CLINICAL SCIENCE OF NUTRITION
Review Article
DOI: 10.62210/ClinSciNutr.2024.93

Innovative approaches to integrating plant-based nutrition in clinical care: a path to better patient outcomes

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Cite this article as: Arslan S, Aydın A, Gerboğa R, et al. Innovative approaches to integrating plant-based nutrition in clinical care: a path to better patient outcomes. *Clin Sci Nutr*. 2024;6(3):175-190.

ABSTRACT

This review examines the impact of plant-based diets on health, focusing on preventing cardiovascular disease (CVD), obesity, type 2 diabetes mellitus (T2DM), and certain cancers. Various plant-based dietary models are assessed, including vegetarian, vegan, flexitarian, Mediterranean, and DASH, considering their nutritional composition and health benefits. Transitioning to plant-based nutrition is crucial not only for individual health but also for environmental sustainability due to its lower ecological footprint compared to animal-based diets. However, ensuring nutritional adequacy, especially for key nutrients like calcium, vitamin D, and B12, requires careful planning. Patient-centered approaches and gradual transitions to plant-based diets are emphasized in clinical practice. Integrating plant-based nutrition into healthcare settings involves patient assessment, dietary counseling, and menu planning to empower patients towards sustainable dietary habits. Overall, evidence strongly supports the health and sustainability benefits of plant-based diets. By incorporating plant-based nutrition into clinical practice, healthcare practitioners can significantly impact healthier dietary choices and improve patient outcomes.

Keywords: plant-based nutrition, clinical practice, dietary patterns, chronic diseases, environmental health

INTRODUCTION

The Impact of Plant-Based Dietary Patterns on Health and Disease

The World Health Organization (WHO) defines a healthy diet as one in which fruits, vegetables (starch-free), whole grains and oilseeds are increased; added sugar (less than 10% of total energy intake) and salt (<5 g/day) are reduced; less than 30% of energy comes from dietary fat (plant sources) and saturated fat (animal sources) is limited.[1] A diet high in highly processed foods and meat is a major cause of chronic diseases such as cardiovascular disease (CVD), cancer, and type 2 diabetes (T2DM). This negative change in dietary habits has been exacerbated by the widespread adoption of a Western-style diet.[2] In this context, there are many healthy eating models, mostly plant-based: Mediterranean, Dietary Approaches to Prevent Hypertension (DASH), pescetarian, vegetarian, vegan, vegan, all plant-based diets (Table 1).[3,4] Traditional dietary habits are generally based on plant foods rather than animal foods, but with the influence of the global food industry, these traditional diets have changed and become more based on meat, dairy, and processed foods.

Nutrition science no longer focuses on individualized nutrients but on healthy foods and dietary patterns. This is because dietary patterns can more comprehensively examine interactions and potential synergistic effects between nutrients. Accordingly, it is important to adopt a dietary pattern that is generally plant-based.[5] Healthy dietary patterns, which have been shown to reduce the risk of heart disease, T2DM, stroke, hypertension, and hyperlipidemia in various clinical trials, contain varying

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Received: May 26, 2024 Accepted: October 3, 2024
Published: October 17, 2024

Table 1. Definitions of plant-based dietary patterns	
Feeding pattern	Definition
Vegetarian	Dietary patterns without meat, poultry, fish
Lacto-ovo vegetarian	Dietary pattern of dairy and egg consumption
Lacto-vegetarian	A dietary pattern in which dairy products are consumed
Pesko-vegetarian	Seafood-based dietary pattern
Vegan	A dietary pattern in which foods of animal origin and their products are not consumed
Flexitarian	A dietary pattern in which small amounts of meat, poultry, eggs and dairy products are consumed, often while actively reducing meat and dairy consumption to reduce the environmental impact of their diet
Mediterranean diet	Dietary pattern typically based on plant foods found in the region, moderate consumption of lean meat, dairy, seafood and olive oil
DASH diet	A dietary pattern with moderate consumption of some animal-derived foods such as lean meat, and low-fat dairy products, and limited salt consumption
Plant-based nutrition	A dietary pattern that includes 85-90% plant-based foods, although there is no consensus definition
A purely plant-based diet	A healthy vegan diet consisting of fruits, vegetables, whole grains, legumes, nuts, minimizing/ avoiding added fat, salt and sugar consumption
DASH: Dietary approaches to prevent hypertension	

amounts of animal-derived nutrients but have in common a reduction in saturated fat, sugar, salt, and processed foods.[2,4] In a systematic review of 153 articles and 6,550,664 individuals, the impact of dietary patterns on all-cause mortality was evaluated. According to the data, dietary patterns that included more vegetables, fruits, legumes, nuts, whole grains, unsaturated vegetable oils, fish, lean meat, or poultry (if meat is included) were found to significantly reduce the risk of all-cause mortality. It has been stated that these dietary habits include relatively lower intakes of red and processed meat and refined carbohydrates.[6] With proper planning, it is possible to meet most nutrient needs with a plant-based diet, but it is key to optimize nutrient diversity and bioavailability of nutrients to meet the needs of individuals in plant-based dietary patterns. Vitamin D and B_{12} are not found in plant-based foods and can be provided by supplements and fortified foods. Other components, such as iodine, omega-3 fatty acids, and selenium, may be inadequate in some plant-based diets, depending on geographical region, food type, processing and cooking, individual needs, and other factors. However, inadequate protein intake can be a problem in the elderly and at-risk groups. On average, 85% of plant-based protein foods are digested due to their high fiber and phytochemical content. It has been shown that about 85-95% of the protein in egg whites, whole eggs, and chicken is absorbed, whereas about 50-75% of the protein in chickpeas, mung beans, and peas is absorbed.[5]

Main Points

- Chronic Disease Reduction: Plant-based nutrition reduces the risk of chronic diseases like cardiovascular disease, type 2 diabetes, obesity, and certain cancers, improving patient outcomes.
- Sustainability: Plant-based diets promote both health and environmental sustainability due to their lower ecological footprint.
- Nutritional Planning: Proper planning ensures that plant-based diets provide essential nutrients like calcium, vitamin D, and B12.
- Clinical Integration: Patient-centered approaches and dietary counseling in clinical settings help patients adopt plant-based diets effectively.
- Strong Evidence: Evidence supports plant-based diets as effective in preventing and managing chronic diseases, making them a valuable tool in healthcare.

There is ample evidence to support a plant-based diet for the prevention and treatment of chronic diseases. The transition to a plant-based food system is also necessary in terms of climate, environmental health, ethics, ideology, and sustainability. This review aims to examine the effects of plant-based diets on health and chronic diseases in various chronic diseases.

Cardiovascular Diseases

CVD, which includes coronary heart disease, cerebrovascular disease, and peripheral vascular disease, is one of the most common non-communicable diseases.[7] The most important underlying cause of CVD is atherosclerosis, a progressive disease of the blood vessels. Underlying risk factors include conditions such as

high blood pressure, dyslipidemia, overweight/obesity, T2DM, and behavioral risk factors such as smoking, unhealthy diet, and reduced physical activity.[8] Managing these risk factors has an important role in slowing the development of the disease and preventing CVD. Given the significant mortality and morbidity, diet represents an important, modifiable risk factor that also influences other cardiovascular risk factors.[9] High amounts of refined carbohydrates, sweets, and sugars, and foods with high animal protein content, especially processed meat and red meat, play a role in CVD formation.[10,11] Plant-based diets that promote higher consumption of plant foods and lower intake of animal foods containing saturated fats such as red meat are associated with improved cardiovascular health and reduced cardiac and all-cause mortality.[12] A healthy plant-based diet shows positive effects on cardiovascular health through different mechanisms.[13] The potential mechanisms underlying these effects are summarized in Figure 1.

Several recent studies have demonstrated the beneficial effects of a plant-based diet on cardiovascular morbidity and mortality.[9,11,14] In a study involving 3678 adults with chronic diseases, the relationship between plant-based diets and CVD risk factors was examined and it was concluded that plant-based diets may improve CVD risk factors in adults with chronic diseases.[14] A meta-analysis of 30 observational and 19 clinical studies found that plant-based diets were associated with decreased total cholesterol, high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) levels, but not with decreased triglyceride (TG) levels.[15] In addition, in a prospective cohort study completed with 4507 people without dyslipidemia and chronic disease at baseline; it was concluded that compliance with a healthy plant-based diet may reduce the risk of dyslipidemia by showing positive effects on LDL-C, HDL-C, and total cholesterol levels.[16] In a study of 70,696 adults followed for 18 years, vegetable protein intake was associated with reduced all-cause and CVD-related mortality. In addition, replacing protein from red or processed meat with plant protein sources was associated with a reduced risk of cancer-related and CVD-related mortality.[17] In a study with identical twins, those on a vegan diet showed improvements in LDL-C and fasting insulin levels compared to those on an omnivorous diet.[18]

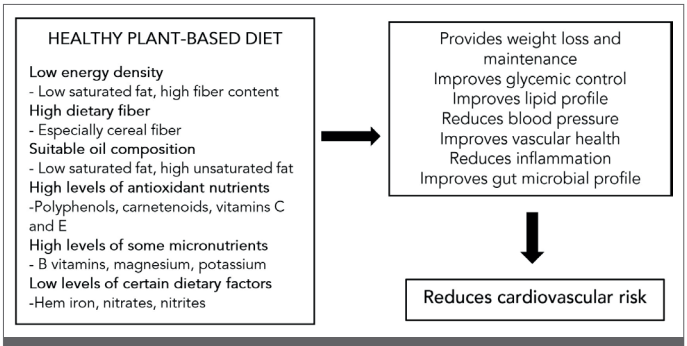

Figure 1. Potential mechanisms underlying the cardiovascular effects of healthy plant-based diets

According to the 2019 ACC/AHA (American College of Cardiology/American Heart Association) guidelines on nutrition, a diet emphasizing the consumption of vegetables, fruits, legumes, nuts, whole grains, and fish is recommended to reduce the risk of Atherosclerotic Cardiovascular Disease (ASCVD) (Stage I). A Stage IIa recommendation suggests that replacing saturated fat with monounsaturated and polyunsaturated fats in the diet and reducing sodium, cholesterol, processed meat, refined carbohydrates, and sugary drinks may be beneficial in reducing ASCVD risk.[19] All evidence for this dietary approach, in combination with other lifestyle interventions, has been shown to reduce symptoms and significantly improve clinically relevant cardiovascular markers.[5] In conclusion, a plant-based diet shows positive effects on CVD prevention through its protective effects mediated by bioactive components.[5,19] These studies suggest that promoting plant-based dietary patterns may contribute to longevity in terms of cardiovascular health.

Cancer

The World Cancer Report emphasizes that the increase in the incidence of cancer, which is an important public health problem, will continue with the increase in the population and that this situation will especially affect low and middle-income countries. According to current estimates, the number of 50.5 million people diagnosed with cancer in the last 5 years in 2020 worldwide is expected to increase further in the coming years.[20] The causes of cancer include environmental (smoking, obesity, dietary patterns, physical/chemical agents) and genetic factors. It is thought that changes in dietary habits can contribute approximately 30-50% to prevent the onset of cancer.[21]

Plant-based foods are the main source of dietary fiber and other bioactive compounds. In particular, plant bioactives including fiber, sulfur compounds, carotenoids, and polyphenols found in foods such as cruciferous and allium vegetables, tomatoes, green tea, and whole grains have well-known anticarcinogenic properties.[22] In one study, 1024 patients with colon cancer (stage III) who preferred whole grains over refined whole grains showed that cancer recurrence and mortality may be lower.[23] In another study, higher long-term adherence to a healthy plant-based diet index was associated with improved survival, and conversely, higher adherence to an unhealthy plant-based diet index was associated with worsened survival.[24] In a prospective cohort study of 1404 colorectal cancer survivors, a plant-based diet index was

inversely associated with all-cause mortality[25], whereas healthy plant-based diet indices were associated with lower mortality and unhealthy plant-based diet indices were associated with higher mortality.[25] In parallel with this study, higher dietary fiber intake after the diagnosis of non-metastatic colorectal cancer was inversely associated with colorectal cancer-specific and all-cause mortality. In a subgroup analysis of fibers from different sources in the study, it was stated that especially cereal fiber may be important for improving survival rate.[26] In a study conducted in China, 3449 breast cancer survivors reported that high consumption of oilseeds was associated with an approximately 50% reduction in the risk of breast cancer recurrence, metastasis, or death.[27] In conclusion, it is shown that plant-based diets and their components may have the potential to improve cancer prognosis, especially in breast and colorectal cancer survivors. In a study conducted in Iran, it is emphasized that dietary fiber reduces cancer risk by removing damaged cells from dilute bile acids in digestion and may reduce the likelihood of mutations and cell proliferation.[28] In another study, a 20 mg daily increase in flavonoid intake was associated with a 10% reduction in the risk of developing lung cancer.[29] In a study conducted in the United Kingdom (UK), the association of plant-based diets with cancer risk was evaluated between individuals who consumed low amounts of meat, and fish and vegetarians and individuals who consumed meat regularly. The 3 groups examined were associated with a lower risk of colorectal cancer, postmenopausal breast cancer, and prostate cancer compared to regular meat consumers.[30] A systematic review found that consumption of 100-120 g of red meat increased the risk of breast cancer by 11%, colorectal cancer by 17%, and advanced prostate cancer by 19%. It was stated that consumption of 50 g of processed meat per day increased the risk of prostate cancer by 4%, breast cancer risk by 9%, colorectal cancer risk by 18%, pancreatic cancer risk by 19%, and cancer mortality risk by 8%.[31]

In the report on diet and cancer published by the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR), it is stated that while an unhealthy diet is a risk factor for many types of cancer, a healthy dietary pattern of plant-based nutrition can reduce cancer risk.[22]

Respiratory Diseases and Sleep Health

Nutrition is an important factor for respiratory and lung health. Vitamins, minerals, antioxidant components, fatty acids, and adherence to certain dietary patterns are associated with the pathophysiology and development of respiratory diseases.[32] While antioxidant deficiency can be seen due to limited fruit and vegetable consumption, oxidative stress levels in the body can increase with the consumption of foods high in saturated fat and Western-style nutrition. This leads to the production of reactive oxygen species (ROS) and subsequent lung damage through various oxidative and inflammatory processes.[33] It is known that diets rich in antioxidant or anti-inflammatory nutrients can modulate the impact of harmful environmental exposures or directly benefit lung health.[34]

Recent epidemiologic studies have reported that consuming antioxidant-rich foods, especially fresh fruits and vegetables, may be beneficial for respiratory function and symptoms in people with chronic respiratory diseases.[35] In a study comparing individuals with chronic obstructive pulmonary disease (COPD) with healthy controls, it was observed that COPD patients consumed fewer fruits and vegetables and followed diets with poorer antioxidant content, which was associated with impaired lung function and increased risk of COPD.[36] Intake of dietary fiber shows potential benefits with both antioxidant and anti-inflammatory properties. In addition, dietary fiber consumption has been associated with lower COPD prevalence.[37] Plant-based diets have been found to decrease proinflammatory molecules and increase anti-inflammatory markers in asthma. Components such as unsaturated fatty acids and antioxidants derived from plant-based foods have been shown to alleviate inflammation and conditions caused by the systemic inflammatory response.[38] The high fat intake seen in Western-style diets can lead to increased airway inflammation, but fruits, vegetables, and their antioxidants can reduce airway inflammation.[39] One study reported an inverse relationship between fruit intake and asthma severity in both adults and children, but studies are needed to explain the mechanism between dietary patterns and asthma symptoms.[38] Many patients with obstructive sleep apnea have reported an improvement in sleep quality and duration after following a plant-based diet. Studies show that a high intake of plant-based protein tends to be positively associated with sleep duration, better sleep quality, and lower insomnia.[40] In six countries (France, Germany, Italy, Spain, UK, United States of America (USA)), plant-based diets or pescetarian diets were associated with a 73% lower risk of moderate to severe coronavirus (COVID-19).[41] In parallel to this study, a diet characterized by healthy plant-based foods was associated with a 9% lower risk of COVID-19 and a 41% lower risk of severe COVID-19.[42] Although plant-based dietary patterns are known to have positive effects on health before the pandemic, it has been reported that they can also be applied to protect against severe COVID-19 and reduce symptoms.[41] With the periodic quarantines implemented between 2019-2022, decreased physical activity, increased stress factors, and low consumption of fruits and vegetables increased the risk of complications of the virus. Since decreased antioxidant and vitamin

intake is one of the important forces in the fight against the virus, it is very important to apply a plant-based diet that is sufficient in terms of vegetables and fruits.[43]

According to the results of studies in the literature, plant-based nutrition may reduce the severity and symptoms of respiratory diseases. However, more studies are needed to determine the mechanism between plant-based nutrition and respiratory diseases.

Weight Management

As a result of all metabolic activities that take place in the human body, the excess of energy intake over expenditure causes an increase in body weight and leads to obesity. According to WHO, obesity is defined as a body mass index (BMI) of 30 kg/m^2 and above or an increase in body fat to the extent that it impairs health.[44]

Obesity, which is a chronic disease related to eating habits, is a risk factor for many diseases (CVD, T2DM, cancer). Therefore, changing dietary habits and body weight management are very important in the prevention and treatment of obesity.[45] The health effects of the rapidly popularizing plant-based diet have led to the need to understand and evaluate its potential implications for weight management.[46] The caloric density of nutrients is very important for body weight loss. The caloric density of plant-based foods is lower than animal-based foods.[47] However, plant-based nutrition is thought to prevent overfeeding by filling the stomach volume with high consumption of fruits, vegetables, and fiber foods, increasing the feeling of satiety, causing gastric emptying, and slowing intestinal absorption.[48] In a randomized controlled study investigating the effects of a plant-based diet, a vegan diet was applied to the intervention group for 16 weeks. A decrease in body weight and fat mass was observed in the vegan diet group.[49] In another similar study, a completely plant-based diet was applied to the intervention group for 6 months and reductions in BMI were found.[50] In a study aiming to minimize the effects of environmental and individual characteristics, omnivorous and vegan diets were applied in identical twins and a significant decrease in body weight was observed in individuals on a vegan diet.[18] In a cross-sectional study examining the prevalence of obesity with the Plant-Based Diet Index, no significant association was found between the dietary index and obesity.[51] Another study using the Plant-Based Diet Index showed that a plant-based diet in general may reduce the risk of obesity and that an unhealthy plant-based diet may be associated with a high risk of obesity.[52] The quality of plant-based nutrition is a very important issue. At this point, unhealthy plant-based diets are plant foods that are highly processed and contain significant amounts of sugar, salt, and fat.[53] In studies, it has been reported that people who follow a healthy plant-based diet have lower BMI, waist circumference, and abdominal adiposity than people who follow an unhealthy plant-based diet.[25,54]

In studies on obesity and weight management, diet quality is as important as dietary patterns. At this point, it is thought that plant-based nutrition has a potential effect on obesity and is beneficial in terms of weight management and chronic diseases when risk factors are considered.

Diabetes

Diabetes is a multifactorial metabolic disorder characterized by dysregulated glucose homeostasis, insulin resistance, and impaired insulin secretion. Poor glucose control in people with T2DM can result in micro- and macrovascular complications, including retinopathy, neuropathy, nephropathy, and cardiovascular disorders.[55] According to the National Diabetes Federation's 2021 Current Diabetes Atlas, 537 million people are estimated to have diabetes in 2021, while this number is projected to reach 643 million by 2030 and 783 million by 2045.[56] The risk factors that lead to the development of T2DM interact with each other, complicating the prevention and treatment of the disease. These factors include unhealthy lifestyle, genetic predisposition, and dietary habits. It has been found that most cases of T2DM develop due to dietary and lifestyle factors, particularly the Western diet, which is high in animal-based and processed foods.[57,58]

In recent years, there has been an increasing number of studies investigating the effectiveness of a plant-based diet in diabetes prevention and management. In the EPIC-Oxford prospective cohort study, it was found that the incidence of T2DM decreased by 37-53% in those who maintained a predominantly or entirely plant-based diet, including vegetarian, vegan, pescetarian diets, whereas there was an increased risk of T2DM in those who consumed processed and unprocessed red meat, eggs and animal protein in general.[59] In parallel with this study, a systematic review of 34 studies reported that a diet rich in red and processed meat before pregnancy was associated with an increased risk of gestational diabetes.[60] A systematic review found that a vegan diet was associated with a lower prevalence and incidence of T2DM, although in some studies it could not be determined whether this was due to a vegan diet alone or healthy lifestyle habits.[61] A meta-analysis of studies examining dietary protein intake and T2DM risk stated that high protein and animal-derived protein intake was associated with an increased risk of T2DM.[62] A systematic review and meta-analysis of 13 randomized controlled trials showed that replacing animal-derived protein with plant-derived protein led to significant reductions in HbA1c, fasting glucose, and fasting insulin levels compared to control groups.[63] A plant-

based diet has advantages for supporting the remission of T2DM. Since this diet consists of foods that are naturally low in calories but rich in nutrients, it eliminates the need to count calories or limit carbohydrates, which may be a more acceptable and sustainable option for patients.[64] While the effect of low-fat vegan diets on blood glucose regulation is generally associated with reduced body weight, factors such as reducing saturated fats and restricting the intake of high glycemic index (GI) foods are also thought to have positive effects on blood glucose regulation.[65] Consumption of 45 g of whole grains per day has been shown to reduce the risk of T2DM by 20%, and consumption of fruits and vegetables (six servings per day) has been shown to reduce the risk of T2DM by 20-30%.[66,67]

In conclusion, there are many studies indicating that a plant-based diet may have a positive effect on the prevention and treatment of T2DM.[62-67] However, more in-depth studies with larger samples are needed to fully understand the certainty of the evidence.

Kidney Diseases

Chronic Renal Failure (CRF) is a nephrological syndrome characterized by chronic, progressive, and irreversible nephron loss due to various diseases. The main factors that increase the risk of CRF are genetic predisposition, family history, advanced age, gender, ethnic characteristics, low birth weight, obesity, smoking, exposure to nephrotoxic substances, acute kidney injury, T2DM, and hypertension.[68] Kidneys have an important role in nutritional homeostasis. Regulation of fluid-electrolyte and acid-base balance and excretion of metabolic wastes are among their important tasks.[69]

Updated in 2020, the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (NKF/KDOQI) guideline recommends the use of low proteins of plant origin (lentils, beans, peas, etc.) in CRF.[70] The amino acids methionine and cysteine in animal-derived proteins form acid due to the presence of organic sulfur oxidized to inorganic sulfate. According to the NKF/KDOQI guidelines, increasing fruit and vegetable intake can reduce body weight, blood pressure, and acid production (Stage II C). Plant-based diets are low in sodium and rich in various phytochemicals, fiber, vitamins, minerals, and antioxidants, unless salt is added during food preparation and processed foods are included. Therefore, plant-based diets are important in preventing micronutrient deficiencies (magnesium, zinc, vitamin K, and vitamin C) in CRF patients.[69] In addition, plant-based low-protein diets are also useful for the prevention and treatment of major comorbidities associated with CRF, such as T2DM, hypertension, and cardiovascular diseases.[71]

Hyperkalemia is one of the common complications in CRF patients. Although plant-based foods are rich in potassium, they are known to have lower bioavailability rates compared to animal-derived and processed products.[72] At this point, it is thought that other effects of these sources can be utilized without accelerating hyperkalemia with the low bioavailability of potassium from plant sources.[69]

Hyperphosphatemia is an independent risk factor for mortality in CRF. Plant-based foods are limited in patients with CRF due to their phosphate content. Phosphates in these foods are bound to phytates, and bioavailability is limited because the enzyme phytase, which releases phytate, is deficient in humans. For this reason, phosphate bioavailability in plant-based foods varies between 10 and 30%, whereas it can range from 40 to 60% or even up to 80% in animal-based foods.[73] In addition, serum phosphate levels have been shown to decrease with plant-based diets compared to animal-based diets.[74]

Plant-based diets may be effective in managing some symptoms and metabolic complications of CRF. It has been suggested that plant-based nutrition carries little risk in the prevention of CRF and that restriction of plant-based nutrients in hyperkalemia and malnutrition should be individualized as it may reduce the potential effects of these nutrients.[69]

Non Alcoholic Fatty Liver Disease

Non-alcoholic steatohepatitis (NAFLD) describes a spectrum of histological and clinical manifestations characterized by the formation of steatosis in more than 5% of the liver, ranging from simple steatosis to fibrosis and cirrhosis.[75] The increasing incidence of NAFLD has been associated with an increase in obesity and T2DM. NAFLD is caused by interrelated environmental and genetic risk factors. Although some genetic risk factors have been identified, obesity and the presence of metabolic syndrome are recognized as the strongest risk factors for the development of NAFLD.[76] Therefore, lifestyle changes, including dietary patterns, play a key role in the management of NAFLD.[77]

Although vegetarian diets are plant-based, some types include animal-based foods. In this respect, studies on complete plant-based diets are limited. In studies, dietary patterns characterized by high consumption of healthy plant-based foods have been associated with a lower prevalence of NAFLD and hepatosteatosis.[78] As fruits and vegetables are primary sources of phytochemicals with antioxidant and anti-inflammatory effects, plant-based diets have been shown to reduce body weight more successfully than omnivorous diets.[79] Dietary indices such as the healthy plant-based diet (hPDI), the Mediterranean diet, the DASH diet, and the Healthy Eating Index-2015

(HEI-2015) encourage high intakes of vegetables and fruits (source of fiber), nuts (source of phytochemicals), legumes and whole grains, while limiting red and processed meat consumption.[80] A study in the United Kingdom associated a healthy plant-based diet with a lower risk of NAFLD and hepatosteatosis, independent of genetic susceptibility. However, an unhealthy plant-based diet was associated with a higher risk of NAFLD and intrahepatic steatosis, but it is emphasized that the quality of plant-based foods is also important at this point.[81] Red and processed meat consumption may promote insulin resistance and increase oxidative stress in the liver, leading to the development of NAFLD. These foods are also naturally high in saturated fat and cholesterol, which are known to worsen NAFLD, as well as potentially harmful sodium, preservatives, and advanced glycation end products.[82]

Gastrointestinal Diseases

The gastrointestinal system (GIS) performs the digestive function, whereby dietary nutrients are broken down into small pieces and incorporated into the bloodstream to provide energy and be used in metabolic activities in the body.[83] Diet is an important regulator of GIS homeostasis and intestinal permeability through the interaction of the immune system and gut microbiota on the mucosal barrier. The GIS is subject to significant chronic inflammatory diseases: Gastroesophageal reflux, colorectal cancer, celiac disease, irritable bowel syndrome, diverticulitis, and inflammatory bowel diseases.[84] These diseases are associated with poor dietary and lifestyle choices, particularly low consumption of plant-based foods (dietary fiber) and high consumption of animal-based foods (saturated fat, cholesterol).[85]

The most common environmental risk factor for inflammatory bowel diseases, which have various risk factors, is thought to be a Western-style diet high in animal fat and low in dietary fiber. Therefore, dietary changes are a frequently recommended approach in the treatment of inflammatory bowel diseases.[85] In a study, when the relationship between the symptoms of individuals with IBD (Inflammatory Bowel Disease) and nutrition was examined, it was concluded that fruit and vegetable intake alone was not sufficient to reduce the risk of active symptoms, but a plant-based diet with high fruit and vegetable consumption and reduced meat and dessert consumption was associated with a lower risk of active symptoms.[86]

It has been found that plant-based diets may mediate their positive effects on gastrointestinal health, especially by increasing bacterial diversity in the gut microbiota.[87] Plant-based diets, which cause an increase in lactic acid bacteria such as *Ruminococcus*, *E. rectale* and *Roseburia* with their high fiber content, cause an increase in *Lactobacillus* and *Bifidobacterium* strains with their polyphenol-rich content and thus reduce inflammation. However, compared to omnivorous individuals, the microbiota of individuals fed plant-based diets contains more *Bacteriodetes* species with anti-pathogenic effects.[88] In a systematic review of 12 studies, the effects of plant-based diets on gut microbiota were examined and it was found that plant-based diets positively affected the gut microbiome composition with a high content of short-chain fatty acids (SCFAs) compared to traditional diets. In addition, it was concluded that it reduced the risk of disease by decreasing trimethylamine-N-oxide (TMAO) intake, which is one of the risk factors of IBD.[89] In a study of 121 individuals, diet composition and fecal microbiota composition were examined and a rich and diverse bacterial content was observed in the microbiome of vegetarian individuals compared to omnivores. The *Firmicutes* / *Bacteroidetes* ratio was lower and the *Prevotella* / *Bacteroides* ratio was higher in vegetarians. A positive relationship was observed between meat consumption level and *Bacteroides* ratio and a negative relationship was observed between *Prevotella* ratio.[90] The effects of the main components of plant-based foods on gastrointestinal health are shown (Table 2).

Table 2. Effects of components in plant-based foods on gastrointestinal health.

Plant-based dietary ingredient	Impact on gastrointestinal health
Vegetable protein	Inflammation is reduced The intestinal barrier increases
Indigestible carbohydrates (plant fibers)	Anti-inflammatory function Strengthening the function of the intestinal barrier Down-regulation of proinflammatory cytokines
Fiber and prebiotics	SCFA construction increases TMAO production decreases
Unsaturated fatty acids	LDL-C and total cholesterol levels decrease Toll-like receptor activation is reduced
Polyphenols	Immunomodulatory effect Antioxidant and anti-inflammatory properties

GIS: Gastrointestinal system, SCFA: Short-chain fatty acids, TMAO: Trimethylamine-N-oxide, LDL-C: Low-density lipoprotein cholesterol

According to these studies, nutrition is an important determinant of the structure of human gut microbiota. In particular, plant foods are involved in the prevention of gastrointestinal diseases by regulating the microbiota through pulp and bioactive compounds. Current research suggests that switching to a plant-based diet may help increase the diversity of health-promoting bacteria in the gut. More observational research is needed to define the links between nutrition, the microbiome, and health outcomes.

Mental Health and Diseases

Mental health and diseases include a variety of disorders that affect mental functioning and combine cognitive deficits and psychiatric symptoms, such as schizophrenia, depression, bipolar disorder, Alzheimer's, Parkinson's, multiple sclerosis, migraine, autism spectrum disorders, and hyperactivity disorder.[91] Considering the side effects of psychiatric medications, easy-to-implement, sustainable adjunctive strategies such as dietary intervention are considered to have high clinical utility in the treatment of disorders.[92] However, the interaction of mental health and diet is not limited to any one biological pathway and interacts with many mechanistic pathways such as gut microbiota, inflammation, oxidative stress, and epigenetics.

The effects of plant-based nutrition on mental health and the mechanisms of how these effects occur are not clear, but it is thought that the microbiota-gut-brain axis and the communication of the intestines with the brain may affect mental health by regulating hormones through the vagus nerve and reducing inflammation.[93] It is thought that plant-based dietary patterns, rich in indigestible plant fibers, antioxidants, and other important nutrients, and low saturated fat content may have a positive effect on mental health by increasing the diversity of intestinal flora. Saturated fats in the diet reduce beneficial *Bifidobacteria* species and increase pro-inflammatory *Bilophila* bacteria. With the increase of these organisms, prebiotic fibers are fermented to produce SCFAs, which are neuroprotective and anti-inflammatory. A reduction in both the amount and balance of microbial species (dysbiosis) has been implicated in many mental disorders, including depression and anxiety.[94,95] It is stated that plant-based nutrition may be beneficial as a short-term intervention, but there is no clarity about its long-term effects.[96] Vitamins, minerals, and long-chain omega-3 fatty acids, which have antioxidant properties in plant-based diets, can affect mood and increase the production of important neurotransmitters such as serotonin, dopamine, epinephrine, and norepinephrine, improving mood and improving cognitive abilities.[97,98] However, most research has examined the relationship between depression, anxiety, stress, and mood disorders and a plant-based diet, with inconsistent results. It is thought that an inadequate vegan dietary pattern may lead to stress, depression, and anxiety, and negatively affect nervous system functioning, as deficiencies in iron, omega-3, omega-6 fatty acids and vitamin B_{12} may be observed.[99] Another perspective is that vegetarian and vegan diets are associated with lower levels of stress, anxiety, and depressive symptoms compared to omnivorous diets due to increased consumption of antioxidants such as vitamin C, vitamin E, and beta-carotene, as well as omega-6, fiber, and phytoestrogens through plant-based diets. This dietary pattern has the potential to show antidepressant properties by increasing serotonin and dopamine levels, inhibiting inflammation in the brain that is associated with depression.[100]

In conclusion, the current findings suggest that a plant-based diet may contribute positively to mood, but more in-depth studies are needed to clarify the mechanisms of these effects.

Women's and Men's Health

WHO defines sexual health as a state of physical, emotional, mental, and social well-being about sexuality.[101] Sexual dysfunction is especially common in women with chronic health problems such as metabolic syndrome, hypertension, dyslipidemia, coronary heart disease, T2DM, obesity, anxiety, and depression.[102] Another important condition related to women's and men's health is infertility. Defined as the inability to conceive despite 12 months of unprotected sexual intercourse, infertility affects 80 million couples every year according to WHO data.[101] Human fertility is a process in which various factors are integrated. These factors include female (ovulation and uterine disorders), male (abnormal sperm production and function), medical conditions (pelvic inflammatory disease and cancer), non-modifiable factors (genetics, gender, age), and modifiable lifestyle factors (physical activity, weight control, nutrition, alcohol, smoking, stress, long-term contraceptive use).[103]

Nutrition and dietary patterns can positively or negatively affect fertility outcomes in men and women. Unhealthy eating habits, especially hypercaloric diets, increased intake of saturated and trans fats, and consumption of high GI and low nutrient foods, can have adverse effects on metabolism. These effects include obesity, T2DM, and insulin resistance. These conditions can lead to increased oxidative stress in the body. Oxidative stress can lead to disorders in the hormonal and immune systems and a decrease in sperm quality, thereby increasing the risk of infertility.[104] In a study, a fertility diet is recommended to eliminate the functional impairment caused by oxidative damage in oocyte mitochondria in infertile women. This diet includes antioxidants, energy enhancers,

and nutrients that are cofactors. Antioxidants such as catechins, N-acetylcysteine, proanthocyanidins, vitamin C, and vitamin E aim to prevent mitochondrial damage by sequestering free radicals.[105] Although there is no dietary recommendation for the prevention of endometriosis in women, there is evidence to suggest that avoiding red meat and eating a high-fiber plant-based diet may help alleviate endometriosis symptoms. In addition, the consumption of animal-based products has the potential to increase the risk of endometriosis due to their effects on steroid hormone levels.[106] A plant-based diet tends to decrease blood estrogen and insulin levels and increase sex hormone-binding globulin levels. Insulin is important because of its agonistic effects on estrogen production and endometrial cell proliferation. Folic acid, which is essential for deoxyribose nucleic acid (DNA) synthesis in sperm and whose deficiency in women can cause neural tube defects, can be provided by a plant-based dietary pattern.[107] In addition, nitric oxide (NO) exerts antioxidant, anti-inflammatory, and vasodilator effects on the contraction and relaxation of penile smooth muscle through the vessel walls. It has been shown that the bioavailability of NO increases with the consumption of plant-based foods rich in polyphenolic compounds and that the number of endothelial progenitor cells may increase when more plant-based foods are consumed. In addition, plant-based nutrition is protective against ROS due to high levels of antioxidants. Consumption of animal-derived foods triggers ROS through iron, animal-derived nitrates, and highly advanced glycation end products.[108]

As a result of the information obtained from the studies, plant-based nutrition positively affects male and female sexual health.

Alzheimer's Disease

Alzheimer's disease is one of the leading causes of dementia and its prevalence is increasing rapidly. Advanced age, gender, family history, genetic predisposition, decreased physical activity, unhealthy diet, and some chronic diseases are among the risk factors. Diet is one of the factors that can be changed to prevent Alzheimer's.[109]

Compared to omnivorous diets, a vegan diet is generally rich in fiber, polyunsaturated fatty acids, folic acid, magnesium, vitamins A, B_1, B_6, C, and E, and has effects on Alzheimer's pathophysiology. At this point, plant-based nutrition may help in the primary and secondary prevention of Alzheimer's disease.[110,111] In a meta-analysis, it was stated that increased fruit and vegetable consumption was associated with a significant 20% reduction in the risk of cognitive impairment and dementia. In addition, a dose-response effect was observed with a gradual increase in the consumption of 100 g of fruits and vegetables, which was associated with a 13% reduction in the risk of cognitive impairment and dementia.[112] In its guidelines for individuals with dementia, WHO recommends a diet rich in at least 5 servings of fruits and vegetables (400 g), legumes, nuts, whole grains (oats, bulgur, unprocessed millet and corn) per day.[113] In contrast, many micronutrients have been found to have a beneficial effect on the course of Alzheimer's disease: Vitamin C, vitamin D, glutathione, polyphenols, Q10, B_6, B_{12} vitamins, folic acid, lecithin, caffeine and some probiotics.[114] In contrast, a diet rich in saturated fatty acids and branched-chain amino acids (BCAA) has been reported to increase the progression of dementia.[115] Since it is difficult to provide especially vitamin B_{12} and vitamin D with plant-based foods, low B_{12} and the associated increase in homocysteine are associated with cognitive impairment. At this point, it is very important to provide micronutrients that cannot be provided by plant-based foods with supplements.[116]

At this point, plant-based diets for Alzheimer's disease reduce the risk of systemic inflammation, T2DM and obesity, proinflammatory bacteria in the gut, and plasma TMAO levels.[117,118] It is stated to be beneficial in terms of pathological mechanisms involved in the development of Alzheimer's disease and dementia. There is no clear recommendation in the plant-based dietary pattern since B_{12}, vitamin D, eicosapentaenoic acid (EPA), and especially docosahexaenoic acid (DHA) are insufficient with dietary sources.[110,111]

Autoimmunity and Chronic Inflammation

The immune system consists of innate immunity including immune system cells such as leukocytes, natural killer (NK) cells, immunoglobulins, dendritic cells, and acquired immunity including cytokines, B and T lymphocytes.[119] The immune system, which plays a role in the prevention of infections, also has tasks such as preventing the growth of some tumors[120], the formation of a response by recognizing newly formed molecules, purification from dead cells, and the initiation of tissue repair.[120]

A healthy immune system is essential for an individual to have an effective immune process. There are many factors affecting the immune system, and especially nutrition plays a role in innate and adaptive immune processes by affecting the intestinal mucous membrane and microbiome.[121] Disruption of the gut microbiome balance with the increase in Western-style nutrition can lead to the formation of inflammatory diseases increasing macrophages and inflammatory cytokines such as interleukin-1 (IL-1) and tumor necrosis factor-alpha (TNF-α).[122] High-fiber plant-based diets regulate homeostasis in the intestines by regulating the cytotoxic effect of pathogens and strengthening intestinal epithelial barrier function.[121] A healthy plant-based diet reduces inflammation through different mechanisms such as

polyphenol content, which is well known for its anti-inflammatory and antioxidant properties, inactivation of nuclear factor kappa-B, and modulation of mitogen-activated protein kinase and arachidonic acid pathways.[123] At the same time, plant-based diets may have positive effects on inflammatory and autoimmune diseases such as systemic lupus and rheumatoid arthritis with their antioxidant nutrient content.[124] Studies are showing that plant foods and the bioactive components they contain modulate immunologic and inflammatory processes (Table 3).

Studies have shown that healthy plant-based diets have a positive effect by regulating the gut microbiome and immune system components with low fat, high fiber, and antioxidant content. To determine whether plant-based diets are effective in reducing chronic inflammation and on the immune system, studies with larger and stronger samples with longer intervention periods and more diverse inflammatory biomarkers are needed.

Bone Health

There are macro and micronutrients that are important for bone health. Vitamin K, magnesium, zinc, and bioactive compounds, especially calcium and vitamin D, play a role in bone health. Inadequate levels of these nutrients can negatively affect bone health.[111]

Deterioration of bone health is directly related to osteoporosis and fracture risk. Therefore, it is extremely important to ensure adequate and balanced nutrition including all nutrients. Individuals with plant-based diets are at risk for deficiency of some nutrients. In a study, it was shown that B_{12} intakes of vegan individuals were very low, while calcium, zinc, and selenium intakes were below the recommended levels.[110] The fact that zinc, which can be obtained from both animal and plant sources, is low in individuals with plant-based diets may be due to insufficient absorption. The high phytate content of plant diets is one of the reasons for this situation.[127] The risk of developing osteoporosis, which occurs with decreased bone density, is higher for individuals with plant-based diets.[128] In a meta-analysis study examining the bone mineral density of vegan, vegetarian, and omnivorous diets, it was concluded that vegans and vegetarians had lower bone density and higher fracture risk than omnivores.[129] Calcium is known to be beneficial for bone and muscle health and milk is considered the primary source of calcium. However, in countries such as Sweden, where milk consumption is the highest, the hip fracture rate is high. In addition, many plant foods (soy products, calcium-enriched vegetable milk and yogurts, tofu, legumes, greens, and oilseeds) contain calcium.[130] Vitamin K and phytochemicals contribute to healthier bone formation and vitamin C can affect bone mass by hydroxylating lysine and proline, which are essential for the formation of stable collagen triple helices. Antioxidant nutrients and phytochemicals such as vitamin C, β-carotene and other carotenoids found in fruits and vegetables can improve bone health by scavenging oxygen radicals and reducing the risk of inflammation caused by free radicals.[131]

Table 3. Literature studies investigating the effect of plant-based diets on inflammation

References	Participants and Method	Conclusion
Craddock et al. 2019[125]	This systematic review and meta-analysis aimed to determine the association between vegetarian dietary patterns and inflammatory and immune markers The review included 30 observational and 10 intervention studies.	Consumption of a vegetarian dietary pattern was found to be associated with significantly lower levels of CRP, fibrinogen, and leukocytes compared with those on a mixed non-vegetarian diet.
Park and Zhang 2021[126]	We examined the associations between plant-based diets and lifestyles and CRP and WBC values in 40,768 adults over 40 years of age from a hospital-based cohort study.	It was concluded that a plant-based diet and lifestyle changes were associated with lower WBC counts and CRP, but a Western-style diet was associated with high CRP.
Clark et al. 2023[122]	152 healthy Australian men and women aged 65 years and older were randomized to MedDiet or a habitual diet (HabDiet, control) for 6 months. A total of 137 participants completed the study (MedDiet n = 74, HabDiet n = 63).	High adherence to the MedDiet for 6 months was observed to lead to improved dietary inflammatory index scores and anti-inflammatory activity compared to the HabDiet group in an older Australian cohort.
Wang et al. 2023[52]	NHANES participants were included in cross-sectional (N = 27,915, cycles 1999-2010, 2015-2018) and longitudinal analyses (N = 11,939, cycles 1999-2008). Diet quality and the association of plant-based diets with inflammatory-related mortality in obesity were examined.	Increased intake of a healthy plant-based diet was associated with lower inflammation, while an unhealthy plant-based diet was associated with higher inflammation.

CRP: C-Reactive Protein, WBC: White blood cells

Although a healthy plant-based diet has benefits for bone health, micronutrient deficiencies should be considered.

Dermatologic Diseases

Plant-based diets have been applied as a complementary therapy for skin health and have beneficial effects in modulating inflammatory and oxidative processes, which are the main mechanisms of inflammatory skin diseases. Therefore, plant-based diets can be considered as a treatment option with fewer side effects in certain skin conditions.[132]

In a study, it was observed that those who consumed milk every day developed more acne than those who consumed milk once a week.[133] Whey proteins, which are responsible for the insulinotropic effects of milk, increase insulin-like growth factor-1 (IGF-1) levels.[134] Acne formation can be seen in athletes who consume high amounts of whey protein.[135] Alternative protein sources derived from plants such as peas, rice, and hemp contain less BCAA. Therefore, they provide less stimulation of the sebaceous glands and support muscle growth.[133] Consumption of soy-derived products has been found to reduce the incidence of acne. Soy contains isoflavones and phytoestrogens that inhibit sebum production caused by androgens. In a study, when acne patients were given 160 mg/day of soybean isoflavones for 12 weeks, acne lesions decreased.[136] Omnivorous diets have high leucine content due to protein sources such as meat and cow's milk. Leucine activates the pathway induced by IGF-1 and has proinflammatory effects.[135] It has been reported that foods high in GI are also responsible for the development of acne. High-GI foods affect the intestinal microbiota by increasing intestinal permeability and causing acne formation. Plant-based diets contain low-GI nutrients and play a protective role due to the anti-inflammatory effect of these nutrients.[137] A study examining the food consumption of patients with psoriasis found that consumption of fresh vegetables and fruits was associated with normal serum lipids and blood pressure, lower waist-to-hip ratio, and reduced psoriasis. Reducing consumption of animal products improves skin and prevents psoriasis-related comorbidities. Therefore, plant-based nutrition improves the symptoms of psoriasis.[137] Increased maternal consumption of meat, milk, and dairy products during pregnancy is associated with an increased risk of atopic dermatitis in infants. Components in the mother's diet that may protect against atopic dermatitis include high antioxidant consumption and dietary fiber.[138] Some skin diseases and dietary patterns for these diseases are shown in Table 4.

In general, the negative effects of animal-derived foods such as milk and dairy products and processed red meat and the positive effects of plant-based diets on skin diseases have been reported. However, more studies are needed to understand the role of plant-based diets in disease management. Considering that all these suggestions and benefits do not cover the world population, according to today's molecular biology studies, individual differences should be taken into consideration, especially after genome studies. To better understand the effects of nutrition on genomics/epigenomics, proteomics, metabolomics, and genetics/epigenomics, PREDIMED and Food4Me studies were conducted to examine the Mediterranean diet especially plant-based diets. In the study involving 7 European countries, it is thought that consuming a diet low in discretionary foods, high in SFA, and low in fiber foods is important to maintain a healthy weight, regardless of fat mass and obesity-associated gene (FTO), which is prone to obesity.[141,142]

CONCLUSION

Plant-based diets are growing in popularity. There is also interest in the development of nutrition guidelines for diets that are sustainable and focus on human and planetary health. Plant-based diets are more sustainable than animal-based diets due to lower use of natural resources and greenhouse gas emissions. Plant-based diets are rich in fiber and phytochemicals and protect against chronic diseases such as CVD, obesity, T2DM, and certain types of cancer. While appropriately planned plant-based diets are largely nutritionally adequate, they may require the use of nutritional supplements such as calcium, vitamin D, and B_{12}. The literature shows that when a patient-centered

Table 4. Dietary patterns and effects in inflammatory skin diseases (modified from Lee et al. 2023)[136]

Inflammatory skin disease	Implemented dietary pattern and its benefits	References
Acne vulgaris	Avoidance of milk and dairy products and low GI diet: Anti-inflammatory effect and reduction in acne lesions	Meixiong et al. 2022[139]
Psoriasis (Psoriasis)	A purely plant-based diet: Anti-inflammatory effect, skin improvement and prevention of concomitant diseases	Fusano 2023[135]
Atopic dermatitis	Increasing fruit and vegetable consumption and avoiding packaged foods: Antioxidant and anti-inflammatory effect	Khan et al. 2022[140]

GI Glycemic index

approach and a gradual transition to a plant-based diet are used in the clinic, patients generally adopt this dietary pattern.

In contrast to the positive effects of plant-based nutrition, more studies are needed on the effects of nutrition on genomics/epigenomics, proteomics, metabolomics and genetics/epigenomics. It should not be forgotten that these effects may create personal limitations. In addition, the sustainable continuity of plant-based diet in geographical regions where animal-based nutrition is culturally widespread can be listed as another limitation. Individual preferences, cultural factors, and access to plant-based foods can be counted among the factors that will limit the implementation of plant-based diet. The lack of sufficient studies on this subject, especially in clinical practice in chronic diseases, limits the recommendations to be made and the guidelines to be created.

To successfully integrate plant-based nutrition into clinical practice, it is recommended that patients' nutritional status and socio-cultural status be evaluated in detail, and a gradual transition to plant-based nutrition should be made by encouraging patients to make simple changes. In addition, encouraging the distribution of plant-based diets in hospital catering services, providing more plant-based options in hospital menus, and guidance from specialized dietitians will facilitate the implementation of plant-based diets in healthcare. Taken together, these strategies can empower patients to make lasting changes that promote better health and well-being.

Author contributions: Concept – S.A.; Design – S.A.; Supervision – S.A., A.A.; Resources – S.A., A.A., R.G., H.A., K.B.K., A.A.M., D.K., E.S.; Materials – S.A., A.A., R.G., H.A., K.B.K., A.A.M., D.K., E.S.; Data Collection and/or Processing – S.A., A.A., R.G., H.A., K.B.K., A.A.M., D.K., E.S.; Analysis and/or Interpretation – S.A., A.A., R.G., H.A., K.B.K., A.A.M., D.K., E.S.; Literature Search – S.A., A.A., R.G., H.A., K.B.K., A.A.M., D.K., E.S.; Writing Manuscript – S.A., A.A., R.G., H.A., K.B.K., A.A.M., D.K., E.S.; Critical Review – S.A.

Funding: The authors declare the study received no funding.

Conflict of interest: The authors declare that there is no conflict of interest.

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