheimer's disease. Barbagallo et al. compared older individuals with Alzheimer's disease to age-matched controls and reported that those with Alzheimer's disease had reduced serum magnesium concentrations [43]. Furthermore, the researchers reported a significant relationship between serum magnesium concentrations and cognitive function, demonstrating that magnesium intake may play a role in supporting cognitive performance. Ozawa et al. found higher self-reported intakes of calcium, magnesium, and potassium in a Japanese population; however, no associations between these minerals and Alzheimer's disease risk were found [44].

Furthermore, magnesium is an essential cofactor for the synthesis of glutathione due to its importance in ATP function [45]. Glutathione is one of the primary antioxidants in the body, and it is important for nutrient metabolism, as well as the regulation of many cellular processes such as gene expression, DNA and protein synthesis, cellular proliferation and apoptosis, signal transduction, cytokine production, immune response, and protein glutathionylation [46]. Inadequate production of glutathione results in increased oxidative stress, and the development of several pathologies such as kwashiorkor, seizures, Alzheimer's disease, Parkinson's disease, liver dysfunction, cystic fibrosis, sickle cell anemia, human immunodeficiency virus (HIV), acquired immunodeficiency syndrome (AIDS), cancer, myocardial infarction, cerebrovascular disease, and T2DM [46]. Magnesium deficiency could reduce the body's capacity for endogenous glutathione synthesis and lead to the development of disease states associated with excessive oxidative stress.

Magnesium is instrumental in attenuating chronic inflammation. Song et al. investigated the relationship between magnesium intake, C-Reactive Protein (CRP) (a standard marker of systemic inflammation), and the incidence of metabolic syndrome in a cohort of middle-aged and older American women. The researchers presented evidence demonstrating an inverse relationship between magnesium intake and CRP concentrations [35]. This relationship was especially prominent in women with a BMI exceeding 25 kg/m^2 and those who had ever smoked in their lifetime [35], indicating the potential role of magnesium status in the development of systemic inflammation. Because metabolic syndrome is known to have a chronic inflammatory component, it is not surprising that magnesium intake was inversely associated with the risk of metabolic syndrome [35, 47].

Magnesium is particularly important as an electrolyte functioning in the cardiovascular system, contributing to normal potassium transport in the myocardium, vasodilation of coronary and peripheral arteries, and reducing the aggregation of platelets [34]. Magnesium assists in the maintenance of normal cardiac function via electrophysiological processes such as nerve transmission, muscle contraction, and gland secretions [23]. Magnesium may also be protective against cardiovascular disease due to its capacity to aid in endothelium-mediated vasodilation [23, 34]. Thus, ensuring adequate magnesium consumption could contribute to a lowered risk of developing cardiovascular disease due to the relationship between abnormal vasoconstriction and the platelet production implicated in blood clotting in the development of myocardial infarction and other cardiovascular events [34].

Magnesium is also essential to proper blood pressure regulation because it decreases the excitability of smooth muscle cells in response to depolarizing stimuli by activating calcium-dependent potassium channels [48]. Thus, via the promotion of vasodilation in vessels and reducing blood pressure, magnesium may be cardioprotective. This may be the mechanism by which magnesium may help prevent cerebrovascular diseases such as strokes, a disease commonly associated with chronic hypertension. Hypertension can lead to vasoconstriction of arteries adjacent to the cerebrum, potentially leading to an aneurysm or other endothelial damage that may lead to ischemic stroke. Larsson et al. conducted a meta-analysis where they examined the relationship between magnesium status and stroke risk. The researchers reported that magnesium intake of greater than 100 mg/day was correlated with an 8% reduced risk of total stroke incidence [49].

Magnesium is implicated in the prevention of T2DM, likely due to its importance in glucose metabolism and insulin function. Magnesium is important for transferring phosphates from ATP to protein, via tyrosine kinases [8]. Tyrosine kinases are involved in the transfer of phosphate of ATP to tyrosine residues on receptors or downstream proteins, which result in the altered activity of various enzymes and the creation of binding sites of various signaling proteins (such as insulin) [50]. Magnesium is implicated in the breakdown of glycogen and the release of glucose-1-phosphate, resulting in altered phosphorylase b kinase activity [8]. Phosphorylase b kinase is important for the activation of glycogen phosphorylase, the primary enzyme responsible for glycogenolysis [51]. Magnesium may also be involved in the translocation of the glucose transporter type 4 (GLUT4), essential for the uptake of blood glucose into cells [8], a process implicated in the prevention and management of diabetes mellitus. Guerrero-Romero et al. reported that magnesium supplementation and higher magnesium intakes improved insulin sensitivity in individuals without diabetes mellitus, but with insulin resistance [52].

4. The Mediterranean Diet as a source of magnesium

As previously mentioned, the MedDiet is characterized by the consumption of foods high in mono- and polyunsaturated fats, seafood, vegetables, fruits, grains, nuts, legumes, EVOO, and fermented dairy products [4]. Some specific fruits that may be incorporated include apples, bananas, oranges, pears, berries, and tomatoes. [4]. Vegetables such as broccoli, kale, and spinach are likely to be included, as well [4]. Many of these foods vary in their magnesium content and are listed in **Tables 1–3**.

We chose to define the United States Recommended Dietary Allowance (RDA) for magnesium as 355 mg/day because it represents the mean RDA for women and men, 19 to 51 years of age. **Tables 1–3** list foods with high, medium, or low amounts of magnesium, considered to be 20%, 10% to 20%, or less than 10% of the mean RDA, respectively. Standard serving size of 100 grams was used as a realistic portion for the

Sunflower seeds	358 mg
Cashews	292 mg
Almond butter	279 mg
Pumpkin seeds	262 mg
Almonds	258 mg
Peanut butter	169 mg
Peanuts	168 mg
Hazelnuts	163 mg
Walnuts	158 mg
Barley	133 mg
Macadamia Nuts	130 mg
Chickpeas	115 mg
Baby Spinach	93 mg
Whole wheat bread	77 mg

Adapted from: FoodData Central. Accessed April 16, 2022. nal.usda.gov/fdc-app.html#/

Table 1.
Common Foods in the Mediterranean Diet with High Magnesium Concentrations per 100 Grams (defined as being greater than 20% of the average United States Recommended Dietary Allowance for women and men, 19 to 51 years of age [355 mg]).

Dried Figs	68 mg
Mackerel	60 mg
Oysters	58 mg
Cooked Brown Rice	43 mg
Dates	43 mg
Canned Sardines	39 mg
Shrimp	39 mg
Mussels	37 mg
Crab	36 mg
Lentils	36 mg

Adapted from: FoodData Central. Accessed April 16, 2022. nal.usda.gov/fdc-app.html#/nal.usda.gov/fdc-app.html#/

Table 2.
Common Foods in the Mediterranean Diet with Moderate Magnesium Concentrations per 100 Grams (defined as 10% to 20% of the average United States Recommended Dietary Allowance for women and men, 19 to 51 years of age [355 mg]).

Peas	33 mg
Pulses	33 mg
Raw Kale	33 mg
Chicken	32 mg
Ground Turkey	29 mg
Bananas	28 mg
Salmon	27 mg
Cheese	27 mg
Sweet Potatoes	25 mg
Trout	25 mg
Brussels Sprouts	23 mg
White Potatoes	23 mg
Raw Broccoli	21 mg
Duck	16 mg
Cauliflower	15 mg
Cantaloupe Melons	13 mg
Turnips	13 mg
Quail Eggs	13 mg
Red Wine	12 mg
Whole Milk	12 mg
Strawberries	12 mg
Chicken Eggs	11 mg
Frozen Carrots	11 mg
Greek Yogurt	11 mg
Oranges	11 mg
Canned Tomatoes	10 mg
Yellow Onions	9 mg
Peaches	8 mg
Pears	6 mg
Grapes	5 mg
Honeycrisp Apples	4 mg

Adapted from: FoodData Central. Accessed April 16, 2022. nal.usda.gov/fdc-app.html#/nal.usda.gov/fdc-app.html#/

Table 3.
Common Foods in the Mediterranean Diet with Low Magnesium Concentrations per 100 Grams (defined as being less than 10% of the average United States Recommended Dietary Allowance for women and men, 19 to 51 years of age [355 mg]).

vast majority of foods; however, for some foods, this may not be the case. Although the tables represent foods with varying amounts of magnesium, some factors that may potentially inhibit the absorption of magnesium are the presence of phytates, oxalates, and to a lesser extent, potassium and zinc [53].

5. Potential health outcomes of the Mediterranean Diet mediated by magnesium intake

Several benefits of the MedDiet may be partially explained by the physiological benefits of magnesium. As previously discussed, the MedDiet has been shown to reduce the incidence of cardiovascular disease, T2DM, peripheral artery disease, atrial fibrillation, certain cancers, cerebrovascular disease, neurodegenerative disease, metabolic syndrome, and improve blood lipid concentrations and glucose metabolism [2, 6, 26–30]. Magnesium, via its several prominent roles in the body, may be implicated in most, if not all of these positive changes.

Several of the aforementioned pathologies are associated with excessive inflammation and oxidative stress, which can be attenuated by processes associated with magnesium. Magnesium intake has been negatively associated with CRP concentrations [35]. Magnesium is also implicated in the production of glutathione (via its importance as an ATP/adenosine diphosphate [ADP] bridge) [45]. Glutathione is the primary antioxidant in human physiology and serves many other functions in cellular processes [46]. Low concentrations of this endogenous antioxidant are associated with many disease states such as neurodegenerative diseases, liver disease, cancer, and T2DM [46].

Magnesium may also contribute to MedDiet's prominent reductions in cardiovascular disease. Magnesium serves an important role as an electrolyte, necessary for potassium transport within the myocardium [34]. Magnesium is also essential in proper cardiac function via its role in electrophysiological processes [23]. Magnesium may also be beneficial in preventing and protecting against hypertension and other cardiovascular diseases via its ability to increase vasodilation of blood vessels, by reducing the excitability of smooth muscle cells, and regulating the endothelium [23, 34, 48]. Estruch et al. compared a MedDiet supplemented with mixed nuts or EVOO to a standard low-fat diet. The group who consumed mixed nuts demonstrated a small reduction in cardiac events compared to the group who consumed EVOO (3.8% vs. 3.4%, respectively) [54]. Nuts are a good source of magnesium, providing some potential evidence that increased magnesium intake within the context of the MedDiet may further enhance its cardioprotective potential.

Magnesium content of the MedDiet may also help partially explain the benefits of the diet on risk of T2DM. Adequate magnesium status may reduce the risk of T2DM, due to its role in glucose and insulin metabolism. As mentioned, magnesium is important as an ATP/ADP bridge, which influences tyrosine kinase activity [8]. Magnesium is important for glycogenolysis and the subsequent release of glucose-1-phosphate, causing changes in phosphorylase b kinase activity. Magnesium is also implicated in GLUT4 translocation, a process essential for glucose uptake into the cell [8]. Magnesium supplementation has also been shown to improve insulin sensitivity [52]. Furthermore, it is possible that MedDiet's potential to reduce neurodegenerative disease may be partly due to magnesium's capacity to bind to the NMDA receptor and block calcium from entering and triggering depolarization [34]. This is important for neurological health because overexcitability of the NMDA receptor is damaging to the brain and implicated in several cerebral pathologies [40].

There is reasonable evidence to support the notion that magnesium intake in the MedDiet may be one of the vectors by which many of the physiological and disease-preventing benefits of the MedDiet are enacted. Therefore, it is important to promote the consumption of foods within the context of MedDiet that are high in magnesium. Magnesium is present in water, consisting of approximately 10% of daily magnesium intake in some estimations [34, 55]. Magnesium is essential for the structure of chlorophyll, the green pigment in plants, which is why leafy green vegetables such as spinach and kale have high magnesium content [23]. However, it is important to keep in mind that some of these sources, such as spinach, also contain some phytochemicals, namely oxalates, that may impair magnesium absorption [53]. Considering the aforementioned information, it is likely beneficial to obtain magnesium from other sources, as well.

6. Comparing magnesium intake with different nutritional strategies

Because many of the benefits of the MedDiet may be attributable to its magnesium content, it is relevant to examine the magnesium intake in the MedDiet compared to other dietary strategies. The standard American diet is lacking in many micronutrients, with magnesium being prominent among these. The United States RDA for magnesium ranges from 310 to 420 mg per day for adults, 19 to 51 years of age, with most of the population failing to meet this recommendation [56]. It is estimated that 60% of the United States population does not meet the RDA for magnesium intake [8]. Castiglione et al. reported that, in a Sicilian cohort, 66.9% of the population met the European recommendations for magnesium intake of around 363 mg of magnesium per day, and 90.4% met the Italian recommendation of approximately 240 mg per day [23–25]. These data indicate that MedDiet is a superior source of magnesium-rich foods compared to the standard American diet.

Other dietary approaches may contain similar amounts of magnesium. The Dietary Approaches to Stop Hypertension (DASH) diet, which is composed predominantly of vegetables, nuts, and fish [57, 58], has been shown to reduce the incidence of T2DM similarly to the MedDiet [59]. Magnesium intake has been shown to be a relevant micronutrient for T2DM prevention in the Mediterranean and DASH diets [59]. One nutritional intervention that attempts to incorporate principles of both the Mediterranean and DASH diets is called the Mediterranean-DASH Intervention for Neurodegenerative Delay, or the MIND Diet [60]. Because the MIND Diet is somewhat of a fusion of the two dietary interventions, the nutritional adequacy of the intervention is comparable to the Mediterranean and DASH diets.

Morris et al. reported that adherence to the MIND diet resulted in significant reductions in the temporal progression of neurodegeneration in 960 participants, about 81 years of age, resulting in a difference equivalent to a reduction of 7.5 years in mental age [61]. Berendsen et al. reported that, in a cohort of 16,000 women, 70 years of age and greater, the MIND Diet attenuated declines in verbal memory, but not overall cognitive decline, over a period of six years [62]. Thus, the MIND Diet may be potentially protective against neurodegenerative disease, but more research comparing it to the Mediterranean and DASH diets separately is needed. This is especially the case for other facets of health such as cardiovascular and cerebrovascular disease risk, insulin sensitivity, quality of life, etc.

7. Conclusion and future perspectives

Overall, the Mediterranean Diet demonstrates incredible potential as a nutritional and lifestyle intervention to help reduce disease risk. The Mediterranean Diet is associated with reduced incidence of several diseases such as cardiovascular disease, type 2 diabetes mellitus, peripheral artery disease, atrial fibrillation, certain cancers, cerebrovascular disease, neurodegenerative disease, metabolic syndrome, improved blood lipid concentrations, and glucose metabolism [2, 6, 26–30]. Due to the Mediterranean Diet's inclusion of foods such as leafy green vegetables, nuts, fish, etc., provides a magnesium-rich nutritional pattern. This high magnesium content may be related to the disease-preventing health effects of the Mediterranean Diet. This is potentially due to the role of magnesium in glucose and insulin metabolism, vasomotor tone regulation, glutathione synthesis, its activity as a calcium blocker on the N-methyl D-aspartate receptor, and its importance in nutrient metabolism [8, 34, 45]. Thus, the consumption of magnesium-rich foods should be highly encouraged in Mediterranean Diet nutritional recommendations.

However, some considerations do exist in widespread adoption of the Mediterranean Diet, such as the required culinary education necessary to work with the foods comprising the diet. Furthermore, some of the qualitative lifestyle factors associated with Mediterranean culture might be more difficult to transfer to non-Mediterranean regions (such as longer meal duration, rest, etc.). However, many of the foods of the Mediterranean Diet fall within the nutritional considerations of many cultures, religions, ethnicities, etc. Thus, overall, the Mediterranean Diet is a promising nutritional intervention for widespread disease prevention, possibly mediated by its magnesium content.

This chapter provides a unique insight into the currently established health effects of the Mediterranean Diet by emphasizing the relevance of magnesium as mediator of these effects. The vast majority of research emphasizes the role of the favorable fatty acid profile and antioxidant content of the Mediterranean Diet as the primary mechanisms by which it exerts its beneficial health outcomes. While this avenue of research is certainly relevant, it is also important to examine the micronutrient density of the Mediterranean Diet as a potential vector for its positive role in the prevention of chronic disease. Due to magnesium's importance in a plethora of physiological activities, many of the widespread health effects of the Mediterranean Diet are likely mediated via the metabolic effects of this micronutrient. Further research is necessary to elucidate the micronutrient density of the Mediterranean Diet. In addition, it would be highly relevant to examine whether some of the health effects of the Mediterranean Diet may be attributable to specific micronutrient concentrations or ratios present in the diet. While significant research exists affirming the benefits of the Mediterranean Diet, some of the mechanisms by which it may exert its effects still remain somewhat unknown. This emphasizes the need for further understanding of the relative importance of differing factors such as fatty acid profile, antioxidant content, micronutrient density, and the macronutrient breakdown of the diet in contributing to the varied health effects of the Mediterranean Diet. This information would also help contribute to designing other nutritional interventions for targeted health outcomes.

Author details

Pierre-Anne Robbin Laird*, Noah Stallard, Yasmin Momenian, Katherine Oshirak and Stella Lucia Volpe
Virginia Polytechnic Institute, Blacksburg, Virginia, United States

*Address all correspondence to: pierre18@vt.edu

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