Contents

Foreword: Mediterranean diet and climatic change 2271
L Serra-Majem, A Bach-Faig, G Miranda and C Clapes-Badrinas

Mediterranean diet pyramid today. Science and cultural updates 2274
A Bach-Faig, EM Berry, D Lairon, J Reguant, A Trichopoulou, S Dernini, FX Medina, M Batino, R Belahsen, G Miranda and L Serra-Majem on behalf of the Mediterranean Diet Foundation Expert Group

Sustainable diets: the Mediterranean diet as an example 2285
B Buringhme and S Dernini

The Middle Eastern and biblical origins of the Mediterranean diet 2288
EM Berry, Y Arnoni and M Aviram

Mediterranean nuts: origins, ancient medicinal benefits and symbolism 2296
P Carro-Agüetech, A Salas-Escott and J Salas-Salcedo

Effects of 3-month Mediterranean-type diet on postprandial TAG and apolipoprotein B48 in the Med-RIVAGE cohort 2302
C Defoort, S Vincent-Baudry and D Lairon

Low consumption of fruit and vegetables and risk of chronic disease: a review of the epidemiological evidence and temporal trends among Spanish graduates 2309
MA Martinez-Gonzalez, C de la Fuente-Arrillaga, C López-del-Burgo, Z Valdez-Perez, S Brune and M Ruiz-Canela

Wholegrain cereals and bread: a duet of the Mediterranean diet for the prevention of chronic disease 2316
A Gil, RM Ortega and J Maldonado

Olive oil, an essential component of the Mediterranean diet, and breast cancer 2323
E Escrich, R Moral and M Solanas

Mediterranean diet in secondary prevention of CHD 2333
M de Lorgeril and P Salén

Comparison and evaluation of the reliability of indices of adherence to the Mediterranean diet 2338
B Mils-Villarreal, A Bach-Faig, J Paig, A Puchal, A Fierum, L Serra-Majen and II. Carmona

Food consumption and civil society: Mediterranean diet as a sustainable resource for the Mediterranean area 2346
FX Medina

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3. Text should be divided under headings (typically to include Introduction, Methods, Results, Discussion and Conclusions), and sub-headings as appropriate. Conclusions should include recommendations that are actionable, practical, and helpful. Manuscripts can be divided into sections that are concrete, feasible, and potentially effective. Emphasising that more research is needed is usually not necessary unless there is a specific reason to say so.

4. Acknowledgements (sources of funding, competing interests declaration, authorship responsibilities, acknowledgements) should be provided during the submission process, not as part of the manuscript.

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FUNDACIÓN
Foreword: Mediterranean diet and climatic change

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Submitted 13 May 2011: Accepted 12 August 2011

Abstract

Changes in diet, reducing animal products and increasing consumption of vegetables can not only benefit human health and the overall use of land, but can also play a decisive role in the politics of climate change mitigation. In this sense, the Mediterranean diet (MD) is presented as a sustainable cultural model, respectful of the environment, whose adherence in Mediterranean countries should contribute to mitigating climate change. The recognition of the MD as an Intangible Cultural Heritage of Humanity by UNESCO in 2010 obliges the Mediterranean Diet Foundation to continue waging this recovery process and to promote our ancient food traditions in a prism of sustainability and commitment to the environment.

In this special issue on collecting the major papers regarding the VIII International Congress of the Mediterranean Diet, organised in Barcelona in 2010, special emphasis is placed on issues concerning the sustainability of food and how the production and transportation of food contributes to enhancing the consequences of climate change.

Climate change is a reality that is already on the political agenda of international organisations and governments. In general, politicians often focus on the energy sector to mitigate this change, whereas agriculture and livestock receive little attention. However, they represent approximately 20% of greenhouse gas emissions and 80% of the land surface used by humans (1).

From a nutritional standpoint, we know that there is a need to moderate the consumption of red meat for strictly health reasons (2). In addition, we know that there are climatic reasons supporting this recommendation. Reducing meat consumption by 50%, for example, would have important implications in: (i) decreasing land devoted to pastures and crops, with the consequent generation of carbon from vegetation; (ii) reducing deforestation intended to obtain crops such as soyabean and other vegetables for animal feed; and (iii) reducing methane and nitrogen dioxide emissions substantially (9–10%) (3,4).

The changes in diet can therefore not only produce benefits in human health and the overall use of land, but can also play a decisive role in the policies to mitigate climate change (4).

In an interesting prediction model, Stehfest et al (4), using four variants of food types (low total meat, low beef and ruminant, low in animal products, healthy or rich in vegetables), analyse the impact between the years 2000 and 2050 of these dietary patterns on some climate change indicators such as livestock production, land use and methane and nitrous oxide emission. The authors conclude on the need to promote some dietary changes within the policies of mitigating climate change. Carlsson-Kanyana and Gonzalez (5) have analysed the greenhouse gas emissions (mainly carbon dioxide and methane) resulting from the production of various food items, also taking into account the environmental costs of transport distance from the place of production to the point of consumption.

The Mediterranean diet (MD) understood not only as a set of food items but also as a culture on ways of producing and elaborating food is an example of sustainability (6). There are examples on how the abandonment of traditional farming practices, livestock and fisheries affects the very sustainability of the MD and its survival. Hence, the importance of it being included on UNESCO’s Intangible Cultural Heritage of Humanity list (7). Its cultural aspects need to be preserved to ensure its own sustainability as well as the cultivation and harvesting methods (8), and hence the landscapes.

In the first paper in the special issue (9), an expert committee from the Mediterranean Diet Foundation (MDF) in collaboration with other institutions presents the new graphic representation of the MD pyramid, conceived as a simplified main frame to be adapted to the different contexts of the Mediterranean region. Its semi-quantitative representation incorporates relative proportions and frequency of the MD pattern food groups, as well as the concepts of seasonality and local products, physical activity, socialisation and so on. Since the recognition of the MD as an Intangible Cultural Heritage of Humanity by UNESCO in 2010 and for its contribution

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to health and general well-being, we hope to contribute to much better adherence and to its preservation with this new graphic representation.

In a second paper, Burlingame and Dernini(10) emphasise that the acknowledgement of the MD as a sustainable diet needs the development of new cross-cutting intersectoral case studies to demonstrate further the synergies among nutrition, biodiversity and sustainability expressed by the MD for the benefit of present and future generations. Berry et al.(11) describe in their paper how the biblical traditional diet, including the seven species (whole grains, fish, wine, pomegranates, figs, walnuts and extra virgin olive oil) and additional Mediterranean fruits, has great health advantages, especially for CVD. In addition to the diet, lifestyle adaptation that involves increasing physical activity and organised meals, together with healthy food choices, is consistent with the traditional MD. Casas-Agustench et al.(12) explain that, like other foods, nuts have a wide variety of cultural connections to the areas where they grow and to the people who live there or eat them. History, symbolism and legends reveal the ancient tradition of nuts and how they are related to the lives of our ancestors.

In an interesting paper by Defoort et al.(13), MD appears efficient in improving postprandial lipemia (TAG and ApoB48, a marker of intestinally derived chylomicrons), a recently acknowledged CVD risk, in men and women with moderate cardiovascular risk. In addition, Martinez-Gonzalez et al.(14) review the evidence on the association between fruit and vegetable (F&V) consumption and risk of major chronic disease and assess trends in the prevalence of low F&V consumption in a cohort of university graduates. Gil et al. empathise the benefits of wholegrain cereals and bread for many non-communicable diseases(15). In addition, Escrich et al.(16) pooling data from sixteen animal experimental series analysing the effects of dietary lipids on mammary carcinogenesis concluded that consumption of extra virgin olive oil in moderate quantities and throughout the lifetime appears to be a healthy choice and may favourably influence a reduction of breast cancer risk. De Lorgeril and Salen(17) recognise that there is now a consensus about recommending the MD pattern for secondary prevention of CHD because no other dietary pattern has been successfully tested so far in these patients. The most important aspect, in contrast with the pharmacological prevention of CHD (including lowering of cholesterol), is that the MD results in a striking effect on survival. They also conclude that the traditional MD is effective in reducing both coronary atherosclerosis/thrombosis and the risk of fatal complications such as sudden cardiac death and chronic heart failure. Both De Lorgeril and Renaud(18) were the scientists responsible for the Lyon Heart Study and for the important experiment that represents a key landmark for the recognition of the MD, and for their outstanding careers, they were recognised with the MDF's VIII Grande Covian Award (Jury: Antonia Trichopoulou, Denis Lairon, Leda Chatzi, Jordi Salas-Salvadó, Carlo La Vecchia, Silvia Franceschi, Walter C Willet, Miguel Angel Martinez and Lluis Serra-Majem (Chairman)). Figure 1 illustrates the historical moment when these researchers shared the common prestigious recognition in Barcelona, 25 March 2010.

Milà-Villarroel et al.(19) in their paper comparing and evaluating the reliability of different indexes of adherence to the MD conclude that indexes perform quite well in measuring the adherence to MD. However, the lack of high correlation among some of them indicates the need for better agreement on the components involved in the MD pattern.

Finally, Medina(20) ends the special issue with a paper that dissects Mediterranean food and diet as a proximity model of consumption that can be, from a local Mediterranean point of view, a sustainable resource for the Mediterranean area.

This collection of selected papers updates once again the trends and developments around the MD, and with that, the MDF aims to contribute to improving its outreach, increasing awareness among health and nutrition professionals and ultimately improving compliance and projection at the population level in a coherent and sustainable way.

References

Mediterranean diet pyramid today. Science and cultural updates

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Abstract

Objective: To present the Mediterranean diet (MD) pyramid: a lifestyle for today.
Design: A new graphic representation has been conceived as a simplified main frame to be adapted to the different nutritional and socio-economic contexts of the Mediterranean region. This review gathers updated recommendations considering the lifestyle, dietary, sociocultural, environmental and health challenges that the current Mediterranean populations are facing.
Setting and Subjects: Mediterranean region and its populations.
Results: Many innovations have arisen since previous graphical representations of the MD. First, the concept of composition of the 'main meals' is introduced to reinforce the plant-based core of the dietary pattern. Second, frugality and moderation is emphasised because of the major public health challenge of obesity. Third, qualitative cultural and lifestyle elements are taken into account, such as conviviality, culinary activities, physical activity and adequate rest, along with proportion and frequency recommendations of food consumption. These innovations are made without omitting other items associated with the production, selection, processing and consumption of foods, such as seasonality, biodiversity, and traditional, local and eco-friendly products.
Conclusions: Adopting a healthy lifestyle and preserving cultural elements should be considered in order to acquire all the benefits from the MD and preserve this cultural heritage. Considering the acknowledgment of the MD as an Intangible Cultural Heritage of Humanity by UNESCO (2010), and taking into account its contribution to health and general well-being, we hope to contribute to a much better adherence to this healthy dietary pattern and its way of life with this new graphic representation.

Keywords
Mediterranean diet
Pyramid
Adult
Dietary pattern
Lifestyle
Culture
Health

The traditional Mediterranean diet (MD) is the heritage of millennia of exchanges of people, cultures and foods of all countries around the Mediterranean basin. It has been the basis of food habits during the twentieth century in all countries of the region, originally based on Mediterranean agricultural and rural models. However, the traditional MD is now progressively eroding due to the widespread dissemination of the Western-type economy, urban and technology-driven culture, as well as the globalisation of food production and consumption, related to the homogenisation of food behaviours in the modern era.

Since the Seven Countries Study in the 1950s, we know which foods were more or less frequently consumed in the Mediterranean area(1), a pattern followed mainly by poor rural societies(2). This led to defining the MD as a dietary pattern rich in plant foods (cereals, fruits, vegetables,
legumes, tree nuts, seeds and olives), with olive oil as the principal source of added fat, along with high to moderate intakes of fish and seafood, moderate consumption of eggs, poultry and dairy products (cheese and yoghurt), low consumption of red meat and a moderate intake of alcohol (mainly wine during meals).

The pioneer Seven Countries Study and numerous and increasing recent epidemiological studies have established the health benefits associated with the adherence to the Mediterranean diet pattern (MDP), mainly in relation to reducing the risk of developing the metabolic syndrome, type 2 diabetes, CVD and some neurodegenerative diseases and cancers (5-6).

This healthy, traditional MDP has been popularised since 1995 using the world famous pyramid representation that graphically highlights the food groups to be consumed daily, weekly or less frequently (7). In addition, in 1995, an index or score was introduced to evaluate the adherence to the MDP, allowing the study of its associated health effects (8). Within the scientific community, there is a consensus on what constitutes the traditional MDP, mentioned above, but issues have been raised about the need to update the present recommendations considering the new lifestyle, dietary, sociocultural, environmental and health challenges the current generations of different countries and sectors of the population are facing, especially low-income groups in which the prevalence of CVD has risen along with the shift from the traditional MD. The following issues, among others, arise and need to be addressed: (i) consumption of fresh, minimally processed, local and seasonal foodstuffs; (ii) the balance between energy-dense and nutrient-dense foods in relation to reduced energy expenditure and the obesity epidemic; (iii) availability, sustainability, accessibility and cost of recommended foods; (iv) adaptation to various geographical, socio-economic and cultural contexts; and (v) understanding the MD as an intangible space for creativity and intercultural dialogue and a common cultural heritage shared by all Mediterranean populations (9).

The incorporation of food consumption as a basic area in Anthropology and Sociology after the 1930s – after the pioneering works of Audrey Richards and Margaret Mead – has brought light to the study of nutrition understood also as a social and cultural process in permanent flux (10). Food represents much more than a pure act of survival for human evolution; eating is a social and cultural phenomenon, while nutrition is a physiological and health issue (11).

After the recognition of the MD as an Intangible Cultural Heritage of Humanity by UNESCO in 2010 (12,13), considering the worldwide interest in the MDP and taking as a framework all the mentioned aspects, scientists present a consensual renewed communication tool for the general public, health professionals and stakeholders. This is a new pyramid with which scientists hope to contribute to a much better adherence to this healthy dietary pattern and its way of life in the Mediterranean area and other countries in the near future.

Consensus on a new pictorial representation of the Mediterranean diet pyramid

The Mediterranean Diet Foundation together with the Forum on Mediterranean Food Cultures initiated the dialogue and process of gathering scientific opinion among international experts to develop a consensus position on a new revised MD pyramid representation (Fig. 1). The new revised MD and food lifestyle pyramid (as a schema) arises from the internal dialogues among scientific experts of the Mediterranean Diet Foundation’s International Scientific Committee and further discussions from a meeting held in the framework of the III CIISCAM Conference ‘The Mediterranean Diet today, a model of sustainable diet’ in Parma (Italy; Fig. 1).

This pyramid results from the aforementioned scientific consensus among experts and is based upon the latest research in the field of nutrition and health, scientific evidence around the healthiness of the MD dietary pattern and its role in the prevention of many chronic diseases by large epidemiological studies published in hundreds of peer-reviewed scientific journal articles during recent decades (5,4).

The final design of the MD pyramid today (Fig. 2) and a brief complementary text for the general public (Fig. 3) have been developed by the gathered opinions of the Mediterranean Diet Foundation Expert Group that includes the Mediterranean Diet Foundation’s International Scientific Committee expertise, the in situ discussions by a representative group of members that met within the Barcelona VIII International Congress on the Mediterranean diet (Fig. 1), and several other experts who provided support on the design, editing and translation to ten different languages (English, French, Italian, Spanish, Catalan, Basque, Galician, Greek, Portuguese and Arabic; see acknowledgements).

Thus, the main purpose of this initiative is to foster dialogue among scientists and experts in public health nutrition, food sciences, metabolism, anthropology, sociology, biology, agriculture and environmental and cultural heritage in order to obtain a common representation of the MDP in the Mediterranean area, meant for non-profit use and promotion without restrictions.

The Mediterranean diet pyramid: a lifestyle for today

The pyramid reflects the changing process that the MD is undergoing within the Mediterranean societies. This new graphic representation (Fig. 2) was conceived as a simplified main frame pyramid, to be adapted to the specific realities of different countries (e.g. portion sizes) and variations in the dietary pattern related to the various geographical, socio-economic and cultural contexts of the Mediterranean region. These guidelines (2010 edition) might be periodically updated according to new consensus and suggestions.
By expressing the goals in terms of foods and referring to a dietary pattern based on a cultural model, the new pyramid may contribute to a higher compliance among the general population. In order to preserve the Intangible Cultural Heritage, adapting the cultural specificity of each food practice to its socio-economic and environmental context is necessary. Thus, the pyramid is developed as a tool to help us adopt a healthier and sustainable lifestyle.

The recommendations target the healthy adult population (18–65 years old) and should be adapted to the special needs of children, pregnant women and those suffering from health conditions.

**Mediterranean diet pattern**

The new MD pyramid provides key elements for the selection of foods, both quantitative and qualitative, indicating the relative proportions and consumption frequency of servings of the main food groups that constitute the MDP. The pattern includes all food groups, and it is just a question of variety of food and culinary techniques, along with adequate frequencies and quantities in the daily diet that make it healthy or unhealthy. A wide variety of foods in the diet minimises the possibility of deficiencies of a particular nutrient. In fact, a higher adherence to the MDP has been associated with a better...
nutrient profile, with a lower prevalence of individuals showing inadequate intakes of micronutrients in comparison to other patterns such as the Western pattern\(^{14}\).

Plant-origin foods are situated at the base of the pyramid. They provide key nutrients, fibre and protective substances that contribute to general well-being, satiety and the maintenance of a balanced diet, and thus should be consumed in high proportions and frequency. This MD core, based on plant-origin foods, is responsible for the prevention of many chronic diseases and for weight control\(^{4,15}\).

The graphic representation follows the previous pattern: at the base, food items that should sustain the diet and provide the highest energy intake; and at the upper levels, foods to be eaten in moderate amounts such as those of animal origin and/or rich in sugars and fats that should be eaten in moderation and some of them left for special occasions. Meals have an essential role in the MD\(^{\text{4}}\), and thus the importance of the meal and its composition is emphasized in the new representation. A balanced composition of the main meals should include fruits, vegetables and cereals, complemented in a lower contribution to daily energy intake with other plant foods, dairy products and protein sources.

The pyramid establishes dietary daily, weekly and occasional guidelines in order to follow a healthy and balanced diet.

**Every day**

- **Main meals** should contain three basic elements, which can also be found throughout the day:
  - **Cereals**: one or two servings per meal in the form of bread, pasta, rice, couscous and others. Preferably whole grain, since processing normally removes fibre and some valuable nutrients (Mg, Fe, vitamins, etc.\(^{17}\)).
  - **Vegetables**: two or more servings per meal. In order to ensure vitamin and mineral daily intakes, at least one of the servings should be consumed raw (one meal/d)\(^{18}\).
  - **Fruit**: one or two servings per meal, as the most frequently chosen dessert. The concept of ‘variety in colours and textures’ is highlighted, in the case of fruit and vegetables, in order to ensure a wide variety of antioxidants and protective compounds\(^{19}\).

- **A daily intake of 1.5–2 l of water** (equivalent to six to eight glasses) should be guaranteed. Proper hydration is essential to maintaining the corporal water equilibrium,
The Mediterranean diet pyramid has adapted to the new way of life

The new model takes into account qualitative and quantitative elements for the selection of foods

The traditional Mediterranean diet (MD) pyramid has evolved to adopt the new way of life. As an initiative of the Mediterranean Diet Foundation and with the collaboration of numerous international entities, a wide range of experts in nutrition, anthropology, sociology and agriculture have reached a consensus in a new richer design with the incorporation of qualitative elements.

The new pyramid follows the previous pattern: at the base, foods that should sustain the diet, and at the upper levels, foods to be eaten in moderate amounts. Moreover, social and cultural elements characteristic of the Mediterranean way of life are incorporated in the graphic design. So, it is not just about prioritising some food groups from others, but also paying attention to the way of selecting, cooking and eating. It also reflects the composition and number of servings per meals.

The Mediterranean diet health benefits and protective effect against chronic diseases have been well established by the scientific community. This new pyramid includes all the food groups; it is in the proportions and the frequencies that relies a healthy or unhealthy diet. This food consumption pattern is addressed to a healthy adult population and should be adapted to the specific needs of children, pregnant women and other health conditions.

Plant-based foods are situated at the base of the pyramid. They provide key nutrients and protective substances that contribute to the general well-being and contribute to maintain a balanced diet, therefore, should be consumed in high proportions and frequency. Foods situated in the upper levels such as from animal origin, rich in sugars and in fats should be eaten in moderation and for special occasions.

The pyramid establishes dietary daily, weekly and occasional guidelines in order to follow a healthy and balanced diet.

**Every day:**

The **three main meals** should contain three basic elements, which can also be found throughout the day:

- **Cereals.** One or two servings per meal in the form of bread, pasta, rice, couscous and others. Preferably whole grain, since some valuable nutrients (magnesium, phosphorus, etc.) and fibre can be lost during processing.

- **Vegetables.** Present at lunch and dinner; or more than two servings per meal, at least one of the serving should be raw. A variety of colours and textures provide a diversity of antioxidants and protective compounds.

- **Fruit.** One or two servings per meal. Should be chosen as the most frequent dessert.

- A daily intake of **1.5–2.0 liter of water** should be guaranteed. A good hydration is essential to maintain the corporal water equilibrium, although needs may vary among people because of age, physical activity, personal circumstances and weather conditions. As well as water, non-sugar rich herbal infusions and broths (with low fat and salt content) may complete the requirements.

- **Dairy products.** Prefer it in the form of **low fat** yoghurt, cheese and other fermented dairy products. They contribute to bone health, but can also be an important source of saturated fat.

- **Olive oil** is located at the centre of the pyramid; should be the **principal source of dietary lipids** because of its high nutritional quality (especially extra virgin). Its unique composition gives it a high resistance to cooking temperatures and should be used for cooking as well as dressings (one tablespoon per person).

- **Spices, herbs, garlic and onions** are a good way to introduce a variety of flavours and palatability to dishes and contribute to the reduction of salt addition. **Olives, nuts and seeds** are good sources of healthy lipids, proteins, vitamins, minerals and fibre. A reasonable consumption of olives, nuts and seeds (such as a handful) make for a healthy snack choice.

- Respecting **religious and social beliefs**, a moderate consumption of **wine and other fermented beverages** (one glass per day for women and two glasses per day for men, as a generic reference) during meals is recommended.

**Weekly:**

A variety of plant and animal origin proteins should be consumed. Mediterranean traditional dishes do not usually have animal origin protein foods as the main ingredient but as a tasty source.

- **Fish** (two or more servings), **white meat** (two servings) and **eggs** (two to four servings) are good sources of animal protein. Fish and shellfish are also a good source of healthy proteins and lipids.

- Consumption of **red meat** (less than two servings, preferably lean cuts) and processed meats (less than one serving) should be in smaller quantity and frequency.

Fig. 3 (colour online) The Mediterranean diet pyramid’s brief complementary text for the general public
The combination of **legumes** (more than two servings) and cereals are a healthy protein and lipid source. **Potatoes** are also included in this group, as they are a part of many traditional recipes with meat and fish (three or less servings per week, preferably fresh potatoes).

**Occasionally:**

In the vertex of the pyramid are represented the sugary and unhealthy fats rich foods (**the sweets**). Sugar, candies, pastries and beverages such as sweetened fruit juices and soft drinks, should be consumed in **small amounts** and left for **special occasions**.

Together with the proportion and frequency recommendations of consumption, the incorporation of **lifestyle and cultural elements** is one of the innovations of the pyramid. Adopting a healthy lifestyle and preserving the cultural elements should also be considered in order to acquire all the benefits from the Mediterranean diet. These elements are:

**Moderation:** Portion sizes should be based on frugality, adapting energy needs to urban and modern sedentary lifestyles.

**Socialisation:** The aspect of conviviality is important for the social and cultural value of the meal, beyond nutritional aspects. Cooking, sitting around the table and sharing food in company of family and friends is a social support and gives a sense of community.

**Cooking:** Make cooking an important activity taking the proper time and space. Cooking can be relaxing, fun and can be done with family, friends and the loved ones.

**Seasonality, biodiversity, eco-friendliness, traditional and local food products** are presented at the bottom of the pyramid to highlight how the new revised modern Mediterranean diet is compatible with the development of a sustainable diet model for the present and future Mediterranean generations. The preference for seasonal, fresh and minimally processed foods maximises the content of protective nutrients and substances in the diet.

**Activity:** Regular practice of moderate **physical activity** (at least 30 min throughout the day) as a basic complement to the diet for balancing energy intake, for healthy body weight maintenance and for many other health benefits. Walking, taking the stairs v. the lift, housework, etc., are simple and easy ways of doing exercise. Practising leisure activities outdoors and preferably with others makes it more enjoyable and strengthens the sense of community.

**Rest:** Resting is also part of a healthy and balanced lifestyle.

This pyramid is the result of an international consensus and is based on the latest scientific evidence on nutrition and health published in hundreds of scientific articles in the last decades. It contributes to the harmonisation of educational tools used in the promotion of the Mediterranean diet and responds to the need for a common framework among the Mediterranean area; to be adapted to the specific realities of each country and region. The use and promotion of this pyramid is recommended without any restrictions and has been translated and is available in English, Spanish, Catalan, Galician, Basque, French, Arabic, Italian, Portuguese and Greek.

The supporting entities of the new design of the Mediterranean diet pyramid are:

- Fundación Dieta Mediterránea
- Forum on Mediterranean Food Cultures
- Hellenic Health Foundation
- Hebrew University
- International Commission on the Anthropology of Food and Nutrition
- Università Politecnica delle Marche
although needs may vary among people due to age, physical activity, personal circumstances and weather conditions. It should be consumed freely, bottled or from the tap, when hygienic circumstances allow it. In addition to water, sugar-free herbal infusions and tea, and low-sodium and low-fat broths may help to complete the requirements.

- Dairy products should be present in moderate amounts (two servings per day), with a preference for low-fat dairy, traditionally in the form of yoghurt, cheese and other fermented dairy products. Although their richness in Ca is important for bone and heart health, dairy products can be a major source of saturated fat([20]).

- Olive oil is located at the centre of the pyramid; it should be the principal source of dietary lipids because of its high nutritional quality (especially extra virgin olive oil). Its unique composition gives it a high resistance to elevated temperatures, and it is recommended for both cooking([21]) and dressings. Olive oil has been reported to be inversely associated with some cancers and is known to positively affect blood lipids and cardiovascular systems([22–20]). This may be related to its high content of monounsaturated oleic acids and abundance of antioxidant compounds, which are primarily present in virgin olive oil([27]). Traditionally, vegetables and other plant foods are cooked with olive oil, thus amplifying their nutritional value.

- Olives, nuts and seeds are good sources of healthy lipids, proteins, vitamins, minerals and fibre([260]). A reasonable consumption of olives, nuts and seeds (such as a handful) make for a healthy snack choice.

- Spices, herbs, garlic and onions are a good way to introduce a variety of flavours and palatability to dishes and allow for a reduction in salt use, as salt is one of the main contributing factors to the development of hypertension among predisposed individuals([20]). Herbs and spices are good sources of micronutrients and antioxidant compounds and also contribute to the regional identities of Mediterranean dishes.

- Respecting religious and social beliefs, a moderate consumption of wine and other fermented beverages during meals (one glass per day for women and two glasses per day for men, as a generic reference) is present in the MDP([30–32]).

Weekly

Consumption of a variety of plant- and animal-origin proteins is recommended. Traditional Mediterranean dishes do not usually have animal-origin protein foods as the main ingredient but rather as a source of flavour.

- Fish and shellfish (two or more servings), white meat (two servings) and eggs (two to four servings) are good sources of animal protein. Fish, white meat (poultry, turkey, rabbit, etc.) and eggs provide high-quality protein. Fish and shellfish are a good source of healthy protein and lipids. Varied consumption (of oily fish, lean fish and shellfish) is recommended. Fish (especially those high in lipids) and shellfish consumption has been reported to reduce the risk of CHD and they have anti-inflammatory properties due to their content of long chain n-3 PUFA([33,34]). White meat is also a good
The conviviality aspect is important for the social and cultural value of the meal beyond nutritional aspects. In this sense, several factors related to food (understood as a social fact) must be kept in mind, such as culinary activities, knowledge transmitted from generation to generation and time devoted to meals related to the daily pace of life. All these aspects contribute to generating or strengthening sociability, communication and the identity of communities. Sharing food in the company of family and friends around the table represents social support and a sense of community. The pleasure associated with the conviviality of meals may positively affect food behaviours, and in return, health status.

Culinary activities
The development of culinary activities such as cooking, making crafts, the organisation of domestic space and other techniques associated with food is basic for the social reproduction of the identity of each particular culture. Thus, devoting enough time and space for such culinary activities is stressed, giving account to their role in everyday meals, celebrations and religious festivals in every culture.

Physical activity
Regular practice of moderate physical activity (at least 30 min throughout the day) serves as a basic complement to the diet by balancing energy intake, maintaining healthy body weight and providing many other health benefits. Physical activity not only involves sports such as football, dancing, jogging, cycling, etc. but also walking, taking the stairs v. the lift, housework, gardening, etc. Practising leisure activities outdoors, and preferably with others, makes them more enjoyable and strengthens the sense of community.

Adequate rest
Resting during the day (nap) as well as adequate night sleep is also part of a healthy and balanced lifestyle. Scientific evidence has shown that a short rest after eating is a healthy and traditional Mediterranean habit that helps promote a balanced lifestyle. An after-meal nap is an increasingly widespread habit in Mediterranean countries and throughout Europe.

Seasonality
The preference for seasonal, fresh and minimally processed foods may in most cases maximise the content of protective nutrients and substances in the diet. Currently and due to the modern lifestyle, the consumption of fresh foods is being substituted by other processed foods. However, progress in modern technology minimises nutrient loss and offers healthy alternatives. Especially in the case of fresh products, several factors influence their nutritional value: the growing methods used, the specific variety chosen, ripeness when harvested, post-harvest handling, storage, extent and type of processing, and the distance transported. Thus, all the decisions and practices along the food system – from seed to table – affect the nutrient content of foods.
Traditional, local, eco-friendly and biodiverse products

Taking into account the traditional, local, eco-friendly and biodiverse products whenever possible contributes to the preservation of Mediterranean landscapes and sea. The MD should be understood not only as a set of foods but also a cultural model incorporating the whole food chain: the way foods are selected, produced, processed and distributed to the consumers. Moreover, the MD, as a plant-centred dietary pattern, further contributes to the preservation of the environment, as it implies a reduction in animal consumption and therefore production compared to Western patterns and, consequently, lowered demands on soil, water and energy resources. All these items express the sustainable character of the MD in an increasingly globalised world.

The MD is an example of a sustainable pattern in which agricultural biodiversity plays an important role. The variety both among and within species contributes to differences in appearance and taste, as well as micronutrient and phytochemical content. However, when making varietal decisions, durability (for instance, to withstand long-distance transport) is sometimes being prioritised over taste and nutritional quality. The large number of endemic species and landscape diversification (cultivated areas, grassland or forest and land use changes over time) that contribute to the biodiversity of the territories bordering the Mediterranean make this area a hot spot of global diversity. In this sense, agricultural biodiversity provides food variety of plant and animal food products from wild and domesticated sources that foster the nutritional guidelines.

The consumption of local and eco-friendly foods has been associated with health and environmental preservation in several ways. First, although there is still no unanimous international consensus on the differences in nutrient content between eco-friendly and conventional products, some literature surveys of nutritional and sanitary aspects of eco-friendly (organic) foods have reported some higher nutrient contents and marginal pesticide residue contaminations. Second, locally grown and harvested foods are normally given more time to ripen. Third, local food products normally have less distance to travel, thus promoting energy saving and reducing pollution, having a lower contribution to climate change and greenhouse gas emissions if compared to long-travelling food products. Moreover, by buying local foods, farmers are encouraged to diversify their crops and decrease their vulnerability to pests. Finally, the consumption of local foods contributes to improving local economies.

Traditional knowledge and practices developed through daily observation, interaction within rural communities, transfer production, procurement and consumption techniques and activities are locally transmitted from generation to generation. All those elements ensure positive, responsible, sustainable and healthy behaviours while reproducing the Intangible Cultural Heritage of the Mediterranean Diet. The modernisation process, including sociocultural changes and new technologies, has transformed food production and threatens sustainable orders of life, such as local foodstuffs and environmental biodiversity. Thus, countries, communities and cultures that maintain their own traditional food systems are better able to conserve local food specialities with a corresponding diversity of crop varieties and animal breeds.

Conclusions

This pyramid is the result of an international consensus and is based on the latest scientific evidence on nutrition and health published in hundreds of scientific articles in recent decades. It contributes to the harmonisation of educational tools used in the promotion of the MD and responds to the need for a common framework in the Mediterranean area, to be adapted to each country's and region's specific realities. The use and promotion of this pyramid is recommended without any restrictions, and the material is available in English, Spanish, Catalan, Galician, Basque, French, Arabic, Italian, Portuguese and Greek.

The 'Mediterranean diet pyramid: a lifestyle for today' summarises and updates the traditional MD of those areas of the Mediterranean basin that have evolved with modernisation. It is a shared and dynamic cultural heritage that was recognised by UNESCO in 2010. Taking into account its contribution to health and general well-being, we hope to contribute to a much better adherence to this healthy dietary pattern and its way of life with this new graphic representation.

Acknowledgements

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Mediterranean diet pyramid today

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Sustainable diets: the Mediterranean diet as an example

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Abstract

Objective: To present the Mediterranean diet as an example of a sustainable diet, in which nutrition, biodiversity, local food production, culture and sustainability are strongly interconnected.

Design: Review of notions and activities contributing towards the acknowledgement of the Mediterranean diet as a sustainable diet.

Setting: The Mediterranean region and its populations.

Subjects: Mediterranean populations.

Results and conclusions: The acknowledgement of the Mediterranean diet as a sustainable diet needs the development of new cross-cutting intersectoral case studies to demonstrate further the synergies among nutrition, biodiversity and sustainability as expressed by the Mediterranean diet for the benefit of present and future generations.

Keywords: Sustainable diets, Mediterranean food cultures, Mediterranean diet, Biodiversity, Nutrition, Sustainable development

The healthy lifestyle of the Mediterranean diet

The traditional Mediterranean diet is the heritage of millennia of exchange of people, cultures and foodstuffs throughout the Mediterranean basin. This diet was the basis of food habits until the mid-twentieth century in all countries of the region, but it is now progressively disappearing because of the widespread dissemination of Western-type lifestyle and globalisation.

The Mediterranean diet, recognised as a healthy dietary pattern and a healthy lifestyle, is still an underexplored resource for valuing biodiversity and understanding human nutrition. More than just food, it is also a potential model of sustainable development, although this too has not been fully realised. In the Mediterranean region, there is widespread awareness of the social, cultural, health and economic dimensions of food, shared by all Mediterranean people.

In 2009, in Parma, Italy, the international conference The Mediterranean Diet as a Model of Sustainable Diet was organised by CIISCAM in collaboration with the FAO Nutrition and Consumer Protection Division, the Forum on Mediterranean Food Cultures, and the CIHEAM-IAM of Bari. Its aim was to promote the Mediterranean diet as an example of a sustainable diet in which nutrition, local food production, biodiversity, culture and sustainability were strongly interconnected, with a low impact on the environment.

The Mediterranean diet, based on a variety of diversified local traditional foods strictly linked to the Mediterranean environment, was presented as an intangible heritage as well as an under-explored resource for biodiversity and nutrition towards nutritional security and sustainable development.

The notion of sustainable diets

In the early 1980s, the notion of ‘sustainable diets’ was described by Gussow and Clancy to recommend diets that are healthier for the environment as well as for consumers. The concept of a ‘sustainable diet’, borrowed from ‘sustainable agriculture’, promoted activities that minimised the waste of natural resources and addressed food production for local and seasonal consumption.

With the food globalisation process and the increased production of agricultural systems, and with no attention paid to the sustainability of ecosystems, the sustainable diet’s concept was neglected for many years. But recently interest in sustainable diets has again been raised by international scientific societies and institutions of various European governments.

There is growing recognition of the complexity of defining sustainability, as well as a growing body of evidence of the unsustainable nature of current diets. A definition of sustainable diets should address sustainability of the whole food chain, while acknowledging the interdependencies of food production systems and food and nutrient requirements.

The notion of a sustainable diet would have been curious a few hundred years ago, when people obtained the majority of their foods out of their ecosystems. Biodiversity was valued and utilised; ecosystems and agro-ecological zones produced the foods that they had produced for millennia.
Traditional knowledge and practices ensured the conservation and sustainable use of food biodiversity within healthy ecosystems. But agriculture, diet and nutrition have changed so dramatically in recent decades that now the concept of a sustainable diet seems novel.

The confounding result, according to FAO estimates, is that the number of undernourished people has increased to nearly one billion\(^6\). This number reflects only the dietary energy supply, whereas micronutrient malnutrition exists on an even larger scale. In addition to the problems of undernourishment, obesity and its associated chronic diseases are rising. This, coupled with the alarming pace of food biodiversity loss and ecosystem degradation, makes a compelling case for re-examining agricultural systems and diets. Although good nutrition should be a goal of agriculture, it is imperative that concerns about sustainability are not lost in the process. Many dietary patterns can be healthy, but they can vary substantially in terms of the cost of their resource.

The Mediterranean diet has been characterised, analysed and promoted through a variety of methods within a number of scientific and applied disciplines. It continues to be recognised and appreciated as a healthy diet, even if its practice in the Mediterranean region is diminishing.

In 2008, delegates at the FAO Regional Conference for Europe made important statements: ‘They highlighted the Mediterranean diet as rich in biodiversity and nutritionally healthy. The promotion of the Mediterranean diet could play a beneficial role of in the sustainable development of agriculture in the Mediterranean region’, and ‘remarked that the goal of increased global food production, including biofuels, should be balanced against the need to protect biodiversity, ecosystems, traditional foods and traditional agricultural practices\(^7\).

In 2010, participants at the international symposium on ‘Biodiversity and Sustainable Diets: United against Hunger’, reached a consensus position on the following definition of sustainable diets: ‘Sustainable diets are those diets with low environmental impacts which contribute to food and nutrition security and to healthy life for present and future generations. Sustainable diets are protective and respectful of biodiversity and ecosystems, culturally acceptable, accessible, economically fair and affordable; nutritionally adequate, safe and healthy; while optimizing natural and human resources\(^8\).

The Mediterranean diet as an example of a sustainable diet

The importance of the Mediterranean diet as an example of a sustainable diet lies not in its specific foods and nutrients but in the methods used to characterise and analyse it and the philosophy of sustainability that is at its core.

The concept of sustainable diets involves economic, environmental and sociocultural issues that influence nutrition and health outcomes. The new approach to present the Mediterranean diet as a sustainable diet, rich in biodiversity, should provide more eco-friendly food-based dietary guidelines and goals to consumers and help clarify what is required for an environmentally sustainable food system.

Integrating the notion of sustainable diets with the food chain approach (i.e. ‘getting biodiversity from the farm to the plate’) should guide an innovative intersectoral effort to counteract the simplification of diets, loss of biodiversity and the degradation of ecosystems and prevent further erosion of food cultures. It will serve to further promote traditional foods of indigenous peoples with their many sources of nutritionally rich species and varieties as readily accessible, locally empowering and sustainable sources of quality nutrition. Furthermore, it will highlight that in an increasingly global, urban and commercial environment, fulfilment of the potential of local resources must successfully integrate production, marketing, consumption and the health of rural and urban dwellers alike as components of sustainable food systems.

The Mediterranean diet provides opportunities for conserving diversity in the cultural knowledge of foods and diets, understanding indigenous or local food systems using a multicultural approach to sustainable diets. It also raises the question of safeguarding traditional knowledge on food and culture.

Conclusions

In conclusion, there is a need to develop new crosscutting, intersectoral case studies on the Mediterranean diet as a sustainable diet to demonstrate the synergies of biodiversity, nutrition and sustainability expressed by the Mediterranean diet for the benefit of present and future generations. More than before, we have to act together by revitalising local capacities to reduce the increasing erosion of the diversity of Mediterranean food cultures, to safeguard it as an intangible cultural heritage, as well as to reinforce the sustainability of the agro-food systems of all Mediterranean countries and food security in the entire region.

These same methods can be used to characterise sustainable diets in other cultures and agro-ecological zones, to identify the necessary new paradigms of reference to solve the many challenges that face humankind, with almost one billion hungry people worldwide.

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References

The Middle Eastern and biblical origins of the Mediterranean diet

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Abstract

Objective: To place the Mediterranean diet (MedDi) in the context of the cultural history of the Middle East and emphasise the health effects of some of the biblical seven species – wheat, barley, grapes, figs, pomegranates, olives and date honey.

Design: Review of the literature concerning the benefits of these foods.

Setting: Middle East and Mediterranean Basin.

Subjects: Mediterranean populations and clinical studies utilising the MedDi.

Results and conclusions: The MedDi has been associated with lower rates of CVD, and epidemiological evidence promotes the benefits of consuming fruit and vegetables. Recommended foods for optimal health include whole grain, fish, wine, pomegranates, figs, walnuts and extra virgin olive oil. The biblical traditional diet, including the seven species and additional Mediterranean fruits, has great health advantages, especially for CVD. In addition to the diet, lifestyle adaptation that involves increasing physical activity and organised meals, together with healthy food choices, is consistent with the traditional MedDi. The MedDi is a manageable, lifestyle-friendly diet that, when fortified with its biblical antecedent attributes, may prove to be even more enjoyable and considerably healthier in combating the obesogenic environment and in decreasing the risks of the non-communicable diseases of modern life than conventional, modern dietary recommendations. The biblical seven species, together with other indigenous foods from the Middle East, are now scientifically recognised as healthy foods, and further improve the many beneficial effects of the MedDi.

Keywords

Biblical foods

Mediterranean diet origins

Seven species

The Mediterranean diet (MedDi) is considered today to be among the healthiest of diets, with evidence of increased longevity and protection against CVD and cancer. The geographic and evolutionary origins of the diet are of interest as they encompass the history of Western civilisation. The rise of agriculture (domestication of crops) and animal husbandry took place from 10,000 to 4000 BCE, while the wheel, metallurgy, writing and city states arose from 4000 to 1000 BCE. These essential developments in the evolution of civilisation originated in the fertile crescent – from Mesopotamia, the ancient near East, Canaan and Egypt. The biblical period from the time of the Patriarchs until King David in Jerusalem was from 1750 to 1100 BCE with the fall of Troy and the Greek colonisation of Ionia occurring in the twelfth century BCE.

Evidence of dietary patterns has been obtained from archaeo-botany and written records. Although there are many similarities between the traditional Greek (Cretan) MedDi and that described in the Pentateuch, the differences are of interest as they have special nutritional benefits – in particular pomegranates and figs. The Bible (Deuteronomy 8:8) speaks of the seven species – wheat, barley, grapes, figs, pomegranates, olives and date honey, as well as a land ‘flowing with milk and (date) honey’, and these are also the basic staples of the MedDi. There are also hieroglyphic records of wine and olive exports from Canaan to Egypt. Further, in Roman times, historians recorded that the produce of the land of Israel was of particularly high quality and was served at the best tables. Such cross-cultural influences may be seen during the Passover meal, which was the basis of Jesus’ Last Supper, and was itself adapted from the Greek symposium brought to the region after the conquests of Alexander the Great in the fourth century BCE. The purpose of the present review is to propose that the MedDi that originated in the Middle East may be beneficially modified by the inclusion of certain food items from biblical times.

Origins of the Mediterranean diet and the biblical diet

The MedDi based on the diet of Crete (before 1960) has been significantly correlated with extended life expectancy

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and the lowest global incidence of CHD, as well as certain cancers and other chronic diseases\textsuperscript{(22)}. The MedDi is not a new diet, which is exactly the reason for its strength. In its traditional form, the food in the region was eaten according to the season and the reason. Climate dictated what was produced agriculturally, and the reason for consumption was determined by daily meal gatherings and festivals. The origins of the MedDi in fact encompass the history of Western civilisation and it has its origins in the diet and lifestyle of the Near Middle East, including those of biblical times.

The dietary laws of the Bible forbade mixing milk with meat (Exodus 23:19, 34:26 and Deuteronomy 14:21) and proscribed eating pig and sea food, allowing only animals with a cloven hoof and which ‘chewed the cud’ (Leviticus 11:3 and following), whereas fish had to have both fins and scales (Leviticus 11:9 and following). The reasons are not clear\textsuperscript{(3)}, but might relate to eating only those animals that were preyed upon and not predators. In addition, the seven species (wheat, barley, vines, figs, pomegranates, olives and honey; Deuteronomy 8:8) in the biblical land ‘flowing with milk and (date) honey’ (Exodus 3:8) were given high priority\textsuperscript{(4)}. Trade between Palestine and Egypt of olive oil and wine has been documented on hieroglyphs some 2000 years before Christ\textsuperscript{(5)}. Archeological excavations have uncovered the products eaten during the Minoan period dating back to the Bronze Age civilization that arose on the island of Crete (2700–1450 BCE). In the Copper Age, plants and sea food were almost the sole source of nutrients. The wall paintings Frescos at Knossos show the prime role of bread in the Cretan diet. Despite the evidence of the early origins of the MedDi, recommendations have been made to revert to the traditional MedDi as consumed in Crete ‘before 1960’. But perhaps we should consider going back much further in time and take into consideration the evolution of the diet from biblical times and even before.

\textbf{Mediterranean lifestyle}

Human genetic profiles have not changed significantly over the past 10 000 years, whereas lifestyle has been revolutionised. Modern industrialised populations are characterised by reduced energy expenditure and increased energy intake. Fat intake in the form of trans and saturated fat has increased and there is a decrease in intakes of fibre, complex carbohydrates, fruit and vegetable antioxidants, protein and calcium\textsuperscript{(6)}. In the USA, there were three times more deaths due to cancer and CHD than in Crete\textsuperscript{(6)} and this differential has only increased recently. Current trends of eating while watching television promote unhealthy, quick meals and exclude social/family communication. In biblical times, meal times (generally twice a day) nurtured relationships and was an opportunity for communication. The social setting for eating promotes fixed meal times and may overcome the reluctance to change in lifestyle experienced today. The Last Supper was the traditional Passover Seder meal and was styled on the Greek symposium in which people reclined and philosophised while eating.

The Lyon Heart Study adapted the Crete diet for the French population and showed cardioprotective and anticancer effects, thereby demonstrating that the MedDi can be modified to suit other populations\textsuperscript{(7)}. Other factors that may contribute to the Mediterranean lifestyle include: relaxing psychosocial environment, mild climate, preservation of the extended-family structure and even a siesta\textsuperscript{(8)}, as well as regular activity, mainly through walking.

The following sections describe the health benefits of different components of the biblical diet in addition to the conventional MedDi recommended today (Table 1). Thus, discussion of the well-known nutritional qualities of grains, legumes, beans, fruit and vegetables and fish is beyond the scope of the present article.

\textbf{The biblical seven species}

The biblical seven species – wheat, barley, grapes, figs, pomegranates, olives and date honey, together with some indigenous foods from the Middle East – are now scientifically recognised as healthy food, and could further improve the beneficial MedDi (Fig. 1).

\textbf{Grains}

The origins and spread of domesticated grains have been traced to the Fertile Crescent spreading from Mesopotamia (the cradle of civilisation)\textsuperscript{(9–12)}. It would appear that such food use reached the Middle East before the Greek Islands. The pivotal role of bread is further emphasised in its important status and use during festivals. In the tenth century BC, carvings on limestone describe the harvest seasons in the land of Israel according to the Gezer calendar, which is a rhythmic enumeration of the agricultural seasons. In the dry summer months, vines were pruned and figs, dates, pomegranates and grapes ripened and the wheat was harvested, whereas in the spring season barley was harvested. Wheat flour and grain have provided the staple (breads, pitas, etc.) for different types of meals throughout the Mediterranean basin. It is the basic food par excellence and is at the centre of food culture. The health benefits of fibre and complex carbohydrates are beyond the scope of the present review.

\textbf{Olives}

In ancient times, olives were consumed by farmers and accompanied travellers and nomads, and in addition were a popular appetizer. Romans served olives as starters and desserts in their rich symposiums. Olive oil is a hallmark of the MedDi, and has a moderate fat content, in the range of 30–40\% of energy derived from fat. The majority
of fat in olive oil is MUFA. Fat from edible olives and olive oil consists of oleic acid (18:1, n-9; 75%), saturated fat (15%) and PUFA (10%). Olive oil is extracted from deeply pigmented olives that are rich in phyttonutrients, including the phenolics hydroxytyrosol and oleuropein. When replacing saturated fat, olive oil reduces absolute levels of serum LDL, inhibits its oxidation and attenuates atherogenesis, with a most impressive effect shown for extra virgin oil that was enriched with green tea polyphenols.

In biblical times, olive oil was cold pressed and stored in dark, opaque glass containers. This was to avoid the powerful oxidative action of sunlight. Unprocessed olive oil has the greatest antioxidant effect. Comparison of extracted phenolic compounds from extra virgin olive oil and processed olive oil showed that extra virgin olive oil had significantly greater antioxidant effects than processed olive oil. It therefore seems that during the modern process of olive oil refinement, some of the phenolic content is reduced. The extra virgin unprocessed olive oil of the biblical diet has a higher concentration of antioxidants, which in turn may prevent LDL oxidation. In addition to its advantageous effects on blood cholesterol quantity, as well as quality, olive oil

Table 1 Some beneficial effects of the components of the biblical diet

<table>
<thead>
<tr>
<th>Component</th>
<th>Health benefit</th>
<th>Source</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olive oil</td>
<td>Heart benefits</td>
<td>MUFA</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>Antithrombotic, anti-inflammatory, antihypertensive effects</td>
<td>Antioxidants: tocopherol, hydroxytyrosol and oleuropein sterols</td>
<td>53</td>
</tr>
<tr>
<td></td>
<td>Reduction in LDL and increase HDL</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Anticarcinogenic</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>High intake of olive oil is not associated with weight gain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Red wine</td>
<td>Antithrombotic</td>
<td>Rich in polyphenols (antioxidants; e.g. resveratrol)</td>
<td>54</td>
</tr>
<tr>
<td></td>
<td>Increase longevity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pomegranates</td>
<td>CVD, LDL oxidation, macrophage oxidative status and foam cell formation</td>
<td>Vitamin C</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>Hypertension: reduces systolic blood pressure through inhibition of serum angiotensin-converting enzyme</td>
<td>Vitamin B6, K</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Viral infections: antibacterial effects against dental plaque</td>
<td>Antioxidant polyphenols</td>
<td></td>
</tr>
<tr>
<td>Barley and wheat</td>
<td>Delays gastric emptying</td>
<td>Fibre in whole grains</td>
<td>56</td>
</tr>
<tr>
<td>Dates + figs (fruit)</td>
<td>Anti-inflammatory, anticarcinogenic, decreases risk heart disease</td>
<td>Vitamins flavonoids</td>
<td>58</td>
</tr>
<tr>
<td>Nuts</td>
<td>Cardio-protective effects</td>
<td>MUFA + PUFA (particularly walnuts)</td>
<td>59</td>
</tr>
<tr>
<td>Legumes (chickpeas)</td>
<td>Lower LDL cholesterol</td>
<td>Rich in arginine</td>
<td>60</td>
</tr>
<tr>
<td>Oily fish and PUFA</td>
<td>Decreases fasting insulin</td>
<td>Protein, fibre, Fe, folic acid and B vitamins</td>
<td>61</td>
</tr>
<tr>
<td></td>
<td>Anti-inflammatory</td>
<td>n-3 anti-inflammatory EPA and DHA</td>
<td>62</td>
</tr>
</tbody>
</table>

Fig. 1 Proposed additions of biblical components to the Mediterranean diet pyramid
also has anti-carcinogenic action. A major component of phenols is lignans, which are found in olive oil. Owen et al.\(^{(17)}\) found that they have a protective function against cancer of the breast, colorectum, oesophagus and prostate. Animal models show that the sterol squalene that is found in olive oil represses tumour growth\(^{(30)}\). Although the high fat content of olives could be of concern due to potential weight gain\(^{(19)}\), obesity is not just the result of high-fat diets\(^{(20)}\). Rather, MUFA have been shown to increase postprandial fat oxidation, diet-induced thermogenesis and energy expenditure\(^{(21)}\); hence, moderate consumption of olive oil is less likely to cause weight gain. It is of interest that in all populations studied, irrespective of geography and diet, oleic acid is the major storage adipose tissue fatty acid derived from the diet, as well as from de novo fatty acid synthesis. The reason for this is not clear, but may relate to oleic acid physico-chemical (fluidity) and biochemical (antioxidant) properties\(^{(22)}\). Oleic acid is the dominant storage adipose tissue fatty acid, irrespective of where people live and what they eat\(^{(23)}\).

**Dates**

Fruit of the date palm (Phoenix Dactylifera L. Arecaceae) are an important component of the diet in the Middle East and North Africa. Dates are an ideal high-energy food as they contain high sugar content. They are also a good source of fibre and minerals, such as Ca, Fe, Mg, K and Zn\(^{(24,25)}\). Date fruit are used in folk medicine for the treatment of various infectious diseases and cancer\(^{(26)}\), probably as a result of their immunomodulatory activity\(^{(26)}\), antibacterial capacity\(^{(27)}\) and antifungal properties\(^{(28)}\). Furthermore, aqueous extracts of dates were shown to have potent antioxidant activity\(^{(29)}\), as they inhibit *in vitro* lipid and protein oxidation, and possess substantial free radical scavenging capacity. The above antioxidant activity is attributed to the wide range of phenolic compounds present in dates, including 30,31). Animal models show that the sterol squalene that is found in olive oil represses tumour growth\(^{(30)}\). Although the high fat content of olives could be of concern due to potential weight gain\(^{(19)}\), obesity is not just the result of high-fat diets\(^{(20)}\). Rather, MUFA have been shown to increase postprandial fat oxidation, diet-induced thermogenesis and energy expenditure\(^{(21)}\); hence, moderate consumption of olive oil is less likely to cause weight gain. It is of interest that in all populations studied, irrespective of geography and diet, oleic acid is the major storage adipose tissue fatty acid derived from the diet, as well as from de novo fatty acid synthesis. The reason for this is not clear, but may relate to oleic acid physico-chemical (fluidity) and biochemical (antioxidant) properties\(^{(22)}\). Oleic acid is the dominant storage adipose tissue fatty acid, irrespective of where people live and what they eat\(^{(23)}\).

**Pomegranates**

The pomegranate has been cultivated in the Mediterranean region since ancient times and was introduced into Egypt from Syria and from Israel around 1600 BC. In the Bible, the coat of the high priest was adorned with pomegranates (Exodus 39: 24–26). Many are the quotations concerning this luscious fruit especially in the Song of Songs: ‘As a piece of pomegranate are thy temples (cheeks)’ (6:7); ‘I would cause thee to drink of spiced wine and the juice of my pomegranate’ (8:2).

In Greek mythology, pomegranates were a symbol of life and rejuvenation. They are a potent antioxidant containing ellagitannin polyphenolic compounds such as punicalagins and punicalins, as well as ellagic acid and gallic acid. The antioxidant health benefits of pomegranate were shown to reduce LDL oxidation and it is helpful in reducing the risk of heart disease\(^{(33)}\). It was also shown to decrease the progression of prostate cancer\(^{(34)}\). Furthermore, drinking just 50 ml of pomegranate juice (PJ) daily can significantly lower blood pressure after 3 months by 5 %. Leaf extracts from pomegranate may also be effective in weight loss as, without affecting plasma TAG levels, pomegranate consumption reduces fat absorption from the intestine and can be cardioprotective\(^{(35)}\).

Pomegranate is a major source of most potent antioxidants (tannins, anthocyanins), which are considered to also be anti-atherogenic. Studies have analysed the effect of PJ on lipoprotein oxidation, aggregation and retention and on macrophage atherogenicity in healthy subjects and atherosclerotic patients, as well as in atherosclerotic apolipoprotein E-deficient (E\(^{-}\)) mice. *In vitro* studies demonstrated a significant dose-dependent antioxidant capability of PJ against lipid peroxidation in plasma (by up to 33 %), in LDL (by up to 43 %) and in HDL (by up to 22 %). The water-soluble fractions of pomegranate’s inner and outer peels, but not the seeds, were even stronger antioxidants against LDL oxidation than the juice itself. The antioxidative effects of PJ against lipid peroxidation in whole plasma and in isolated lipoproteins were also shown *ex vivo* in humans and mice. Furthermore, PJ consumption in humans increased the activity of serum paraoxonase, an HDL-associated esterase (lipo-lactonase) that acts as a potent protector against lipid peroxidation. PJ not only inhibited LDL oxidation, but also reduced two other related modifications of the lipoprotein, that is, its retention to extracellular matrix proteoglycans and its susceptibility to aggregation. The inhibitory effects of PJ consumption on macrophage ability to oxidise LDL on
the one hand, and on the uptake of oxidised LDL on the other, contributed substantially to the attenuation of cellular cholesterol accumulation and foam cell formation, as observed in atherosclerotic mice and in atherosclerotic patients\(^3\). PJ supplementation to E\(^\circ\) mice significantly reduced the number of macrophage foam cells and the size of the atherosclerotic lesion, in comparison to controls. PJ consumption by patients with carotid artery stenosis for 1 year reduced systolic blood pressure (by 18\%), oxidative stress (by 65\%) and, most importantly, the lesion size as measured by intima-media thickness (IMT; by \(\sim 30\%)\(^5\).

Altogether, the results of the above studies clearly demonstrate that PJ may be considered as a potent nutraceutical agent against CVD\(^3\).\(^6\).\(^7\).

### Figs

The fig is the fruit of lust and is believed to be a symbol of fertility. The high levels of fibre in figs stimulate bowel movement. Excavations at Gezer have uncovered remains of dried figs from the Neolithic Age and an old seed was recently germinated from the Dead Sea\(^3\). Figs are native to the Mediterranean and grow on the ficus tree (Ficus carica), and were one of the first fruits to be cultivated. The fruit is rich in natural and simple sugars, minerals and fibre and is a good source of K, Ca, Mg, Fe, Cu and Mn. Dried figs are popular as they last for a long time and have high calcium content (250mg of Ca/100g fruit weight). Potassium is also essential in regulation of blood pressure. Recently, Aviram's group observed high total polyphenol content in fig juice (with some phenolics that are unique to figs), which was associated with significant antioxidant activity against LDL oxidation (M Aviram, unpublished results).

### Grapes

Vine cultivation and wine production originated in Mesopotamia. However, the culture of wine consumption belongs to the Mediterranean. An Egyptian inscription from 2375 BC records how a military governor, Uni under the reign of Pharaoh Pepi I, sent troops to put down a revolt in Israel and how they 'destroyed the fortresses ... and felled the fig trees and vines'. A mural from the reign of Amenopsis II (fifteenth century BCE) shows the preparation of wine in Egypt by the Apirou, thought to be the Hebrews\(^8\).\(^9\). From early Egyptian civilisation through the classical period and the Roman Empire, wine has been of importance and value and exclusive to the civilised elite. Consumption of wine in the MedDi is subject to different cultural norms, especially in Muslim countries.

Red wine is rich in antioxidants from the flavonoid phenolics family, and includes catechin, querchitin, anthocyanins and resveratrol. Resveratrol is a trihydroxy-stilbene phenolic compound found in the grape's seeds and skin and it has been shown to increase blood HDL cholesterol, to protect against LDL oxidation and to attenuate blood clotting. It is found in several vegetal sources and has also been shown to possess lifespan-promoting properties that mimic energy restriction in yeast and metazoans, including small mammals. While in yeast and lower metazoans resveratrol acts mainly by activating the histone deacetylase Sir2, in mammals it appears to target – in addition to the Sir2 homologue SIRT1 – several crucial pathways for the control of metabolism, including the AMPK and the insulin-IGF1 receptor axis\(^4\).

In the Mediterranean culture, wine is consumed in conjunction with a meal, whereas Western cultures may consume wine independent of meals and it is a more alcoholic, less acidic and a less phenolic-rich wine. Alcohol consumption on an empty stomach leads to rapid alcohol absorption and increases the risk of intoxication. It is of interest that the Rambam (Maimonides) recognised the health benefits of wine already more than 800 years ago\(^4\).

Red wine, but not white wine, consumption (400 ml/d, for a period of 2 weeks) by healthy volunteers, resulted in a reduced propensity of their LDL to lipid peroxidation as determined by a 46\%, 72\% and 54\% decrement in the content of aldehydes, lipid peroxides and conjugated dienes, respectively. It appeared that some phenolic substances present in red wine are absorbed, bind to serum LDL and may be responsible for the antioxidant properties of red wine against LDL oxidation.

The lower antioxidant activity in white wines, in comparison to red wines, lies in the reduced content of polyphenols extracted from the grape skin, as red wine, but not white wine, is prepared following long contact time (~1 month) of the grape skin with the produced wine. Nevertheless, it is possible to enrich white wine with the grape skin polyphenols. White wine derived from whole squeezed grapes stored for a short period of time (up to 18h) contained increased concentrations of polyphenols (from 0.35 after 3h, up to 0.55 mmol/l after 18h of storage), and in parallel, exhibited increased capacity to scavenge free radicals and to inhibit copper ion-induced LDL oxidation. Addition of increasing concentrations of alcohol (up to 18\%) to the whole squeezed grapes remarkably augmented the extraction of grape skin polyphenols into the wine (up to 1.25 mmol/l), and thus resulted in increased capacity of the wine to scavenge free radicals and to inhibit LDL oxidation to an extent similar to that of red wine. LDL oxidation inhibition was directly related to the wine's polyphenolic content (\(r = 0.986\)). Thus, processing white wine with a short period of grape skins' contact in the presence of increased alcohol concentration led to extraction of their polyphenols and produced polyphenol-rich white wine with antioxidant characteristics similar to those of red wine\(^4\).

The potent antioxidant activity first shown for the Israeli red wine consumption was also demonstrated later on in a UK study, although the antioxidant capability of this wine was lower than that of the Israeli wine. Analyses of both red wines revealed five-fold increased levels of the polyphenolic subfracion flavonols in the studied Israeli
red wine. Flavonols are potent polyphenolic antioxidants, and this may explain the above results. There is wide variation in the flavonol content of different red wines throughout the world and a major determinant for the production of grape flavonols is the amount of sunlight to which the grapes are exposed during cultivation, when flavonols are synthesised. Thus, the climatic conditions under which grapes are grown could explain the five-fold increased content of flavonols in the specific studied Israeli red wine compared to the studied UK wine, and hence the high antioxidant potency observed in the Israeli red wine\(^{(45)}\).

The effect of consuming red wine, or its major flavonoid constituents, the flavonol catechin or the flavonol quercetin, on the development of atherosclerotic lesions was studied, in relation to LDL oxidation and aggregation, using the atherosclerotic, apolipoprotein E-deficient (E\(^{-}\)) mice model\(^{(44)}\). The atherosclerotic lesion area was significantly decreased in the treated mice. These results were associated with reduced susceptibility to oxidation (induced by copper ions, free radical generators or by macrophages) of LDL, isolated after consumption of red wine, quercetin and, to a lesser extent, catechin, in comparison with LDL isolated from control mice. Furthermore, PON1 activity was preserved in red wine-treated mice in comparison to PON1 inactivation in the placebo-treated mice.

LDL oxidation was previously shown to lead to its aggregation. The susceptibility of LDL to aggregation was decreased, in comparison with control mice, by 63\%, 48\% or 50\% on consuming catechin, quercetin or whole red wine, respectively. In vitro studies revealed that the inhibition of LDL aggregation by the above polyphenols could be related, at least in part, to a direct effect of the polyphenols on the LDL particle\(^{(45, 46)}\).

**Additional biblical foods**

The MedDi, particularly that from Crete, has a balanced intake of polyunsaturated essential fatty acids (EFA) in a ratio of 2:1 (\(n\)-6:\(n\)-3) in contrast to the much higher ratios observed in the Western and Northern European diets, and in the USA\(^{(5, 47)}\). In the traditional MedDi, a sweet tooth was satisfied by intake of carob, and figs stuffed with walnuts as a snack.

**Carob**

During the Roman persecutions, Rabbi Shimon Bar Yochai and his son survived for 13 years in a cave and survived on carob, dates and water. (Kohelet Raba 10:8)\(^{(39)}\). Carob is a legume native to the Mediterranean. The word ‘carob’ is derived from the Arab kharrub and means ‘pod’, and it also gave the name carat to the measure of gold. Carob beans can be dried, ground and roasted to produce carob flour or powder. Carob is caffeine-free and naturally sweet and a rich source of calcium and potassium and smaller amounts of iron and some B vitamins. Carob binds to the intestinal tract and acts as a remedy for diarrhoea.

Aviram’s research group recently measured the total polyphenol concentration in carob pod honey and found that it was comparable to concentrated PJ. The carob pod honey contained 25.8 (\(\pm\) 2.4) mg, whereas concentrated PJ contained only 28.3 (\(\pm\) 2.4) mg of gallic acid equivalents/ml. The carob pod honey also exhibited significant dose-dependent free radical scavenging capacity. These studies demonstrated that carob pod honey contains high concentrations of total polyphenols, even in comparison to polyphenol-rich PJ.

**Nuts**

Nut consumption has an inverse relationship with risk for CVD. Nuts are rich in protein, fibre, phytonutrients and polyphenolic antioxidants, as well as MUFA and PUFA.

The US Food and Drug Administration have promoted the intakes of almonds, hazelnuts, peanuts, pecans, pistachios and walnuts as they contain <8 g of saturated fat per 100 g. Walnuts have a particularly high content of \(n\)-3 fatty acids, in addition to being high in fibre, vitamin B, magnesium and several types of antioxidants. Walnuts are active in improvement of blood vessel elasticity and in reducing atherosclerotic plaque accumulation, blood LDL cholesterol concentration and the inflammatory C-reactive protein biomarker.

Nuts are also rich sources of fibre, vitamin E and phytochemicals such as ellagic acid, flavonoids, phenolics, luteolin, isoflavones and tocotrienols. Nuts are also an excellent source of Mg, Zn, Se, Cu, riboflavin, niacin, Fe and folic acid. Of interest is that peanuts were shown to contain the flavonoid resveratrol (~70 µg/ounce of peanuts), whereas almonds contain the flavonoids quercetin and kaempferol.

Nut consumption reduces the risk of CHD, as shown in the Iowa Women’s Health Study and that on California Seventh-Day Adventists\(^{(48–50)}\).

Additional antiatherogenic properties of nuts may be related to the type of the nut’s proteins that are rich in the amino acid arginine and low in lysine. Arginine is a precursor of the vasodilator, antiatherogenic agent nitric oxide. Reduced arginine/lysine ratio is directly related to accelerated atherogenesis\(^{(51)}\).

An additional important mechanism for the protective effect of nut consumption against atherogenesis is the attenuation of oxidative stress by nut antioxidants such as vitamin E, polyphenols, flavonoids and other phytochemicals\(^{(52)}\).

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Mediterranean nuts: origins, ancient medicinal benefits and symbolism

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Abstract

Objective: To consider historical aspects of nuts in relation to origin and distribution, attributed medicinal benefits, symbolism, legends and superstitions.

Design: Review of historical aspects of nuts.

Setting: Mediterranean region.

Subjects: The varieties reviewed include almonds, walnuts, hazelnuts, pine nuts and pistachios.

Results and conclusions: Like other foods, nuts have a wide variety of cultural connections to the areas where they grow and to the people who live there or eat them. History, symbolism and legends reveal the ancient tradition of nuts and how they are related to the lives of our ancestors. Archaeological excavations in eastern Turkey have uncovered the existence of a non-migratory society whose economy centred on harvesting nuts. This shows that nuts have been a staple in the human diet since the beginnings of history. Moreover, since ancient times nuts have been used for their medicinal properties. They also play a role in many old legends and traditions.

Keywords
Nuts
Almonds
Walnuts
Hazelnuts
Pine nuts
Pistachios

Tree nuts: origin and distribution

Almonds
Almonds are native to the Mediterranean climate region of the Middle East, Pakistan, Syria and Turkey(1), and other areas in Asia Minor. They were spread by Egyptians, Greeks and Romans in ancient times throughout the Mediterranean and into northern Africa and southern Europe.

The first evidence of the existence of wild almonds comes from Israel during the Pleistocene (780,000 b.c.e. ‘before the common era’). The Acheulian site of Gesher Benot Ya’aqov (Israel) has revealed a unique association of edible nuts with pitted hammers and anvils, which indicates a nut-cracking activity and supports the hypothesis that the pitted stones served as nut-cracking tools(2).

Domesticated almonds appear in the Early Bronze Age (3000–2000 b.c.e.) in the Near East, or possibly a little earlier at the dawn of agriculture. A well-known archaeological example of the almond is the fruit found in Tutankhamun’s tomb in Egypt (c. 1325 b.c.e.) and at Deir el-Medina(3), which was probably imported from the Levant(4). Almonds have also been found at the Neolithic level under the palace of Knossos, and in Bronze Age storerooms at Hagia Triada, both on Crete.

Around 500–600 C.E. (‘of the common era’), Arabs conquered North Africa and brought almonds into Tunisia and Morocco, and eventually into the Iberian Peninsula across the Strait of Gibraltar(5). In the culture of Al-Andalus, almonds were used in many recipes(6).

In the mid-1700s, Spanish Franciscan Friars started to cultivate almonds in their missions along the Royal Road from San Diego to Sonoma. Because of the climatic conditions, almonds were soon grown around the Sacramento area and San Joaquin in the Central Valley. California is currently the leading producer of almonds worldwide(7).

Walnuts
Walnuts (Juglans regia) are also considered to be one of the oldest tree foods known to man. Historical references date back to Persia in 7000 b.c.e., but they were originally found throughout southeastern Europe and all the way to the Himalayas(8).

The oldest archaeological site where walnuts have been unearthed is in the Shanidar caves in northern Iraq. After this find, at a considerable distance from Persia, evidence of walnuts was discovered in a Mesolithic dunghill in Switzerland(9).
The Americans, however, had their own native walnuts: the eastern black walnut (*J. nigra*). Archaeological findings also indicate that native Americans had been eating black walnuts since at least 2000 B.C.E.⁹. Of all the walnuts, the Persian or English walnut (*J. regia*) was the most common, probably the tastiest and certainly the most important.¹⁰

In ancient Persia, only royalty ate walnuts, and they came to be known as Royal Walnuts. Around 2000 B.C.E. in Mesopotamia, the Chaldeans left inscriptions on clay tablets revealing the existence of walnut groves within the famed Hanging Gardens of Babylon. Evidence of walnut consumption dating from the same era can also be found on carved stelae containing the ‘Code of Hammurabi’, in the section on laws governing food.¹¹

The first people to cultivate walnuts were the ancient Greeks, who used them not only for food, but also as medicine and dyes for hair, wool and cloth. The Romans, imitators of the Greeks, discovered their merits and were willing to pay dearly for the luxury of serving them along with fruits for dessert. In the ruins of Pompeii, whole, unshelled walnuts were among the foods on the table at the Temple of Isis on that fateful day of 24 August, 79 C.E. when Mount Vesuvius erupted. Although some reports are just myths, walnuts are mentioned in the principal Roman treatises on agriculture: ‘De Re Rustica Varro’, ‘De Re Rustica Columella’ and ‘Naturalis Historia’.¹²

Although there are no written records of the arrival of walnuts in Kashmir, they were an established presence and may have journeyed from there to China during the Han dynasty, sometime between 206 B.C.E and 220 C.E. Although walnuts are often referred to as English walnuts, they did not become popular in England until after World War I when they became a commercial enterprise.¹³ They acquired this name because they were frequently imported by English ships. The species was taken to the New World by English settlers and to California by missionaries. Nowadays, California is also the largest producer of walnuts.¹⁴

**Hazelnuts**

Hazelnuts or filberts come from a number of similar trees of the genus *Corylus* that are native to Europe, Asia and continental America. The hazel grew wild, forming part of the subsoil of deciduous forests from the most recent glacial period, between around 18,000 and 17,000 B.C.E.¹⁵ Hazelnuts have been cultivated in China for more than 5000 years.¹⁶

In 1995, archaeologists found evidence of large-scale Mesolithic nut processing on the Hebridean island of Colonsay. Carbon dating shows that the finds date back 9000 years. Hundreds of thousands of burnt hazelnut shells were found in a shallow pit or midden at Staosnaig, on the east coast of this small island. The nuts had been harvested in a single year and pollen analysis suggests that the hazel trees were all cut down at the same time. The scale and location of the activity is unusual, suggesting that the island community was trading processed hazelnuts with other island and mainland communities.¹⁷ On a smaller scale than Staosnaig, there are similar hazelnut middens at Kinloch and Papadil on Rhum.¹⁸

Hazelnuts were also used extensively in the Roman Empire. Carbonised hazelnuts have been recovered from sites destroyed by Mount Vesuvius and provide valuable historical evidence that hazelnuts were used by the ancient Campanians of the first century C.E.¹⁹ For example, in the garden of the House of the Ship Europa at Pompeii, two pieces of carbonised hazelnut shell were found in 1972.²⁰ Moreover, carbonised fragments of one of the stakes used to prop up the limbs of a large tree in the garden in the House of Julius Polybius were identified as hazelnut.²¹

The leading producer of hazelnuts today is Turkey.²²

**Pine nuts**

Pine nuts are the seeds of the pine tree *Pinus pinea*, which belongs to the Pinaceae family. Some authors maintain that the species is native to the entire Mediterranean basin, whereas others limit its natural range exclusively to the eastern Mediterranean and Asia Minor.²³

Remains of pine nuts from the Mesolithic period have been found in various caves, such as those in Nerja (Málaga) and Lattes in southern France, which show the presence of the pine tree and the use of pine nuts, as well as other nuts, in the diet of human groups.²⁴

The Hebrew prophet Hosea (ca. 734–732 B.C.E.), who lived in the Northern Kingdom (ancient Israel), referred to pine nuts in the Old Testament (14:8). The ancient Greeks and Romans appreciated the taste of pine nuts. Archaeologists have found pine nuts among household foodstuffs in the ruins of Pompeii (79 C.E.). The Roman legions carried pine nuts among their provisions, and pine-nut shells have been uncovered in refuse dumps of Roman encampments in Britain from the middle of the first century.²⁵

The current world leader in pine nut production is Spain.²⁶

**Pistachios**

According to Vavilov,²¹ a prominent Russian and Soviet botanist and geneticist, Pistachios originally came from: (i) central Asia, including northeast India, Afghanistan, Tajikistan and Uzbekistan; and (ii) the near-east, which covers Asia Minor, Caucasus, Iran and the mountain region of Turkmenistan. The presence of pistachio nuts in archaeological excavations provides evidence that the pistachio has long been associated with human activities, and was used as fuel. Pistachio (*Pistacia vera* L.) cultivation probably began in areas near to which the pistachio grew wild. Remains of pistachio nuts dating from the sixth millennium B.C.E. have been found in Afghanistan and southeastern Iran.²² Pistachio cultivation was widespread in the ancient Persian Empire, from where it gradually expanded westward. In Assyria,
Ancient medicinal benefits of tree nuts

Almonds
The Greek physician Hippocrates (ca. 460–370 b.c.e.), considered the ‘father of medicine’\(^{(29)}\), was the author of the Corpus Hippocraticum, a collection of medical works in which the medicinal effects attributed to almonds are first mentioned. He records that ‘Almonds are burning but nutritious, burning because they are oily and nutritious because they are fleshy’\(^{(31)}\). In the Greek system of humoral physiology, almonds would have been categorised as a hot and dry food: that is to say, one that stimulates choler in the body. Logically, as a medicine in this allopathic system, in which ailments are cured by the administration of substances with opposite qualities, almonds would have been ideal for treating colds and other phlegmatic disorders.

The ancients also attributed other wonderful virtues to almonds, such as its supposed ability to prevent intoxication. Almonds were thought to prevent inebriation if consumed before drinking began. The Greek historian Plutarch (c. 46–120 c.e.) mentions a great wine drinker who ate five or six bitter almonds and did not fall victim to intoxication (Plutarch, Mor. 624 c.). The same property is referred to by Dioscorides (40–90 c.e.), a Greek physician (Diosc. i.123,2), and Pliny (Plin xxxiii.145), who even managed to agree on the number of almonds that should be consumed.

Raw or toasted almonds were consumed extensively in Rome. Pliny also gives many medical uses for bitter almonds: ‘they provoke sleep and sharpen the appetite, act as a diuretic and emmenagogue. They are also used topically for head-ache, when there is fever more particularly. (…) Used in combination with amylum and mint, they arrest haemorrhage. They are useful, also, for lethargy and epilepsy, and the head is anointed with them for the cure of epynictis. In combination with wine, they heal putrid ulcers of an inveterate nature, and, with honey, bites inflicted by dogs. They are employed, also, for the cure of scaly eruptions of the face; the parts affected being fomented first’. Pliny only says of sweet almonds, ‘their remedial properties are not so extensive; still however, they are of a purgative nature, and are diuretic. Eaten fresh they are difficult to digest\(^{(12)}\).

Walnuts
This fruit was considered astringent\(^{(32)}\), stomachic and suitable to facilitate digestion\(^{(33)}\). Heraclides of Tarentum (c. second century b.c.e.), a Greek physician, suggested they were a stimulant to the appetite, and advised that they be eaten at the beginning of a meal\(^{(27)}\).

When Pompey (106–48 b.c.e.) had made himself master of the palace of Mithridates, he searched everywhere for the recipe for the famous antidote against poison used by the previous king. At length it was found, and it was very simple: ‘Take two dried walnuts, two figs, and twenty leaves of rue; pound them all together, with the addition of a grain of salt; if a person takes this mixture fasting, he will be proof against all poisons for that day’ (Plin. xviii. 4).

It is said that, if chewed by a fasting man and applied to a wound, walnut kernels can instantaneously cure bites inflicted by a mad dog\(^{(12)}\).

An infusion of powdered walnut leaves (supposed to have an astringent quality) used to be applied both internally and externally to treat swollen glands, shingles and sores. Walnut oil was prescribed for colic and to soothe the intestines. The juice of green walnut husks, diluted in warm water, was recommended as a mouthwash and to stop diarrhoea. A green walnut, boiled in sugar, was said to relieve constipation. Powdered walnut bark was prescribed to treat ringworm\(^{(10)}\).

Until the end of the eighteenth century, walnut milk was considered a nourishing substitute for dairy milk in European households. The Chinese, too, have an ancient custom of making walnut milk, which was thought to be a strength-building food and to possess medical properties\(^{(10)}\).

Hazelnuts
In ancient times, hazelnuts were used as a medicine and tonic. Greek doctors thought they were moderately nutritional and, if eaten raw, they believed they were difficult to digest and so recommended that they be toasted\(^{(34)}\). They also believed that consuming too many led to dizziness and headaches. In the first century c.e., the Greek physician Dioscorides emphasised the properties of hazelnuts as a medium to cure colds and grow hair\(^{(35)}\).
Ancient healthy benefits of nuts

In the Middle Ages, both fresh fruit and nuts were consumed very little. Because of the influence of Galen's doctrines, they were considered to be a poor foodstuff and were often seen as the cause of illnesses. In his book *Regimen*, Arnau de Vilanova (1255–1311 c.e.), an alchemist, astrologer and physician of Catalan origin, tells us that, ‘Hazel nuts, due to their nature, give some comfort to the liver, but harm the stomach and the head’ (36). Hazel nuts were only used as thickeners, and rarely as ingredients of a dish. They were eaten alone, and with other nuts, but were not seen as worthy of mention in cooking documents or agricultural treatises.

**Pine nuts**
Pine nuts were used for medical purposes in the Egyptian culture. In the book *The Physicians of Pharaonic Egypt*, pine nuts are mentioned as one of the products that the ancient Egyptians used to cure illnesses (37). Both Galen of Pergamum (129–199/217 c.e.), a Roman physician, and Dioscorides believed their properties counteracted cough and chest pain. Galen thought they had clearing properties, and recommended them for patients with expectorant chests and lungs (38). In his book *De Materia Medica*, Dioscorides says that pine nuts are astringent, have some energetic value and relieve cough and chest infections, either on their own or after being mixed with honey (39).

Pine nuts were used in the Al-Andalus culture as food, and also as a drug. Abû‘Alî al-Husayn ibn Sinâ (40), the doctor, philosopher, mathematician and astronomer born in Persia (980–1037 c.e.), wrote in his most famous work the *Kitâb al-qânîn (Canon of Medicine)* (40), ‘Pine nuts are useful against rotten fluid in the lungs, bleeding, and chronic cough, particularly with boiled fresh grape juice. If you boil them in a sweet wine, they are very good for cleansing lungs of pus. They also give energy and increase sexual appetite and the amount of semen. If pine nuts are eaten together with honey, they cleanse the kidneys and bladder and also protect the bladder from stones and ulcers’. Averroes (1126–1198 c.e.), a renowned Andalusî jurist, physician and scholar, also believed that pine nuts, like onions and chickpeas, increased the amount of semen and recommended using their oil as a remedy for stroke and weakness (41).

**Pistachios**
Pistachios were known to the Assyrians and the Greeks as a medicinal drug, a potent aphrodisiac and an antidote against bites by poisonous animals. Galen doubted whether pistachio nuts were good for the stomach (Plin. xvii. 5, 8). Avicenna (980–1037 c.e.), a polymath of Persian origin and the foremost physician and philosopher of his time, proved the contrary (Varro. i. 13, 38; Columell. ii. 5, 6, 9), and several centuries before him, the Roman epicures had courageously demonstrated that this fruit never does any harm, whether raw or roasted, alone or accompanied with garum and salt.

In his *Canon of Medicine*, Avicenna, considered the greatest doctor and scientist of the Islamic Middle East, prescribed pistachios for liver disease and described them as an aphrodisiac. As they are rich in oil, they were used both as food and medicine in Al-Andalus. Averroes says, ‘it is hot and dry, with great warmth. Its oil is a balanced cure, strengthening the stomach and the liver due to its nature as a whole. In general, it is one of the medicines considered to be of great usefulness’ (41). This belief was passed on to medieval Christian doctors. Arnau de Vilanova states that pistachios are good for liver colds (liver cold) and they damage the stomach and harm the head to a lesser extent than other nuts (36).

Pistachios have also been reported as a remedy for sclerosis of the liver, abdominal ailments, abscesses, bruises and sores, chest ailments, circulation problems and other problems (36).

**Symbolism, legends and superstitions**

**Almonds**
In the ancient religion of Cybele, the goddess of Mother Earth, life, death and resurrection was worshipped in Anatolia since Neolithic times, and the almond was considered to be the goddess’ vulva, from which life emerged. The almond is the first tree to flower in spring and therefore a sign of rebirth. It is the symbol of Attis, who was born of a virgin, and was conceived from an almond (39). This legend is a possible explanation for the relationship in the Bible between the almond and the Virgin Mary. Christian symbolism often uses almond branches as a symbol of the virgin birth of Jesus. In the Bible, the almond is mentioned ten times, beginning with the Book of Genesis 43:11, in which it is described as ‘among the best of fruits’.

Almonds have symbolised good luck for many centuries in southern Europe; traditionally, candied almond nuts are given away at weddings in Greece as tokens of long life and happiness. In Spain, glistening, ceremonial ‘Jordan’ almonds from Malaga are usually sugar coated. ‘Jordan’ refers to a renowned Spanish almond variety, the name of which is probably a corruption of the French word for garden (*jardin*) (10).

**Walnuts**
The scientific name ‘Juglans’ means ‘Jupiter’s nut’ and ‘regia’ means ‘royal’ (38). An old story recounts that in ancient days when men lived upon acorns, the gods lived upon walnuts. This shows that walnuts were highly valued far back in history (40).

According to some authors the walnut originated when Bacchus, the Greek god of wine and ecstasy, fell in love with Carya, the youngest of the three daughters of Dion, King of Laconia (44). When the jealous elder sisters endeavoured to prevent the two lovers from meeting, Bacchus turned them into stone and, for reasons clear only to a god, transformed his beloved into a walnut tree.
Greeks and Romans considered walnuts a symbol of fertility(10). After the wedding feast the bridegroom strewed in the nuptial chamber, at night, several baskets of walnuts, which children hastened to pick up(45). This was, as the Romans said, a kind of offering to Jupiter, and thus he was entertained to grant his supreme patronage to the husband, and to adorn the wife with the virtues of Juno (Juvenal. Sat. xv. 10). The god could not have failed to smile at this part of the request of blind mortals, and it is asserted that, at times, he did not deign to grant it.

The walnut tree also holds a few dark superstitions. In seventeenth-century Italy there was a walnut tree, the Tree of Benevento, that was believed to be the place where witches gathered. According to legend, the Bishop removed the tree, roots and all, but another witch-haunted tree grew where the original had stood(8).

Superstitions and fears also surrounded the shade of the walnut tree. A passage in Pliny’s writings states that the shadow of the walnut tree dulls the brain. He also considered the walnut tree a nuisance wherever it was planted and that nothing should be grown near it, because it contains evil or poison(8).

**Hazelnuts**

In many texts hazel and rowan trees, which are not always clearly distinguished lexicographically, are considered to be magical. Druids used hazels in their spells. In Celtic customs, hazels were linked to magical practices. In medieval times, they were attributed with divinatory properties. Warlocks, gold prospectors and water diviners used hazel branches for their practices. In Normandy, cows were beaten three times to give milk. The proceedings of a trial for witchcraft in 1596, in Hesse, contains the following quote: ‘If the witch had hit the cow with the branch of the devil, that cow gave milk all the year’. Hazel is therefore sometimes the devil tree(46). However, it is also a symbol of patience and perseverance in the development of mystical experience(46) and in many traditions a symbol of procreation and fertility. For example, in Norse mythology, Ægunn, goddess of life and fertility, is released by Loki, in the form of a falcon, who turns her into a hazelnut to take her back to Asgard(47).

The tree was also the symbol of marriage, wealth and family happiness. In Hanover, Germany, crowds shouted ‘Hazelnuts, hazelnuts!’ at the groom, and 3 d after the wedding the bride handed out hazelnuts to symbolise that the marriage had been consummated(46,48). In Russia, during wedding receptions, the mother-in-law threw hazelnuts and oats at the son-in-law, while in Ciutadella (Menorca, Balearic Islands) young men threw hazelnut shells at marriageable girls during the ‘Sant Joan’ festivities(42).

**Pistachios**

Legend has it that the Queen of Sheba decreed pistachios to be an exclusively royal food, going so far as to forbid commoners from growing the nut for personal use(24). They were a symbol of happiness(46). Nebuchadnezzar, the ancient king of Babylon, had pistachio trees planted in his fabled hanging gardens. In the first century c.e., the Emperor Vitellius debuted this prized nut in his capital city of Rome. According to Muslim legend, the pistachio nut was one of the foods brought to earth by Adam(43).

In short, nuts have cultural values that go beyond nutrition and cuisine.

**Acknowledgements**

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Ancient healthy benefits of nuts


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Effects of 3-month Mediterranean-type diet on postprandial TAG and apolipoprotein B48 in the Medi-RIVAGE cohort

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Abstract

Objective: To determine the postprandial lipaemia response before and after intervention with healthy diets in the Medi-RIVAGE cohort of subjects with moderate risk factors of CVD.

Design: One hundred and thirty-five adults (fifty-two men and eighty-three women) followed either a Mediterranean-type (MED) diet or a low-fat American Heart Association-type diet in a parallel design for 3 months. At entry and after 3 months, lipids, glucose and insulin were measured in the fasting samples; TAG and apolipoprotein B48 (ApoB48; a marker of intestinally derived chylomicrons) levels were measured in the fasting and postprandial samples after a standard test meal.

Results: The MED diet only lowered ($P < 0.028$) fasting TAG and both diets reduced TAG and ApoB48 levels 5 h after the test meal. The overall 5 h postprandial ApoB48 response (area under curve (AUC)/incremental AUC) was lowered after both diets but this effect was more marked after the MED-diet intervention. Whatever the TAG level at entry, normo- and hyper TAG subjects showed a reduction in the post-prandial ApoB48 levels after 3-month diets. BMI at entry did not impact the effect of diets given subjects with BMI $< 25$ kg/m$^2$ showed reduced postprandial ApoB48. Men and women displayed comparable postprandial changes after dietary challenges.

Conclusions: A MED diet appears efficient to improve postprandial lipaemia, a recently acknowledged CVD risk, in men and women at moderate cardiovascular risk.

Keywords

Nutrition
Metabolism
Men
Women
Cardiovascular risk

Postprandial lipaemia has received increasing attention during the past two decades$^{(1,2)}$. Indeed, following a typical fat-containing meal (30–60 g fat), circulating TAG shows a marked elevation within 1–2 h and can remain elevated for 5–8 h in healthy subjects and longer in dyslipidaemic patients$^{(3,4)}$. On the basis of dietary habits, it is clear that the dominant state of TAG metabolism for most humans is postprandial$^{(1,5–7)}$.

The specificity of the postprandial period is a physiological transient accumulation of TAG-rich lipoprotein (TRL) particles in the circulation as provided by both the liver (very LDL) and the small intestine (chylomicrons secreted after lipid digestion and absorption)$^{(1,8)}$. The capacity of individuals to regulate circulating TAG levels, that is, to secrete and clear TRL postprandially, is obviously an important reflection of their metabolic homeostasis as challenged by dietary intakes$^{(9)}$.

It is now well recognised that elevated postprandial lipaemia and TRL is a characteristic metabolic abnormality of a number of lifestyle-related diseases and conditions that are associated with increased cardiovascular morbidity and mortality$^{(10–12)}$. Exacerbated postprandial lipaemia has been repeatedly associated with cardiovascular risk during clinical studies$^{(13)}$. Moreover, recent and large epidemiological surveys have clearly evidenced the strong association between the extent of non-fasting TAG and the relative risk for cardiovascular events in men and women$^{(14,15)}$.

Thus, the habitual high-saturated fat, high-carbohydrate/sugar diets (and sedentary lifestyles) that typify the present time in industrialised countries are prone to cause exacerbated postprandial lipaemia$^{(1,5–7)}$, even in healthy subjects. Only a limited number of clinical studies have addressed the effect of chronic dietary regimen on the extent of postprandial lipaemia. While most of them have tested the effects of changes in single nutrients or fibres as reviewed$^{(16)}$, very few have investigated the effects of global dietary challenges on postprandial lipid metabolism$^{(17)}$. Hence, during the 3-month Medi-RIVAGE intervention study$^{(18)}$, we aimed to investigate the influence of dietary changes on postprandial lipid metabolism in subjects at moderate cardiovascular risk. We hypothesised that substituting a Western-type diet for either a Mediterranean (MED) diet or a low-fat diet alters the postprandial levels of circulating TAG or apolipoprotein B48 (ApoB48), a specific marker of intestinally derived TRL particles$^{(19)}$. 
Subjects and methods

Subjects and study design

The design and methods of the Medi-RIVAGE intervention study have been reported previously in detail(17). Briefly, volunteers were men and women aged 22–70 years who met at least one of the following eligibility criteria: fasting plasma cholesterol concentration of 6.5–7.7 mmol/l; TAG concentration of 2.1–4.6 mmol/l; glucose concentration of 6.1–6.9 mmol/l; blood pressure between 140–180 and 90–105 mmHg; BMI > 27 kg/m² or family history of CVD. Subjects treated with hypolipaemic or hypoglycaemic drugs were excluded.

At entry, eligible volunteers relied on a Western-type diet as reported previously in detail(17). They were provided with nutritional recommendations and follow-up by dietitians. The subjects were randomly assigned to consume one of the two slightly restricted and reduced-fat diets for 3 months, that is, either an MED diet adapted from the traditional model(20) or an adaptation of the commonly prescribed low-fat American Heart Association-type diet (LFAT). To summarise the published detailed changes in nutrient intakes after 3 months in 169 subjects(18), the two intervention diets had comparable reduced total fat (~34% energy), saturated fat (~10% energy) and cholesterol (~190 mg/d), and comparable increased PUFA (~6% energy) and increased MUFA in the MED group (up to 15-6% energy). Fruit, vegetable and fish intakes increased in both diet groups, whereas nut and fibre intakes increased in the MED group only. In fact, the nutrient and fibre intakes did not markedly differ between the two diet groups as reported elsewhere(18).

One hundred and thirty-five volunteers (fifty-two men and eighty-three women) enrolled in the postprandial study provided a full data set including postprandial tests and eighty-three women) enrolled in the postprandial study provided a full data set including postprandial tests.

Analytical methods

At entry and after 3 months, biochemical analyses were performed as described previously(18). Briefly, plasma and serum samples were immediately separated from whole blood by centrifugation. Glucose, insulin and TAG were determined using routine laboratory techniques in fasting and postprandial plasma samples from all subjects and ApoB48 quantification was performed using a competitive ELISA(22).

Statistical analyses

Statistical analyses were performed using the Statistical Package for Social Sciences statistical software version 17.0 (SPSS Inc., Chicago, IL, USA).

Absolute postprandial changes are given as concentration values. The data for postprandial parameters response following the test meal were expressed as area under the curve (AUC; 0–5 h) and were calculated by the trapezoidal method. Incremental AUC (IAUC) was calculated by subtracting the fasting concentration value.

Identified covariables such as sex, BMI, variation in body weight, alcohol consumption, smoking status (smoker/former smoker/never smoker) and menopausal status in women (yes/no or treated) were entered into the models.

Time effect within diet group was calculated using paired t test. Group effect at entry was assessed by univariate ANOVA. General linear models (GLM) were used to compare the postprandial response profiles between the different groups (diet groups, the low- and high-BMI groups, the low- and high-TAG groups). Two-tailed values of P<0.05 were considered significant.

Results

The characteristics of the 135 volunteers at entry are shown in Table 1. We did not observe significant differences between the two diet groups for the markers of fasting lipaemia (TAG and ApoB48) and postprandial lipaemia (AUC/IAUC for TAG and ApoB48) and for most lipid parameters. The HOMA score (Homeostasis Model Assessment of Insulin Resistance) reflecting the insulin-resistant status was not different in the two groups. HDL and LDL cholesterol levels were slightly different between the two diet groups.

Influence of 3-month intervention diets on fasting and postprandial parameters

In the present study, after 3-month consumption of the intervention MED or LFAT diets, the MED group only elicited a small but significant decrease in fasting TAG levels (ΔTAG = −0.15 (sd 0.07) mmol/l vs. −0.13 (sd 0.09) mmol/l for MED and LFAT groups, respectively; Table 2). The changes observed in postprandial TAG and ApoB48 levels after the test meal are shown in Fig. 1. After 3-month intervention, TAG levels significantly decreased 5 h after the test meal in both intervention groups (ΔTAG = −0.33 (sd 0.09) mmol/l vs. −0.27 (sd 0.10) mmol/l for MED and LFAT groups, respectively). Nevertheless, the changes in TAG AUC or TAG IAUC after 3 months were not significantly different from those at entry, whatever the group.
After 3-month consumption of the MED or LFAT diets, no significant change in fasting ApoB48 levels was observed (Fig. 1, Table 2). After 3-month intervention, subjects in the MED group had a significantly reduced ApoB48 level (ΔApoB48 = −0.013 (sd 0.09) mg/l v. −0.010 (sd 0.09) mg/l for MED and LFAT groups, respectively) and ΔApoB48 IAUC : −0.01 (sd 0.02) mg/l for MED and LFAT groups, respectively; Table 2). Repeated measures (0 and 3 months) GLM indicated that the type of diet modulated the reduction in ApoB48 IAUC and AUC (time and diet, P = 0.045 and 0.046, respectively) but not for TAG variables. Thus, the two diet groups have been merged for further analysis on postprandial parameters, with diet used as a covariable.

### Effects of fasting TAG, BMI, waist-to-biop ratio and gender at entry on the postprandial parameters

As shown in Fig. 2a (left panel), after stratifying the cohort (n 135) according to the fasting TAG level at entry, subjects with a higher fasting TAG level (>1.7 mmol/l; n 34) also had higher TAG levels 2.5 and 5 h after the test meal at entry (P < 0.001 for each time point). This was also observed after 3-month dietary intervention (P < 0.001 for each time point). Nevertheless, the level of fasting TAG at entry did not alter the TAG IAUC or AUC after 3-month dietary intervention.

At entry, subjects with a higher fasting TAG level also presented a higher fasting ApoB48 level (P = 0.009) as shown in Fig. 2a (right panel). ApoB48 levels 2.5 and 5 h after the test meal did not differ between the low- and high-TAG groups. After 3-month dietary intervention, both groups showed a significant and comparable decrease in ApoB48 IAUC (P = 0.001) and fasting ApoB48 levels were no longer different between the low- and high-TAG groups.

There were no significant differences between the two TAG subgroups for other fasting lipid parameters, age or BMI.

As shown in Fig. 2b (left panel), when stratifying the cohort according to subjects’ BMI at entry, after 3-month dietary intervention overweight/obese subjects (with BMI > 25 kg/m²) presented higher fasting TAG and higher postprandial TAG at the 2.5 h time point (P = 0.003 and 0.012, respectively). After dietary intervention, the reductions in TAG IAUC were not significant whatever the BMI group. As shown in Fig. 2b (right panel), subjects with low and high BMI had comparable ApoB48 levels at fasting and postprandially. After 3-month dietary intervention, the two BMI groups showed a significant and comparable decrease in ApoB48 IAUC (P = 0.001).

### Table 1 Characteristics of subjects in MED and LFAT intervention groups at entry

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Diet</th>
<th>n</th>
<th>Mean</th>
<th>SD</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>MED</td>
<td>72</td>
<td>51.50</td>
<td>5.50</td>
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</tr>
<tr>
<td></td>
<td>LFAT</td>
<td>63</td>
<td>52.80</td>
<td>2.00</td>
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<tr>
<td>BMI (kg/m²)</td>
<td>MED</td>
<td>72</td>
<td>28.43</td>
<td>4.27</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>LFAT</td>
<td>63</td>
<td>28.18</td>
<td>4.70</td>
<td>NS</td>
</tr>
<tr>
<td>Waist-to-hip ratio</td>
<td>MED</td>
<td>69</td>
<td>0.88</td>
<td>0.14</td>
<td>NS</td>
</tr>
<tr>
<td></td>
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<td>59</td>
<td>0.89</td>
<td>0.13</td>
<td>NS</td>
</tr>
<tr>
<td>ApoB48</td>
<td>MED</td>
<td>72</td>
<td>0.22</td>
<td>0.17</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>LFAT</td>
<td>60</td>
<td>0.25</td>
<td>0.18</td>
<td>NS</td>
</tr>
<tr>
<td>ApoB48 IAUC</td>
<td>MED</td>
<td>72</td>
<td>0.37</td>
<td>0.38</td>
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</tr>
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<td>60</td>
<td>0.28</td>
<td>0.25</td>
<td>NS</td>
</tr>
<tr>
<td>TAG</td>
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<td>72</td>
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<td>0.97</td>
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<td>1.44</td>
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<tr>
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<td>0.58</td>
<td>0.76</td>
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</tr>
<tr>
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<td>0.53</td>
<td>0.67</td>
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<tr>
<td>Cholesterol</td>
<td>MED</td>
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<tr>
<td>HDL cholesterol</td>
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<td>1.63</td>
<td>0.50</td>
<td>NS</td>
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<td>LDL cholesterol</td>
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<td>Glucose</td>
<td>MED</td>
<td>72</td>
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<td>0.60</td>
<td>NS</td>
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<td>LFAT</td>
<td>63</td>
<td>5.22</td>
<td>0.60</td>
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</tr>
<tr>
<td>Insulin</td>
<td>MED</td>
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<td>7.34</td>
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<tr>
<td></td>
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<td>63</td>
<td>2.48</td>
<td>1.85</td>
<td>NS</td>
</tr>
</tbody>
</table>

MED, Mediterranean diet; LFAT, low-fat American Heart Association-type diet; ApoB48, apolipoprotein B48; IAUC, incremental area under curve. Subjects in MED diet (n 72) and LFAT diet (n 63) groups at entry with thirty men and forty-two women, respectively, in MED group and twenty-two men and forty-one women in LFAT group. P values give significance between the two diet groups using ANOVA model.

### Table 2 Effects of MED (n 72) and LFAT (n 63) on LSD and postprandial ApoB48 and TAG

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>MED (month 0)</th>
<th>MED (month 3)</th>
<th>Time effect</th>
<th>MED (month 0)</th>
<th>MED (month 3)</th>
<th>Time effect</th>
<th>Time × diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting B48</td>
<td>0.22</td>
<td>0.17</td>
<td>0.26</td>
<td>0.23</td>
<td>NS</td>
<td>0.25</td>
<td>0.18</td>
</tr>
<tr>
<td>IAUC B48</td>
<td>0.39</td>
<td>0.39</td>
<td>0.10</td>
<td>0.32</td>
<td>&lt;0.001</td>
<td>0.27</td>
<td>0.25</td>
</tr>
<tr>
<td>Fasting TAG</td>
<td>1.58</td>
<td>0.97</td>
<td>1.43</td>
<td>0.99</td>
<td>0.028</td>
<td>1.44</td>
<td>0.77</td>
</tr>
<tr>
<td>IAUC TAG</td>
<td>0.58</td>
<td>0.76</td>
<td>0.56</td>
<td>0.61</td>
<td>NS</td>
<td>0.52</td>
<td>0.67</td>
</tr>
</tbody>
</table>

MED, Mediterranean diet; LFAT, low-fat American Heart Association-type diet; ApoB48, apolipoprotein B48; IAUC, incremental area under curve. Fasting and postprandial ApoB48 (mg/l) and TAG (mmol/l). Time effect was calculated using paired t test; time × diet significance was calculated using general linear models.
The waist-to-hip ratio (WHR) reflects abdominal obesity. After stratification of the cohort according to the presence or absence of this risk factor (WHR $>1.0$ in men and $>0.8$ in women), only women without this risk factor showed a significant lower fasting TAG at entry ($0.99$ (SD $0.097$) v. $1.57$ (SD $0.11$) mmol/l for WHR $<0.8$ and $>0.8$ respectively, $P<0.001$) and a significant variation after the dietary intervention regarding the TAG IAUC ($-0.04$ (SD $0.08$) v. $0.30$ (SD $0.09$) mmol/l for WHR $<0.8$ and $>0.8$ respectively, $P=0.016$) after adjustment for age and menopausal status. No statistical difference was observed for ApoB48 parameters.

Regarding gender, we observed that fasting TAG at entry was significantly higher in men compared with women ($1.83$ (SD $0.15$) v. $1.31$ (SD $0.08$) mmol/l, $P=0.001$), but no other difference was observed between genders regarding TAG AUC/IAUC and ApoB48 parameters at entry and after the dietary intervention.

**Discussion**

We have previously reported the lowering effects of the 3-month dietary interventions on fasting total and LDL cholesterol, TAG, glucose and insulin levels in the Medi-RIVAGE cohort$^{(18)}$. In the present paper, we aimed to determine the effect of two global diets on postprandial parameters in 135 volunteers. We clearly show herein the favourable effects of the MED diet, and to a lesser extent of the LFAT diet, on relevant postprandial parameters such as TAG and ApoB48.

We observed that the MED diet, and to a lesser extent the low-fat diet, markedly blunted the response to the test meal by significantly reducing the TAG and ApoB48 levels after 5 h (Fig. 1). This time point is of clear importance because it reflects the second part of the postprandial event, that is, the clearance phase of TRL particles. It has been repeatedly shown that an exaggerated delayed postprandial TAG and TRL excursion is associated with an increased CVD risk$^{(1,13–15,24)}$. This was the case at entry when the subjects involved exhibited a noticeable clearance defect with elevated 5 h TAG levels. In a recent meta-analysis of about hundred trials, it was indeed found that the 4 h time point is the best suited to detect abnormal postprandial lipaemia$^{(25)}$. We observed that the TAG level 5 h postprandially was reduced by 13.7% after the MED diet and 12.5% after the LFAT diet. Considering the available evidence associating elevated/delayed postprandial or non-fasting TAG and the risk for CHD in both men and women, the present data support the new idea...
that an MED diet markedly reduces the postprandial lipaemia risk factor and, thus, can be protective against CVD. A previous study comparing European with northern or southern dietary patterns reported a difference in postprandial TAG kinetics in the two groups(26). This is in line with numerous other studies reporting a reduced cardiovascular mortality and events in subjects relying on a traditional MED diet(27,28).

It was also very interesting to observe that at the same time (i.e. 5h postprandially), the ApoB48 level was markedly reduced after the MED diet and to a lesser extent the LFAT diet. Therefore, the blunting of the ApoB48 level after 2.5h as well as the overall 5h postprandial ApoB48 accumulation under the MED diet (−74.4%) is a remarkable observation. The LFAT diet only reduced ApoB48 AUC by 41.7%. Because ApoB48 is a specific marker of intestinally derived chylomicrons in humans, this indicates that an MED diet markedly limits the number of chylomicron particles in the circulation postprandially. This could account for native chylomicrons as secreted by the small intestine after meal fat digestion and/or clearance of chylomicrons remnants that are quickly generated upon endovascular lipolysis of native chylomicrons. Although no clear explanations are available regarding chylomicron remnant clearance, the reduction of insulinaemia and HOMA score reported in the subjects on the MED diet(18) can be associated with a decrease in chylomicron ApoB48 synthesis, as demonstrated by others(29).

Taken together, the markedly reduced late accumulation of both TAG and ApoB48 levels elicited by the MED diet supports its beneficial effect on lipid metabolism. It could also play a role in explaining the observed inverse relationship between obesity, especially central obesity, and adherence to a traditional MED diet as repeatedly reported(30,31). Indeed, filling adipocytes with TAG is a postprandial phenomenon wherein TRL TAG are released.

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**Fig. 2** Impact of fasting TAG (■, TAG > 1.7 mmol/l; Δ, TAG < 1.7 mmol/l; a) or BMI (■, BMI > 25 kg/m²; Δ, BMI < 25 kg/m²; b) at entry on postprandial TAG (left) and postprandial apolipoprotein B48 (ApoB48; right) responses to a 3-month Mediterranean-type diet (——, at entry; ·····, after 3 months). Values are expressed as mean and SEM.
from TRL and taken up by adipocytes while hyperinsulinaemia block the intracellular TAG hydrolysis. In fact, there are number of foods and nutrients (fatty acids, carbohydrate, fibres) that could play a role in the global beneficial effect of the MED diet as observed on postprandial lipaemia (1,5–7). This remains to be further documented.

Obesity is known to promote exaggerated postprandial lipaemia (2,22–34) and a positive relationship between BMI and plasma TAG levels has been observed. Most subjects included in the Medi-RIVAGE cohort were overweight (70%) and lost weight (mean = -3±4 kg) after the 3-month diet. We found (Fig. 2) that whatever the subject’s BMI at entry (< or > 25 kg/m²), the 3-month regimen promoted a higher clearance of ApoB48-containing particles based on the reduced ApoB48 IAUC or AUC. Thus, the overweight/obese as well as the lean subjects benefited from the dietary change accompanied by a small weight loss.

Regarding the impact of fasting TAG on the subsequent postprandial response (Fig. 2), we observed that those subjects with abnormally high fasting TAG have an exaggerated postprandial TAG response in agreement with the literature (3,5,8). It is noteworthy that the lowering effect of the 3-month diet was comparable in subjects with normal or elevated TAG.

In conclusion, we report herein for the first time the efficiency of an MED in improving postprandial lipaemia, a recently acknowledged CVD risk, in men and women at moderate cardiovascular risk.

Acknowledgements

The authors declare that they have no conflict of interest. All authors conceived and designed the study. C.D. and D.L. analysed, interpreted the data and wrote the paper. The authors thank Claudine Antona for her technical help.

References


Low consumption of fruit and vegetables and risk of chronic disease: a review of the epidemiological evidence and temporal trends among Spanish graduates

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Abstract

Objective: To review the evidence on the association between fruit and vegetable (F&V) consumption and risk of chronic disease, and to assess trends in the prevalence of low F&V consumption.

Design: Systematic review and cross-sectional analyses of a Mediterranean cohort.

Setting: The Seguimiento University of Navarra (SUN) project (Spanish dynamic cohort of graduates).

Subjects: A systematic review of prospective studies aimed to assess the relationship between fruit and/or vegetables consumption and chronic disease incidence was conducted. We also assessed 18,457 university graduates (59–64% women; mean age = 39 (±12) years) enrolled in a dynamic cohort with permanently open recruitment. Baseline data were collected between 1999 and 2010 using a validated 136-item FFQ. Four definitions for low F&V consumption were used (<400 g/d, <200 g/4184 kJ (1000 kcal) per d, ≤2 servings/d and ≤1 serving/d). Multivariate-adjusted cross-sectional associations between the prevalence of low F&V consumption and the year of recruitment were estimated.

Results: The systematic review found that a high F&V consumption is inversely associated with CVD incidence and mortality. This association is not so clear for cancer. Inconsistent findings have been reported for diabetes. In all, 13% of participants in the SUN cohort did not meet the goal of consuming at least 400 g/d of F&V and 2–1% of them did not reach >1 serving/d. Between 1999 and 2010 the consumption of F&V significantly increased.

Conclusions: Even among health-conscious university graduates, low F&V consumption is fairly prevalent. Although the temporal trends suggest an improvement, preventive strategies addressed to increase F&V consumption are needed.

Methods

Literature review

We searched electronic databases (1980–2009) for published prospective studies that assessed the relationship between the consumption of fruit and/or vegetables and the incidence or mortality from CVD, cancer or diabetes and included a quantitative assessment of F&V intake.

The Seguimiento University of Navarra prospective cohort

The Seguimiento University of Navarra (SUN) cohort is a Mediterranean epidemiological study with a prospective design. All participants are university graduates. The SUN cohort is patterned after the models of the Nurses’ Health...
Study or the Health Professionals Follow-up Study, which are composed only of highly educated participants, thus ensuring a more complete follow-up and a better quality of self-reported information. A major difference of the SUN cohort is that the recruitment is permanently open, because a dynamic design has been chosen for this cohort. New participants have been admitted every year since 1999, thus allowing for estimation of temporal trends in lifestyle and food habits of recruited participants. Extensive information about the methods, objectives and design of this cohort has been published previously\(^{(6-10)}\). Information on exposure was gathered by mailed questionnaires at baseline. Outcomes were assessed through follow-up questionnaires collected biennially.

A previously validated and extensively used 136-item FFQ\(^{(9-11)}\) was collected at baseline together with a wide array of information about sociodemographic characteristics, anthropometric variables, lifestyles and health-related habits\(^{(8)}\). The baseline questionnaire included 554 items\(^{(50)}\). The validity of self-reported information has been assessed in specific studies using subsamples of the SUN cohort\(^{(12-15)}\).

Up to May 2010, 20 426 participants had been admitted to the SUN cohort and had completed their baseline evaluation. From them, we excluded participants who reported very low or very high values for total energy intake according to predefined limits\(^{(16)}\), because they were more likely to have failed to properly complete the questionnaire (<3547 kJ (<800 kcal)/d in men or <2092 kJ (<500 kcal)/d in women or >16736 kJ (>4000 kcal)/d in men or >14644 kJ (>3500 kcal)/d in women) \(^{(n 1969)}\). Therefore, 18 457 participants were included in the following analyses.

The present study was approved by the Institutional Review Board of the University of Navarra. Voluntary completion of the first questionnaire was considered to imply informed consent.

**Definition of low fruit and vegetable consumption**

The FFQ included sixteen items for fruits and eleven items for vegetables (plus potatoes and French fries, which were excluded). Each item in the FFQ included a typical portion size\(^{(9-11)}\). Daily food consumption was estimated by multiplying the portion size by the consumption frequency, for each food item (nine options ranging from never or almost never to six or more times per day). A team of trained dietitians updated the nutrient databank using the latest available information included in food composition tables for Spain. We used three alternative operative definitions for low F&V consumption: (i) \(\leq 400\) g/d; (ii) \(\leq 200\) g/4184 kJ (1000 kcal)/d; and (iii) \(\leq 2\) servings/d. The operative definition of very low F&V consumption was \(\leq 1\) serving/d.

**Statistical methods**

Differences in sociodemographic or behavioural characteristics of participants according to the period of recruitment were estimated with one-way ANOVA or Pearson’s \(\chi^2\).

Logistic regression models were fit with each of the definitions for low or very low F&V consumption as outcome. Potential confounders included in all models were age, sex and the higher educational status achieved by the participant (four levels: only college, postgraduate school, masters degree, doctoral degree). Tests of linear trend were conducted using the likelihood ratio test with the calendar year of entering the cohort introduced as a continuous independent variable and adjusting for the potential confounders. All these analyses were repeated after stratifying by sex. In sensitivity analyses, we also additionally adjusted for baseline BMI (continuous), marital status (married/others), current smoking at baseline, leisure-time physical activity (METs-h/week, continuous) and alcohol consumption (g/d, continuous).

All \(P\) values presented are two-tailed: \(P<0.05\) was considered statistically significant. The Statistical Package for the Social Sciences software package for Windows version 15.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analyses.

**Results**

**Literature review**

Table 1 shows the results of some recently published meta-analyses on F&V consumption and the risk of CVD. All of them included only prospective cohort studies. A pooled analysis of eleven cohort studies conducted by Pereira et al.\(^{(177)}\) found that fruit fibre was inversely associated with the incidence of CHD events and also with CHD mortality. Null associations were found for vegetable fibre. Subsequently, two meta-analyses on F&V intake and CHD were published\(^{(18,19)}\). The meta-analysis conducted by Dauchet et al.\(^{(18)}\) found stronger inverse associations for fruit than for vegetable intake. The meta-analysis by He et al.\(^{(20)}\) showed an inverse dose–response trend.

In addition to the traditional narrative review by Ness and Powles\(^{(20)}\), two recent meta-analyses of fruit or vegetable consumption and stroke risk have been published\(^{(21,22)}\). The meta-analysis by Dauchet\(^{(21)}\) showed that stroke risk was reduced by 11% for each additional serving/d of fruit and by a non-significant 3% for each additional serving/d of vegetables. The estimates of relative risk in the meta-analysis by He et al.\(^{(22)}\) were 0·72 (95% CI 0·66, 0·79) for fruits and 0·81 (95% CI 0·72, 0·90) for vegetables for the comparison between the highest (>5 servings/d) and the lowest (<3 servings/d) intake categories. There were no statistically significant differences in the risk of stroke when the intermediate category of vegetable consumption was compared with the lowest category of consumption. Some meta-analyses suggested the possibility of publication bias (some small studies with null results might have remained unpublished), but
Table 1  Recent meta-analyses of F&V consumption and the risk of CVD

<table>
<thead>
<tr>
<th>First author(ref.)</th>
<th>Year</th>
<th>Exposure</th>
<th>Outcome</th>
<th>Number of studies</th>
<th>Pooled RR</th>
<th>95% CI</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pereira(17)</td>
<td>2004</td>
<td>Fruit fibre (≥10 g/d)</td>
<td>CHD</td>
<td>11</td>
<td>0·84</td>
<td>0·70, 0·99</td>
<td>Pooled analysis; the inverse association was also apparent for cereal fibre and total fibre.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vegetable fibre (≥10 g/d)</td>
<td>CHD</td>
<td>11</td>
<td>1·00</td>
<td>0·88, 1·13</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fruit fibre (≥10 g/d)</td>
<td>Fatal CHD</td>
<td>10</td>
<td>0·70</td>
<td>0·55, 0·89</td>
<td>Evidence of publication bias.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vegetable fibre (≥10 g/d)</td>
<td>Fatal CHD</td>
<td>10</td>
<td>1·00</td>
<td>0·82, 1·23</td>
<td></td>
</tr>
<tr>
<td>Dauchet(18)</td>
<td>2006</td>
<td>Fruit (≥1 serving/d)</td>
<td>CHD</td>
<td>7</td>
<td>0·93</td>
<td>0·89, 0·98</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vegetable (≥1 serving/d)</td>
<td>CHD</td>
<td>8</td>
<td>0·95</td>
<td>0·92, 0·99</td>
<td>Evidence of publication bias.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fruit (≥1 serving/d)</td>
<td>Fatal CHD</td>
<td>10</td>
<td>0·70</td>
<td>0·55, 0·89</td>
<td>The inverse association for 3–5 servings of F&amp;V v. &lt;3 servings/d was borderline significant (P = 0·06).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vegetable (≥1 serving/d)</td>
<td>Fatal CHD</td>
<td>10</td>
<td>1·00</td>
<td>0·82, 1·23</td>
<td></td>
</tr>
<tr>
<td>He(19)</td>
<td>2007</td>
<td>F&amp;V (3–5 v. &lt;3 servings/d)</td>
<td>CHD</td>
<td>12</td>
<td>0·93</td>
<td>0·86, 1·00</td>
<td>Significant heterogeneity was found that also remained within many subgroup analyses. No evidence of substantial publication bias.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>F&amp;V (&gt;5 v. &lt;3 servings/d)</td>
<td>CHD</td>
<td>12</td>
<td>0·83</td>
<td>0·77, 0·90</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fruit (1–3 v. &lt;1·3 servings/d)</td>
<td>CHD</td>
<td>9</td>
<td>0·90</td>
<td>0·83, 0·98</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vegetables (1·7–3·0 v. &lt;1·7 servings/d)</td>
<td>CHD</td>
<td>9</td>
<td>0·92</td>
<td>0·87, 0·97</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>F&amp;V (&gt;3 v. &gt;1·7 servings/d)</td>
<td>CHD</td>
<td>9</td>
<td>0·84</td>
<td>0·76, 0·92</td>
<td></td>
</tr>
<tr>
<td>Dauchet(21)</td>
<td>2005</td>
<td>Fruit (≥1 serving/d)</td>
<td>Stroke</td>
<td>6</td>
<td>0·89</td>
<td>0·85, 0·93</td>
<td>Consistent results for &gt;5 v. &lt;3 servings/d.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vegetable (≥1 serving/d)</td>
<td>Stroke</td>
<td>4</td>
<td>0·97</td>
<td>0·92, 1·02</td>
<td>Some heterogeneity in subgroups for 3–5 v. &lt;3 servings/d.</td>
</tr>
<tr>
<td>He(22)</td>
<td>2007</td>
<td>F&amp;V (3–5 v. &lt;3 servings/d)</td>
<td>Stroke</td>
<td>8</td>
<td>0·89</td>
<td>0·83, 0·97</td>
<td>A small publication bias was suggested.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>F&amp;V (&gt;5 v. &lt;3 servings/d)</td>
<td>Stroke</td>
<td>12</td>
<td>0·74</td>
<td>0·69, 0·79</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fruit (2–3 v. 1 serving/d)</td>
<td>Stroke</td>
<td>6</td>
<td>0·52</td>
<td>0·48, 0·56</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fruit (≥3 v. ≥1 serving/d)</td>
<td>Stroke</td>
<td>6</td>
<td>0·72</td>
<td>0·66, 0·79</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vegetables (2–4 v. ≥1 serving/d)</td>
<td>Stroke</td>
<td>6</td>
<td>0·93</td>
<td>0·82, 1·06</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vegetables (&gt;4 v. ≥1 serving/d)</td>
<td>Stroke</td>
<td>6</td>
<td>0·81</td>
<td>0·72, 0·90</td>
<td></td>
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</table>

F&V, fruit and vegetables; ref., reference; RR, relative risk.
However, when the first definition of low F&V consumption (≤400 g/d) was used among men, the results only approached statistical significance ($P = 0.06$). The results were similar and remained statistically significant (data not shown) after additionally adjusting the models for baseline BMI, marital status, current smoking at baseline, leisure-time physical activity and alcohol consumption.

**Discussion**

The health promotion advice to select diets largely based on plant foods and to increase the consumption of F&V has not changed in the past 50 years (36). However, the actual global levels of F&V consumption are far from optimal (4,5,35). Whereas the potential benefits of F&V against cancer incidence are only weak and restricted to certain types of cancer, the results of large cohort studies consistently provide enough evidence to support strong benefits against CVD. In particular, fruit consumption is associated with relative reductions in risk higher than 25% for stroke and higher than 15% for CHD. The commonly proposed goal of consuming at least five portions (or at least 400 g) of vegetables and fruits per day (4,35) to reduce the risk of CHD or stroke is well supported by prospective epidemiological evidence (37). There is, however, a need for further evidence regarding diabetes prevention.

The more recent results of cohort studies, as compared with previous case–control studies, provide only weak evidence of the association of F&V consumption with reduced cancer risk. The inconsistencies between cohort and case–control studies on this issue may be related to recall and selection biases in case–control studies (33). A lower participation rate among controls than among cases is very likely in most case–control scenarios. Control subjects who agree to participate are typically very health conscious persons who tend to consume more F&V than those who did not choose to participate (32). This would lead to an apparent inverse association of F&V with cancer in case–control studies even if that association is not true. These false benefits might be further exaggerated if the groups of control and cases differentially recall or report their past diets due to the fact that many cases recently received a dismal diagnosis, whereas controls were not under this psychological impact.

On the other hand, an underestimation of a true inverse association between F&V consumption and the risk of chronic disease may happen in any epidemiological study because of imprecise dietary measurements, regression-dilution bias (38) or limited between-subjects variability in F&V consumption (35). Some degree of non-differential misclassification (measurement error) is unavoidable in nutritional epidemiology and may account for losing the ability to detect some real associations if they are not strong enough. However, in a large cohort study that
Table 3 Characteristics of graduates entering the SUN cohort according to the recruitment period (1999–2010)

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>% Women</td>
<td>60</td>
<td>57</td>
<td>57</td>
<td>67</td>
<td>51</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age (years)</td>
<td>37 13</td>
<td>37 11</td>
<td>42 12</td>
<td>40 12</td>
<td>39 14</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>% University degree</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Only college</td>
<td>35</td>
<td>28</td>
<td>39</td>
<td>16</td>
<td>19</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Masters degree</td>
<td>7</td>
<td>8</td>
<td>4</td>
<td>10</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>PhD</td>
<td>10</td>
<td>11</td>
<td>11</td>
<td>10</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>% Married</td>
<td>45</td>
<td>51</td>
<td>61</td>
<td>53</td>
<td>47</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>% Current smokers</td>
<td>25</td>
<td>25</td>
<td>18</td>
<td>18</td>
<td>17</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.3 3.4</td>
<td>23.3 3.5</td>
<td>24.2 3.5</td>
<td>23.6 3.8</td>
<td>23.7 3.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Physical activity (METS-h/week)</td>
<td>24</td>
<td>21</td>
<td>24</td>
<td>23</td>
<td>25</td>
<td>0.08</td>
</tr>
</tbody>
</table>

Table 4 Trends in the prevalence of low F&V consumption among graduates entering the SUN cohort (1999–2010)

<table>
<thead>
<tr>
<th>Low F&amp;V consumption</th>
<th>Very low consumption</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤400 g/d</td>
<td>≤200 g/1000 kcal/d</td>
</tr>
<tr>
<td></td>
<td>≤2 servings/d</td>
</tr>
<tr>
<td></td>
<td>≤1 serving/d</td>
</tr>
<tr>
<td>Adjusted*</td>
<td>Adjusted*</td>
</tr>
<tr>
<td></td>
<td>Adjusted*</td>
</tr>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>% Fruit and vegetables</td>
<td>2313</td>
<td>2117</td>
<td>2117</td>
<td>2117</td>
<td>2117</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

In summary, the benefits of F&V consumption for cardiovascular health are well substantiated by empirical epidemiological research. As CVD is the leading cause of global mortality, the promotion of F&V consumption represents a priority for global public health. In this context, the assessment of trends among highly educated subjects might be important because of the potential exemplary role that these sectors of the population with higher levels of education may play in achieving behavioural changes in society at large. Their lifestyles
tend to be eventually adopted by the rest of the society. The assessment of trends among university graduates is a uniquely appropriate setting to provide the knowledge to design adequate intervention strategies to enhance the adoption of healthy eating habits (40, 41).

In our Mediterranean cohort of university graduates (the SUN project), we found that the prevalence of adequate consumption of F&V has recently increased in Spanish university graduates, with a highly significant trend for improvement. This improvement might be related to better information and to successful public health efforts to promote a healthy diet in Spain. Sectors of the population with a higher educational level might be more easily reached by these efforts and might be more likely to adopt healthier diets.

Our study may have some potential limitations. A potential caveat is related to possible unmeasured confounders, as we only adjusted for age, sex and education. Some other baseline characteristics of recruited participants for this cohort might have changed during the assessment period (1999–2010). However, additional adjustment for potentially important known confounders (BMI, alcohol intake, smoking and physical activity) did not substantially change the results with respect to the analyses presented in the tables. In fully adjusted models, the P values for linear trend strongly suggested a decreasing trend for low F&V consumption during the assessment period (P = 0.001 for ≤400 g/d; P < 0.001 for ≤200 g/1841 kJ (1000 kcal)/d; P < 0.001 for ≤2 servings/d; P = 0.002 for ≤1 serving/d). Therefore, we do not consider residual confounding as the most likely explanation for our results.

Social desirability bias might have partially accounted for an apparent higher consumption of F&V. However, to be able to explain the observed temporal trend, this social desirability bias should have increased with calendar time. We do not have any evidence to support this possibility. The criteria for admitting participants in the cohort and the recruitment strategies remained essentially the same for the SUN cohort during the assessed period. However, the adjustment for other lifestyle and sociodemographic characteristics of recruited participants renders them more comparable. In addition, in the design of the SUN cohort, our aim was not to gather a ‘representative’ sample in the statistical sense of being a probability sample of a target population. We intended to obtain a fairly homogenous cohort with the ability to conduct valid within-cohort comparisons. Our goal was to select a study group for homogeneity with respect to important confounders, for highly cooperative behaviour and for availability of accurate information, as recommended in epidemiological research (42).

Taking into account these characteristics of our cohort, we acknowledge that our absolute estimates for the prevalence of low F&V consumption would be overly optimistic to be applied to the less-educated sectors of the population and that it would be inappropriate to generalise these findings to the general Spanish population. We can only conclude that in this well-educated Mediterranean cohort the adequacy of F&V consumption has improved in the past 10 years, but the room for improvement is still large.

Acknowledgements

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References


Wholegrain cereals and bread: a duet of the Mediterranean diet for the prevention of chronic diseases

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Abstract

Objective: The promotion of healthy lifestyles is one of the major goals of governments and international agencies all over the world. Wholegrain cereals are rich in nutrients and many phytochemical compounds, with recognised benefits for health, including dietary fibre, a number of phenolic compounds, lignans, vitamins and minerals and other bioactive components. The aim of the present work is to review the fundamental studies that support the consumption of wholegrain cereals and bread to prevent chronic diseases.

Design: Descriptive review considering human studies.

Setting and subjects: Subjects included in randomised intervention trials and cohort studies from different countries published up to 2010.

Results: Several studies show consistently that subjects who ingest three or more portions of foods per day based on wholegrain cereals have a 20–30% lower risk of CVD than subjects who ingest low quantities of cereals. This level of protection is not observed with the ingestion of refined cereals, these being even higher than with the intake of fruit and vegetables. Likewise, high intake of wholegrain cereals and their products, such as whole-wheat bread, is associated with a 20–30% reduction in the risk of type 2 diabetes. Finally, protection against the risk of colorectal cancer and polyps, other cancers of the digestive tract, cancers related to hormones and pancreatic cancer has been associated with the regular consumption of wholegrain cereals and derived products.

Conclusions: The regular intake of wholegrain cereals can contribute to reduction of risk factors related to non-communicable chronic diseases.

Keywords

Bread

Cereals

Chronic disease

Grains

Diet

Mediterranean

Foods based on wholegrain cereals, including bread, play an important part in health and well-being. Thus, research consistently indicates that the regular consumption of wholegrain cereals reduces the risk of CVD, type 2 diabetes mellitus (DM2) and certain types of cancer, as well as several gastrointestinal pathologies (1–5).

Wholegrain cereals, those containing all the parts of the grain (bran, germ and endosperm), are rich in nutrients and phytochemical compounds, with recognised benefits for health, such as dietary fibre, antioxidants, including phenolic compounds, phytoestrogens including lignans, vitamins and minerals. In fact, the advantages of wholegrain cereals are related not only to greater fibre content but also to higher content of essential fatty acids, vitamin-B complex, vitamin E, Fe, K, Mg, Zn, Se and other bioactive components (2,6).

Most of the substances that promote health in wholegrain cereals are found in the germ and bran. It is believed that these compounds exert an additive, synergetic effect on health when consumed together (7). In particular, cereals contain various non-amylaceous polysaccharides, namely cellulose, pentosans and β-glucans. These compounds are hydrolysed by endogenous digestive enzymes and, being cell-wall constituents, abound in the external parts of the grain. Therefore, their content is greater in wholegrain or less processed flours.

The major compound in bread is starch. Starch is classified into rapidly digestible starch (RDS), slowly digestible starch (SDS) and resistant starch (RS) (8) according to the rate of glucose release and its absorption in the gastrointestinal tract. SDS, which leads to a slower entry of glucose into the blood stream and a lower glycaemic response, is digested completely in the small intestine at a lower rate as compared to RDS, whereas RS is the starch portion that cannot be digested in the small intestine, but is fermented in the large intestine. Experimentally, each starch fraction can be quantified on the
basis of the \textit{in vitro} Englyst method\textsuperscript{(8,9)}: starch digested within 20 min belongs to RDS, whereas SDS represents the digested starch between 20 and 120 min, and the remaining fraction is RS. Bread has a variable proportion of SDS and of RS, according to the variety of grain. In white breads, the proportion of RS is high, reaching 5.6–8.1\% due to the incomplete gelatinisation of the starch in the crust. Starch in bread tends to retrograde, so that from the moment the bread is made, the portion of resistant starch increases over time, this being more pronounced in pre-cooked breads\textsuperscript{(10)}.

Some varieties of French bread (the traditional baguette) have lower insulinaemic index in healthy subjects, and lower glycaemic index (GI) in type 2 diabetic subjects, than that of the other varieties; these results might be due to bread processing difference rather than fibre content\textsuperscript{(11)}.

Soluble fibres present in bread are partially hydrolysed and used as a substrate by the intestinal microbiota, augmenting the mass of colon bacteria and the synthesis of volatile fatty acids – acetic, propionic and butyric acids – as well as gases such as nitrogen and methane. These fatty acids can be used by the colonocyte as an energy source. Its ingestion in the appropriate quantity is associated with lower levels of plasma cholesterol and TAG as well as a reduced risk of coronary disease\textsuperscript{(10,11)}. Subjects who relate the consumption of wholegrain cereals with a reduced risk of coronary disease\textsuperscript{(18)}.

There is ample epidemiological and clinical evidence that relates the consumption of wholegrain cereals with a reduced risk of coronary disease\textsuperscript{(10,11)}: Subjects who ingest three or more rations of foods per day based on integral cereals have a 20–30\% lower risk than subjects who ingest low quantities of cereals, and this level of protection is not observed with the ingestion of refined cereals, these being even higher than with the intake of fruits and vegetables\textsuperscript{(1,6,12–16)}.

Morris et al.\textsuperscript{(17)}, after studying 337 subjects for 10–20 years, concluded that the reduction in the risk of CVD was attributable to a greater consumption of cereal fibre, whereas other sources of soluble fibre such as pectin and guar gum did not present the same effect. In addition, an analysis of several cohort studies on dietary fibre and coronary disease risk showed that the consumption of dietary fibre from cereals and fruits was inversely associated with the risk of coronary disease\textsuperscript{(180)}. Other large surveys have found a moderate association between the intake of wholegrain cereal and the lowering of CVD risk. In an extensive prospective health study in Iowa (USA), 34 492 postmenopausal women aged 55–69 years and free of CVD were tracked to determine the occurrence of mortality by CVD (n 387) from 1986 to 1994\textsuperscript{(15)}. The lowering of the risk in the highest quintile of wholegrain cereal intake was controlled for more than fifteen variables and was not explained by the adjustment of the consumption of dietary fibre. This suggests that other components of wholegrain cereal that are not dietary fibre may reduce the risk of CVD.

A Finnish study of 21 930 men who smoked (50–69 years of age) was monitored for 6–1 years\textsuperscript{(16)}. The lower risk of CVD was associated with the increase in the intake of products containing rye. Rimm et al.\textsuperscript{(19)} examined the association between cereal consumption and the risk of myocardial infarction (MI) in 43 757 health professionals in the USA, aged 40–75 years. Cereal fibre was the factor most strongly associated with a reduced risk of MI, with a 0.71 decline in the risk per 10 g increase in the ingestion of cereal fibre.

The Nurses’ Health Study, an extensive prospective cohort study tracking women in the USA for 10 years, was also used to examine the relationship between cereal consumption and cardiovascular risk\textsuperscript{(13)}. A total of 68 782 women aged between 37 and 64 years without prior diagnosis of angina, MI, apoplexy, cancer, hypercholesterolaemia or diabetes were examined at the beginning of the study. The authors controlled for age, cardiovascular risk factors, dietary factors and the use of multivitamin supplements. For an increase of 10 g/d in the total consumption of fibre, the risk of CVD was 0.81 (95 % CI 0.66, 0.99). Among the different sources of dietary fibre (cereal, vegetables and fruit), only cereal fibre proved to be strongly associated with a lower risk of CVD.

As wholegrain cereals are a major source of dietary fibre in many countries, it is difficult to separate the protection of dietary fibre from that of wholegrain cereals. In a study tracking health professionals, Jensen et al.\textsuperscript{(6)} examined the consumption of wholegrain cereals, bran and germ in relation to the risk of coronary disease from the data on food consumption frequency. Added germ was not associated with CVD risk, leading the authors to conclude that the study supported the association of the benefits described between the consumption of wholegrain cereals and the reduction of CVD, suggesting that the bran of wholegrain cereal could be a key factor in this relation. The regular consumption of foods that include wholegrain cereals appears to protect against CVD. Van Dam et al.\textsuperscript{(20)} reported that the consumption of refined diets that did not include wholegrain cereals was associated with higher levels of blood cholesterol and lower consumption of micronutrients. Prudent eating habits, including the intake of wholegrain cereals, was associated with a lower level of reactive protein C and endothelial dysfunction, an early step in the development of atherosclerosis\textsuperscript{(21)}. The consumption of foods based on wholegrain cereals was also associated with lower reactive protein-C concentrations in the Nurses’ Health Study\textsuperscript{(22)}. In addition, a prospective
in the blood sugar response, in 1981 the concept of GI was introduced. For this index to be established, healthy volunteers who had fasted for the night had their glycaemia levels measured after ingesting a set quantity of the food in question (the quantity of food was adjusted to provide 50 g of glycaemic or biologically available carbohydrate). The glycaemia was measured in previously established time intervals up to a maximum of 120 min. These measurements were compared with those of a reference product such as glucose (50 g), to which an index of 100 was arbitrarily assigned. The quotient between the areas of the respective curves was called the GI. Initially, the reference product for the determination of the GI was white bread, but the bread generated a variable glycaemic curve, depending on its composition and preparation, especially the variable content of RS. In fact, traditional white breads can vary their GI with respect to glucose from 74 % to 100 %.

The concept of GI appears to be a useful tool for glycaemic tracking in diabetic patients. In addition, diets with a low GI have the capacity to reduce the secretion of insulin and diminish blood lipid concentrations, as demonstrated in several clinical tests. Diabetic patients who ingested bread having a low GI and made with the addition of fibre from wholegrain cereals registered a reduction in the blood glucose values as well as in the cholesterol and TAG levels, compared with those who followed a diet with a high GI. However, the GI did not take into account the quantity of carbohydrates consumed, an important determinant of the glycaemic response. For example, most fruits have a high GI and would appear not to be a good choice as part of a diet with a low GI. Nevertheless, fruit usually have a low content of carbohydrates, and therefore their glycaemic effect is minimal.

Another important concept is that of the glycaemic equivalent (GGE) of a food. The GGE refers to the relative tendency of a given quantity of food consumed at a single time, such as a portion, to induce a postprandial glycaemic response. The GGE is measured directly by the quantity of reference glucose necessary to give the same glycaemic response as a relevant quantity of a given food.

Bread belongs to a group of foods that increase the insulin response, as its main carbohydrate is gelatinised starch, easily digested by human amylases, and therefore usually gives rise to high glycaemic responses. Wholegrain breads have a lower GL than do corresponding white breads and therefore offer better control for postprandial glycaemia.

Breads made with wholegrain cereals, for reasons discussed for the whole grains in terms of their content of fibre and resistant starches, present lower GI values. The incorporation of soluble fibre in great quantities (bread made of oat bran) augments viscosity of the bolus, limits
Wholegrain cereals, bread and chronic diseases

the access of amylotic enzymes and diminishes the diffusion of the glucose through the mucosa, giving these products a far lower GI. In addition, rye breads made with sour dough, due to the presence of organic acids, appear to diminish postprandial glycaemia and insulinemia. In addition, flatbread has a more compact structure and therefore slower digestion and a lower GI. For all the above, breads made traditionally with high fibre contents are useful for controlling postprandial glycaemia in subjects with intolerance to glucose and with diabetes.

It has been reported that the ingestion of fibre from wholegrain cereals is inversely related to DM2. In a long-term study of almost 90,000 women(33), and in a similar study of nearly 45,000 men(32), it was found that those who consumed more cereal fibre had an approximately 30% lower risk of developing DM2, compared with those with lower consumption. In addition, in the study on women's health in Iowa (USA), it was found that the consumption of dietary fibre and wholegrain cereal protected against DM2(35). In another study, individuals who consumed mainly refined cereals and little wholegrain cereal had a 57% greater risk of DM2 than those who consumed higher quantities of wholegrain cereals(34). In the Study Tracking Health Professionals, one part monitoring 42,986 men consuming approximately three rations of wholegrain cereal per day associated this consumption with a 37% lower risk of DM2(35). In addition, when the data were brought together for prospective cohort studies, the consumption of wholegrain cereal was found to reduce the relative risk of DM2 by 30%(36,37).

Pereira et al.(38), studying hyperinsulinaemic subjects who were overweight or obese, tested the hypothesis that the consumption of wholegrain cereal improves the tissue sensibility of the insulin in overweight and obese adults. Eleven adults followed two diets, each for 6 weeks. The two diets were identical except that in one of them the products of refined cereal, mainly bread, were replaced by wholegrain products. The insulin during fasting proved 10% lower during the diet with the integral cereal. Thus, the authors concluded that sensitivity to insulin may be an important mechanism by which foods based on whole grains reduce the risk of DM2 and cardiac disease.

Juntunen et al.(39), evaluating plasma glucose and the insulin response after the ingestion of cereal products. Several subjects consumed different cereal products: bread with wholegrain rye, wholegrain rye bread with β-glucan concentrate from oats, pasta made of dark Durum wheat and wheat bread made from white wheat flour. The glucose responses and the index of gastric emptying after the consumption of the two rye breads and the pasta did not differ from those after the consumption of white wheat bread. However, the insulin, the glucose-dependent insulino-tropic polypeptide and the peptide analogous to type-1 glucagon were lower after the consumption of the rye breads and dark pasta than after the consumption of white wheat bread. Thus, the postprandial insulin responses to cereal products may be determined by the form of the food and the botanical structure more than by the quantity of fibre or the type of cereal in the food. McKeown et al.(40) have reported that the consumption of wholegrain cereal in the Framingham Children's Study is inversely associated with the index of body mass and insulin during fasting.

Juntunen et al.(41), studying postmenopausal women who consumed high-fibre rye bread and white wheat bread, measured the glucose and insulin metabolism. The acute response of insulin significantly augmented more during the period of consuming rye bread than during that of consuming white wheat bread. This suggests that high-fibre rye bread favours the secretion of insulin. In another study, foods based on rye and wheat was offered to middle-aged overweight men(42). The men consumed cereals low in fibre that provided 5 g of dietary fibre in the diet of refined cereals and 18 g of fibre in the diet of the wholegrain cereal, whether high in rye or wheat. All this was additional to a basal diet that contained 14 g of fibre. The postprandial insulin fell 46–49% and postprandial glucose dipped 16–19% after the consumption of the wholegrain diet.

Qi et al.(43), examining whether the ingestion of wholegrain cereals and dietary fibre was associated with inflammatory indicators among 902 diabetic women in the Nurses' Health Study, suggested that the wholegrain cereals and a diet with a low GI could reduce systemic inflammation among women with DM2. In addition, Jensen et al.(24) found in 938 healthy men and women that the consumption of wholegrain cereal was inversely related more strongly to the plasma markers of glycaemic control (insulin during fasting, glycosylated Hb A1c, peptide C and leptin).

Cancer

The consumption of wholegrain cereals has in several studies been associated with a reduced risk of some types of gastrointestinal cancer. In a meta-analysis on the consumption of wholegrain cereals and cancer that analysed all the studies conducted up to 1998 indicated protection against the risk of colorectal cancer and polyps, other cancers of the digestive tract, cancers related to hormones and pancreatic cancer(44). In addition, a systematic review of case-control studies carried out using a common protocol in northern Italy between 1983 and 1996 indicated that a greater frequency in the consumption of wholegrain cereal is associated with a lower risk of cancer(45).

Wholegrain cereal is consumed primarily as wholegrain bread and some as wholegrain pasta. Cohort studies have shown a lower risk for specific cancers, such as colorectal in women(46), stomach(47), mouth/throat and the upper digestive tract(48) and endometrium(49).

A review of forty studies on gastrointestinal cancer has found a reduction in cancer risk from 21% to 43% in subjects with high consumption of wholegrain cereals
compared to those with low consumption\(^{(2)}\). In addition, in more recent cohort studies, the intake of wholegrain cereals has been associated with a moderate reduction in colorectal cancer risk\(^{(50,51)}\). Furthermore, in a recent meta-analysis, it was shown that the intake of products having a low GI and GL, including products based on cereals with a high fibre content, was associated with a lower risk of colorectal, pancreatic, endometrium and breast cancer\(^{(52)}\). However, a recent study published jointly between the World Cancer Research Fund and the Institute for Cancer Research on the relative risk of different types of cancer in relation to different lifestyles found no association between the specific consumption of cereals and colorectal cancer\(^{(53)}\). On the other hand, another meta-analysis indicated that the consumption of foods with a low GI or GL was not associated with a reduction in colorectal or pancreatic cancer\(^{(54)}\). However, the studies that examine the association of the consumption of cereals with hormone-dependent cancers are very limited.

Several mechanisms have been proposed for the action of cereals in relation to cancer. The fibre and certain resistant starches found in cereals and their products, as in the case of bread, ferment in the colon and contribute to reduction of the intestinal transit and improvement of intestinal health. Cereals also contain antioxidants that can protect against oxidative damage, which can play a fundamental role in the development of cancer. Other bioactive compounds in wholegrain cereals may affect the hormonal levels and probably the hormone-dependent cancers. The potential mechanisms include shifts in the plasma-glucose values and weight loss\(^{(2)}\). In addition, the lowering of insulin levels by wholegrain cereals can be an indirect way by which cancer risk is reduced, given that several epidemiological studies have suggested that higher levels of insulin are associated with a greater risk of colon, breast and possibly other types of cancer.

Dietary factors, such as the intake of fibre, vegetables, fruits, antioxidants, vitamin B\(_6\) and phytoestrogen, as well as lifestyle factors such as exercise, smoking and alcohol intake, which are controlled for in most epidemiological studies, do not explain the apparent protective effect of wholegrain cereals against cancer, again suggesting that it is the complete package of the wholegrain cereal that is effective\(^{(11)}\).

Various theories have been proposed to explain the protective effects of wholegrain cereals. Thus, the increase in the faecal mass and the decrease in transit time give less opportunity to the faecal mutagens to interact with the intestinal epithelium. Secondarily, it is thought that the sequestration by fibre of the bile acids, which promote cell proliferation, can diminish the frequency of mutations. Wholegrain cereals also contain anti-nutrients, such as protease inhibitors, phytic acid, phenolic compounds and saponins, which until recently were thought to have only a negative nutritional consequence. Some of these anti-nutrient compounds may act as cancer inhibitors by preventing the formation of carcinogens and blocking the interaction of carcinogens with cells. Other potential mechanisms of wholegrain cereals to lower cancer risk include effects of lignans. Lignans are compounds that have a 2,3-dibenzylbutane structure, and there are minority constituents of many plants that form construction blocks to create lignin in the cell wall of the plant. Owing the relation of the excretion of lignans with fibre consumption, it is assumed that vegetable lignans are contained in external layers of the grain. Concentrated sources of lignans include whole wheat, whole oats and whole rye. Seeds are also a concentrated source of lignans, including flax seeds (the most concentrated source), pumpkin seeds, caraway seeds and sunflower seeds\(^{(2)}\).

Cereals and other foods rich in fibre increase the urinary excretion of lignans, an indirect measure of the lignan content in food\(^{(55,56)}\). In addition, they are positively related to the consumption of products based on wholegrain cereals\(^{(57)}\). Similar results were found in a study in the USA\(^{(58)}\) in which the subjects consumed either wholegrain-based foods or refined-grain foods (especially bread) for 6 weeks. Most of the increase in serum enterolactone occurred when the subjects consumed the diet based on wholegrain bread. Serum enterolactone has been associated not only with a decline in the risk of cancer, but also with a lower CVD related to all the causes of mortality in middle-aged Finnish men\(^{(59)}\).

**Gastrointestinal pathologies**

The components of wholegrain cereals, including fibre, RS and oligosaccharides, play a fundamental role in the maintenance of intestinal homeostasis. Several studies have suggested that the dietary fibre from grains and whole cereals augments the weight of the stool and absorb water, and the partial fermentation of the fibre in the colon as well as of the oligosaccharides promotes the growth of beneficial bacteria in the faeces\(^{(2,27)}\). RS is not digested in the same way as ordinary starch, passing through the intestine to the colon, where it is fermented, and behaving in all senses like soluble dietary fibre. The main content of faecal residue facilitates intestinal peristalsis and defecation. All this helps alleviate symptoms of constipation and contributes to lowering the risk of developing diverticulosis and diverticulitis\(^{(60)}\).

McIntosh et al\(^{(42)}\) offered foods based on rye and wheat to overweight middle-aged men and measured markers of intestinal health. The food based on rye and wheat with high fibre content increased the faecal evacuation by 33–36% and diminished the activity of faecal \(\beta\)-glucuronidase by 29%.

**Conclusion**

The regular intake of wholegrain cereals may contribute to reduction of the risk factors related to non-communicable
chronic diseases, particularly those of CVD, DM2 and certain types of cancer, as well as several gastrointestinal pathologies.

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2322 A Gil et al.


Olive oil, an essential component of the Mediterranean diet, and breast cancer

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Abstract

Objective: The Mediterranean diet has been related to a lower risk of some chronic diseases, including cancer. We aim to gain insight into the effects of the main source of fat of this diet on breast cancer, the most common type of malignancy in women.

Design: Data from sixteen experimental series analysing the effects of dietary lipids on mammary carcinogenesis in an animal model, in the context of the international literature on the Mediterranean diet, olive oil and breast cancer risk.

Setting: Experimental and human data on the effects of olive oil and Mediterranean diet on breast cancer.

Subjects: An animal model of induced breast cancer and other human and experimental studies in the literature.

Results: Diets rich in extra virgin olive oil (EVOO) exert a negative modulatory effect on experimental breast cancer to a weak promoting effect, much lower than that obtained with a high-corn oil diet. EVOO confers to the mammary adenocarcinomas a clinical behaviour and morphological features compatible with low tumour aggressiveness. This differential effect, in relation to other dietary lipids, may be related to a lower effect on body weight and sexual maturation. In addition, EVOO induced different molecular changes in tumours, such as in the composition of cell membranes, activity of signalling proteins and gene expression. All these modifications could induce lower proliferation, higher apoptosis and lower DNA damage. These results, together with the favourable effect of olive oil reported in the literature when it is consumed in moderate quantities, suggest a beneficial influence of EVOO on breast cancer risk.

Conclusions: Consumption of EVOO in moderate quantities and throughout the lifetime appears to be a healthy choice and may favourably influence breast cancer risk.

Keywords
Mediterranean diet
Olive oil
Breast cancer

The Mediterranean diet includes a variety of food patterns from different regions of the Mediterranean, and it is characterised by the consumption of an abundance of plant foods (fruit, vegetables, cereals, grains and nuts), dairy products, fish and olive oil as the principal source of fat. This diet has been traditionally linked to the longevity of populations from the Mediterranean countries, and it has been associated with a significant improvement in health status, as seen by a reduction in overall mortality, mortality from CVD, incidence of or mortality from cancer, and incidence of other chronic diseases. Olive oil, as a major energy source in the Mediterranean diet, is being investigated for its contribution to the reported health benefits of this diet. The main active components of olive oil include monounsaturated lipids (especially oleic acid), phenolic constituents (such as hydroxytyrosol, tyrosol and oleuropein) and squalene.

Cancer is a major health problem and a leading cause of mortality worldwide. The most commonly diagnosed cancers in men are lung (16-5% of the total), prostate (13-8%) and colorectum (10-0%), whereas in women they are breast (22-9%), colorectum (9-4%) and cervix uteri (8-8%). Geographical differences in cancer incidence rates indicate a role of environmental factors in the aetiology of this disease, nutrition being one of the most relevant. Epidemiological and especially experimental studies have found a relationship between dietary lipids and some cancers, such as breast and colorectum. Human data have also shown that women in the Mediterranean European countries have a lower incidence of breast cancer than women in other Western countries, and recent prospective studies have associated the Mediterranean diet with a reduction of breast cancer risk. In fact, it has been proposed that up to...
25% of colorectal, 15% of breast and 10% of prostate, pancreas and endometrial cancers could be prevented by adhering to this diet.

Thus, because strong evidence suggests that consuming the Mediterranean diet may have a protective effect, the aim of the present paper is to analyse the influence of the main source of fat of this diet (olive oil) on breast cancer and the mechanisms involved in this effect.

Effects of extra virgin olive oil on experimental breast cancer: clinical parameters

The relationship between dietetic factors, especially dietary lipids, and breast cancer has long been analyzed. Although experimental studies in animals have clearly shown an influence of dietary lipids on breast cancer, heterogeneous human epidemiological results have been reported. While cohort studies have generated conflicting results, case–control analyses and new prospective studies have shown that high fat intake is an important modulator of breast cancer risk. The main source of fat in the Mediterranean diet is olive oil, but the effects of this oil on breast cancer risk are not well elucidated. Moreover, although dietary habits in the Mediterranean countries have been traditionally linked to the high consumption of olive oil, in recent years the consumption of seed oils rich in n-6 PUFA – such as sunflower or corn oils – and other oils has increased. Thus, more scientific evidence is needed in relation to the effects of olive oil and high-n-6 PUFA oils on breast cancer. Owing to the difficulty in obtaining data with controlled variables in humans, animal models are widely used to gain insight into the influence of dietetic factors on health. For more than 20 years, we have been using the experimental model of breast cancer chemically induced with 7,12-dimethylbenz[a]anthracene (DMBA) in the female Sprague-Dawley rat. The suitability of this model for the possible application of the results in human breast cancer was previously validated, and it is used extensively in breast cancer studies. For the investigation of the different effects that olive oil and n-6 lipids may have on the initiation and promotion of mammary adenocarcinomas, a low-fat diet (with 3% of corn oil), a high-fat n-6 diet (with 20% of corn oil) and high-fat n-9 (with a 17% of extra virgin olive oil (EVOO) and 3% of corn oil) diets have been designed and validated.

To study the effects of dietary lipids on experimental breast cancer, several clinical parameters have been defined, in addition to suitable statistical analysis. In sixteen experimental series developed in our laboratory, results have always been conclusive: diets with a high content of n-6 PUFA (corn oil) exert a clear stimulating effect of the experimental mammary carcinogenesis in all the clinical parameters studied (Fig. 1). This stimulating influence has been mainly observed in the promotion stage of carcinogenesis, although an influence on the initiation stage cannot be ruled out. In contrast, the diet high in EVOO, with the same total content in fat as the high-corn oil (HCO) diet, has noticeably shown a different effect (Fig. 1). Thus, depending on the parameter studied, the high-olive oil diet exerted a weak stimulatory effect to a protective effect on mammary carcinogenesis. In all the experimental studies developed in our laboratory, the high-EVOO diet, in comparison with the HCO diet, consistently increased tumour latency (retarding the appearance of tumours) and decreased tumour incidence, multiplicity and volume. Moreover, in some of the experimental series, we have observed that the olive oil diet reduced tumour content and volume, even in comparison with a control low-fat diet, which suggested a protective effect of the olive oil on mammary carcinogenesis. The study of tumour regression, as a proposed protective effect of this high-olive oil diet, showed a slow progression of tumours in the animals fed that diet, rather than a real regression.
interest considering the high percentage of olive oil used in this experimental diet, as it should be taken into consideration that all high-fat diets may have an unspecific stimulatory effect on carcinogenesis. In this sense, a positive association between the dietary energy supply and cancer mortality rates has been shown, and energy restriction has an indiscriminate inhibitory effect on carcinogenesis. In the literature, experimental studies on the effects of olive oil in the diet have reported inconsistent results. Administration of diets with a lower percentage of oil (7% and 15%) during prenatal life has significantly increased the number of tumour-free rats.

Effects of extra virgin olive oil on experimental breast cancer: histopathological characteristics

Our group has also characterised morphologically, for the first time according to our knowledge, the effect that dietary lipids may exert on experimental breast cancer. Previously, a histological grading system adapted to rat mammary carcinomas was developed. These studies first showed the correspondence between the histological pattern and the clinical characteristics of each tumour, finding a higher degree of biological aggressiveness in tumours with higher histopathological degrees, desmoplastic reaction, limfoplasmocitic infiltrate, tumour necrosis and prevalent cribiform architectural patterns. Furthermore, the analysis of the effects of different diets showed that the HCO diet promoted adenocarcinomas with a high histological degree, stromal invasion, more prominent tumour necrosis and a frequent cribiform pattern in comparison with the controls and high-olive oil diet. In contrast, animals fed a diet rich in EVOO developed adenocarcinomas with a low histopathological grade, few invasive and necrotic areas (similar to the tumours from the control group) and extensive papillary areas. In conclusion, tumours from the animals fed the high-EVOO diet clearly showed a lower degree of tumour malignancy than those from the animals fed the HCO diet, being more similar to control tumours. All these results are compatible with the lower degree of clinical malignancy and with the non-promoting effect of a diet rich in EVOO.

Mechanisms of action of extra virgin olive oil on breast cancer: growth and sexual maturation

The mammary gland has the particularity that, unlike other organs, after birth it remains highly undifferentiated until the onset of puberty. Reproductive events increasing the number of menstrual cycles and therefore lifetime exposure to oestrogens, such as early menarche, have been associated with increased risk of breast cancer. Thus, modifications in growth and sexual maturation due to the effect of nutrition may modify the susceptibility to mammary transformation, advancing, retarding or expanding the windows of this susceptibility.

We observed that a diet high in corn oil increased the body weight of the rats as well as the BMI. In contrast, the high-olive oil diet, with the same percentage of fat as the HCO diet, did not modify body weight or mass in relation to the low-fat diet (Fig. 2). Several studies have also reported an effect of the high-ω-6 PUFA diet on body weight, but there are few experimental data regarding the effects of the olive oil diet. In this sense, a 30% EVOO diet has also been shown to produce lower bodyweight gain in rats when compared to a 30% corn oil diet. On the other hand, there are human epidemiological data suggesting
that the Mediterranean diet may have a protective effect on obesity\(^{42-45}\).

Sexual maturation has also been studied in rats fed these high-fat diets. Although a high amount of fat in the diet generally advances the onset of puberty, we observed different effects depending on the type of oil consumed. The onset of puberty in animals fed the HCO diet was significantly advanced, followed by animals fed a high-EVOO diet, and the control animals\(^{31}\) (Table 1). No differences were found either in body weight or mass when arriving at each stage, thus suggesting that the reproductive morphological changes are related to the acquisition of a threshold level of body mass, as has been already reported in humans\(^{40}\). This threshold weight would appear earlier in the animals of the HCO group, followed by the high-EVOO group and the controls. These results were in accordance with the study of a marker of puberty, the hypothalamic expression of kisspeptin\(^{47}\). The mRNA levels of kisspeptin in the hypothalamus of rats fed the HCO diet suggested higher expression of this marker at around puberty, while no differences were observed in the animals fed the EVOO diet in relation to the controls. No differences were observed in other parameters of maturation due to the effect of diets (uterine weight, time span among stages, time from vaginal opening to first oestrus or cycle), which also suggested that high-fat diets may advance the process of maturation but did not change its evolution\(^{31}\).

| Table 1 Effect of an LF, HCO and an HEVOO diet on day of arrival at different states of maturation in female rats |
|-----------------|-----------------|-----------------|
|                  | LF (n 81)       | HCO (n 31)      | HEVOO (n 31)    |
| Day of arrival at: | Mean SE Median | Mean SE Median | Mean SE Median |
| Maturation state 1 | 34±8 0±31 34   | 32±2* 0±36 32±t | 32±7* 0±33 34   |
| Maturation state 2 | 38±1 0±21 38   | 36±6* 0±23 36±* | 36±5* 0±23 36±* |
| Maturation state 3 | 44±1 0±33 44   | 42±2* 0±47 42±* | 42±8 0±54 43    |

LF, low fat; HCO, high-corn oil; HEVOO, high-extra virgin olive oil.
*\(P<0.05\) compared to control LF group.
†\(P<0.05\) compared to HEVOO group (parametric Tukey’s test for mean, non-parametric Mann-Whitney’s \(U\) test for median).

Mechanisms of action of extra virgin olive oil on breast cancer: hormonal status

Breast cancer is an oestrogen-dependent neoplasia, and thus may be influenced by modifications in hormonal status\(^{40}\). Thus, the possible effect of dietary lipids on serum concentrations of luteinizing hormone, follicle-stimulating hormone, oestradiol, progesterone, prolactin, insulin and corticosterone has been analysed, but no significant modifications due to the effect of high-olive oil or HCO diets\(^{48}\) (E Escrich, unpublished results) have been found. In the literature, there are discordant results regarding the influence of dietary lipids on hormone levels. For example, pregnant rats fed with a high-\(\alpha\)-6 PUFA diet have been shown to either increase\(^{49}\) or not modify\(^{50}\) serum oestradiol levels. Other authors have found lower concentrations of oestradiol in lactating dams fed a 7% olive oil diet in comparison to those fed a 7% corn oil diet\(^{31}\). The discrepancy among results may be related to the cycling nature of hormones, as their serum concentrations are highly dependent on the hour of the day and the phase of the oestrous cycle\(^{52}\).

To better understand the effects that dietary lipids may have on hormonal status, we also analysed the expression levels of hormone receptors in the mammary gland and in the experimental tumours, finding little difference due to the effect of the high-fat diets. Thus, analyses of the expression of estrogen receptors (ER\(\alpha\), ER\(\beta\)1 and ER\(\beta\)2) showed no significant differences due to the effect of diets. We observed higher levels of progesterone receptors in the mammary gland of rats fed the EVOO diet in relation to the animals fed the HCO diet at the age around puberty, which may be related to the development of lobulo-alveolar structures\(^{31}\). The few changes observed suggest that the modulation of the expression levels of these hormone receptors are not a major mechanism by which these high-fat diets may influence mammary gland biology.

Mechanisms of action of extra virgin olive oil on breast cancer: morphology and differentiation of the mammary gland

The mammary gland is a target of sexual maturity. Various studies on animals have shown that the risk of malignant transformation of this tissue can be highly dependent on the influence of early life events, and highlight the importance of the degree of differentiation at the time of a carcinogenic insult\(^{53}\). Thus, we characterised the differentiation degree of the mammary gland by quantifying the different epithelial structures in the periphery of the gland. Other authors have suggested that high-fat diets, such as HCO diet, may influence mammary carcinogenesis by increasing the number of the epithelial structures that are target of the carcinogen (the undifferentiated terminal end buds (TEB))\(^{49,53}\). However, we found little influence from either of the high-fat diets on the number of TEB, terminal buds, alveolar buds or lobular structures of the breast tissue\(^{31}\).
To further characterise the degree of differentiation of the mammary gland, mRNA expression of β-casein, classically considered a molecular differentiation marker of this gland, has also been analysed. β-Casein expression increased in the mammary tissue over time, but no significant differences were found due to the effect of dietary lipids. Although β-casein mRNA levels inversely correlated with the number of undifferentiated terminal ducts, we did not find a correlation with TEB, the main target of carcinogens, or, therefore, with the susceptibility of the mammary gland to transformation.

**Mechanisms of action of extra virgin olive oil on breast cancer: molecular changes in tumours**

The molecular mechanisms by which dietary lipids may exert their effects on the development of mammary cancer are not well understood. Experimental studies support the hypothesis of the existence of a specific effect aside from the unspecific one derived from the energy supply. Some of the proposed mechanisms, to which we have contributed with experimental data, include modifications of the structure and function of cell membranes, modulation of gene expression or influence on cell signalling pathways. Moreover, several studies have reported beneficial effects of olive oil through other mechanisms, such as modifications in oxidative stress and changes in immune system function. Lipids could act through several of these and other mechanisms in an integrated, simultaneous and/or sequential way.

**Modifications of cell membranes**

Lipids are an essential component of cell membranes and thus regulate their biological activity. Membrane lipid composition may be altered by dietary lipids, mainly by n-3 PUFA and the n-3/n-6 ratio of the diet. Few studies have been carried out regarding the influence of olive oil on membrane composition, but there is evidence that adherence to the Mediterranean diet may affect the structural properties of the erythrocyte cell membrane of hypertensive patients. This influence has been related to the beneficial effect of the Mediterranean diet on hypertension. A high content of polyunsaturated lipids in membranes increases the fluidity and the susceptibility to peroxidation. We have studied the membrane composition of experimental tumours by analysing fourteen different fatty acids in six lipidic fractions. A high-n-6 PUFA diet changed the tumour lipid profile, increasing the 18:2n-6 relative content and decreasing that of the 18:1n-9 (significantly in three lipidic fractions: phosphatidylcholine, free fatty acids and TAG). Taking into consideration that those tumours had more aggressive clinical and histopathological behaviour, these results would be in accordance with the lower effect of MUFA on membrane fluidity and the lower susceptibility of these lipids to peroxidation, thus decreasing the oxidative damage in membranes.

**Effects on gene expression**

It has long been known that different dietary components can modulate the expression of specific genes. Although data regarding the effect of dietary lipids in genes with a role in cancer are scarce, there is a wealth of information reporting the effects of such dietary compounds on genes of the metabolism. Moreover, the effects of dietary lipids could be modified by the disease, as we have observed changes in the normal regulation of the expression of CPT-I, HMGCa synthase and PPARα by high-fat diets in the liver of tumour-bearing rats.

The healthy benefits of the Mediterranean diet have been partly associated with changes in the expression of atherosclerosis-related genes through olive oil polyphenols. Thus, olive oil may exert some of its influence on breast cancer through the modulation of expression of genes involved in the carcinogenesis process. We found in experimental mammary tumours that the high-EVOO diet and the HCO diet had different influences on the modulation of the expression of the ErbB family of membrane receptors, especially c-erbB1. Hence, the HCO diet increased the ratio between the 9:5 kb mRNA of EGFR (coding the functional full-length receptor) and the 2:7 kb mRNA (coding an inactive truncated receptor), whereas the high-EVOO diet decreased this ratio in the mammary tumours. On the other hand, the expression levels of p21Ras, a key transductor of ErbB proliferative signalling that is frequently involved in human mammary carcinogenesis, were not modified by these dietary lipids. High-fat diets did not modify either the expression levels of HMG-CoA reductase or squalene synthase, two genes that codify enzymes of the mevalonate pathway. The healthy benefits of the Mediterranean diet have been partly associated with changes in the expression of atherosclerosis-related genes through olive oil polyphenols. Thus, olive oil may exert some of its influence on breast cancer through the modulation of expression of genes involved in the carcinogenesis process. We found in experimental mammary tumours that the high-EVOO diet and the HCO diet had different influences on the modulation of the expression of the ErbB family of membrane receptors, especially c-erbB1. Hence, the HCO diet increased the ratio between the 9:5 kb mRNA of EGFR (coding the functional full-length receptor) and the 2:7 kb mRNA (coding an inactive truncated receptor), whereas the high-EVOO diet decreased this ratio in the mammary tumours. On the other hand, the expression levels of p21Ras, a key transductor of ErbB proliferative signalling that is frequently involved in human mammary carcinogenesis, were not modified by these dietary lipids.

Cell dedifferentiation is part of the alterations linked to cancer, and thus our group studied whether a high-EVOO diet and a HCO diet changed the degree of molecular differentiation of DMBA-induced mammary tumours. We analysed the expression of known mammary differentiation markers, α-casein, β-casein and transferrin, in addition to β-actin and its transporter protein ZBP1. In the mammary adenocarcinomas, the expression levels of α-casein, β-casein and transferrin were not related to the degree of morphological differentiation or to the clinical behaviour of the tumours, which suggested that these genes were not good biomarkers of the modifications that the experimental diets conferred to the adenocarcinomas. The HCO diet, but not the high-EVOO diet, increased the β-actin mRNA levels but not those of the protein. This last result, in addition to the increase observed in the transporter ZBP1 as a result of the HCO diet, suggested a deregulated transport and translation of β-actin that was
associated with the most malignant phenotype of the tumours from animals fed a diet rich in corn oil, but not with those of the animals fed the high-EVOO diet\(^{(64)}\).

New screening technologies allowed different experimental approaches in order to gain insight into the modulation of gene expression by dietary lipids. cDNA microarrays analyses were used to discover four genes significantly downregulated due to the effect of the HCO diet in tumours\(^{(65)}\) but not modified by the high-EVOO diet\(^{(66)}\). The genes differentially modulated in the adenocarcinomas of animals fed a diet rich in \(n\)-6 PUFA were \(\alpha\)-2u-globulin, VDUP1, the imprinted gene \(H19\) and an unknown gene (Fig. 3). Experimental evidence suggests that these known genes are potentially related to differentiation and cell proliferation, thus being involved in the tumour-stimulating effect of the HCO diet\(^{(65)}\). Moreover, the \(IGFII\) gene, related to proliferation and reciprocally imprinted with \(H19\), was upregulated by the HCO diet and downregulated by the high-EVOO diet. Furthermore, both high-fat diets had an opposing effect on the activity of thioredoxin, an oxidoreductase inhibited by VDUP1 that promotes cell growth and has an antiapoptotic action. This result was in accordance with the opposing effect of the HCO and EVOO diets on mammary carcinogenesis\(^{(65,66)}\).

**Influence on signalling pathways**

Our investigations have also focused on the effects that olive oil diet may have on signalling pathways with an important role in mammary development and human breast cancer, such as the ErbB-Ras and their main effectors (Erk1/2, PI3K/Akt, RalGDS/Ral)\(^{(61)}\). The protein levels and activity of the ErbB1, ErbB2 and ErbB3 were not altered due to the HCO diet or the high-olive oil diet, but we observed a significantly decreased expression in the 80 kDa ErbB4-truncated protein due to the effect of the high-EVOO diet\(^{(62)}\).

We next investigated the effect of the olive oil diet on p21Ras expression and activity. Animals fed this diet developed tumours with significantly higher levels of p21Ras protein, but with a significantly decreased activity (Fig. 3). In contrast, no changes were observed in p21Ras function as a result of the HCO diet, suggesting that p21Ras may have a role in the negative modulatory effect...
of olive oil on breast cancer, whereas it is not involved in the stimulatory effect of the HCO diet\(^{62}\). Several mechanisms of action for this decreased activity have been addressed: the tumour mutation status of Ha-ras1 and the expression of two key enzymes of the mevalonate pathway, the HMG-CoA reductase and squalene synthase (SQS). The experimental diets did not modify the rate of the activating point mutation in the codon 61 of the gene c-Ha-ras1, or the mRNA expression levels of HMG-CoA and SQS in the mammary adenocarcinomas (as mentioned above). Other experimental studies have suggested that an olive oil diet may have a protective effect on colon cancer through the effect of squalene, a minor compound of olive oil, inhibiting the HMG-CoA reductase\(^{67}\). However, such effects have been observed at very high concentrations of squalene (1% of diet), and our results did not support the hypothesis of a chemopreventive effect of olive oil diet through squalene on HMG-CoA reductase inhibition, at least at the expression level\(^{62}\).

The analysis of the main effectors of p21Ras showed increased ERK1/2 activity and reduced ERK1/2 expression due to the effect of both high-fat diets. These results suggested an unspecific effect of such diets upregulating the ERK1/2 proliferating pathway, which would not be elicited by ErbB receptors and could be mediated, at least partly, by a p21Ras-independent mechanism. No differences were found in the expression or activity of RalA and RalB proteins due to the effect of the experimental diets. On the other hand, the EVOO diet decreased both Akt expression and activation, whereas the HCO diet only decreased Akt protein levels\(^{62}\) (Fig. 3). A reduced activity of Akt has been associated with induction of apoptosis\(^{68}\); thus, these results suggested that the high-olive oil diet may downregulate the pro-survival p21Ras/Akt pathway in the mammary tumours. Few data have been published regarding the effects of olive oil on these pathways, but it has been shown that in breast cancer cells oleic acid both increased\(^{69}\) and decreased\(^{70}\) active Akt, whereas hydroxytirosol abolished Akt phosphorylation and induced transient Erk1/2 phosphorylation-dephosphorylation in colon cancer cells\(^{71}\).

The influence of the high-olive oil diet on mammary tumours may thus result in upregulation of ERK1/2 pathway concomitantly with a downregulation in Akt signalling. There are experimental data in the literature suggesting that this relative balance between ERK1/2 and Akt pathways may result in pro-apoptotic signalling\(^{72,75}\). To address the hypothesis that the EVOO diet induced cell apoptosis, we analysed the levels of the activated caspase-3, which is considered the main executor of the caspase cascade involved in both extrinsic and intrinsic apoptosis\(^{74}\). The tumours from the animals fed the olive oil diet had significantly higher levels of this protein, which was concordant with the proposed pro-apoptotic effect of the olive oil\(^{62}\) (Fig. 3). These results are in line with other studies that have reported that olive oil, oleic acid and minor compounds of olive oil can modulate apoptosis\(^{51,75–77}\).

Apoptosis is a crucial process in cancer development, and it has been suggested that tumour growth is partly determined by the balance between cell proliferation and apoptosis. The histopathological analysis of the mitotic activity and the protein expression levels of the mitotic marker proliferating cell nuclear antigen (PCNA) indicated that the high-EVOO diet did not exert a significant effect on tumour cell proliferation, in contrast to the HCO diet, which significantly increased tumour mitotic activity\(^{40,62}\). This last result was consistent with an influence of HCO diet on the survival and proliferation signalling pathways and with its stimulatory effect on mammary carcinogenesis\(^{7,22,27–33}\). Moreover, the high-EVOO diet decreased the levels of monoubiquitylated PCNA, which is associated with DNA damage, in the mammary tumours\(^{62}\) (Fig. 3). The effect that olive oil may have on the proliferation of tumour cells is still not well elucidated. In vitro experiments have found evidence that some minor compounds of olive oil, such as hydroxytyrosol and oleuropein, inhibit proliferation of breast cancer cells\(^{75}\), while oleate has been reported to have a stimulatory effect on cell proliferation\(^{70}\).

**Conclusions**

There is increasing epidemiological and experimental evidence indicating the beneficial effect of the Mediterranean diet, and in particular of EVOO, on the progression of some cancers, especially breast cancer. This effect could be the result of its MUFA (oleic acid) and its minor compounds.

In an experimental model of mammary cancer, we have observed that a high-EVOO diet clearly has a different effect on breast carcinogenesis if compared with the effect of other diets (an n-6 PUFA enriched diet) with the same amount of fat, showing the importance of the type of oil consumed beyond its energy content. Some of the parameters that we have studied in relation to the clinical and histopathological behaviour of tumours, in addition to experimental data published in the literature using lower percentages of olive oil in the diet, suggest that EVOO may have a beneficial effect on breast cancer risk if its consumption is moderated. The mechanisms by which this type of oil may exert its effects are diverse, such as a protective effect on obesity or molecular influences eliciting a balance between proliferation and apoptosis shifted in favour of apoptosis or lower levels of DNA damage in tumours. These data may contribute to the published evidence of the healthy effect of the Mediterranean diet and highlight that the use of EVOO as the source of fat from childhood may be considered as a healthy choice.
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References

Mediterranean diet, olive oil and cancer


Mediterranean diet in secondary prevention of CHD

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Abstract

Objective: To summarise our present knowledge on the Mediterranean diet in secondary prevention of CHD.

Design: Review of literature.

Setting: Adult coronary patients.

Subjects: CHD patients at high risk of cardiac death.

Results: The two main causes of death in these patients are sudden cardiac death (SCD) and chronic heart failure (CHF). The main mechanism underlying recurrent cardiac events is coronary thrombosis resulting from atherosclerotic plaque erosion or ulceration. The occurrence of thrombosis is usually associated with plaque weakness in relation to high lipid content of the lesion where cholesterol only represents a very small part compared with other lipids (i.e. fatty acids). Thus, the three main aims of the preventive strategy are to prevent coronary thrombosis, malignant ventricular arrhythmia and the development of left ventricular dysfunction (and CHF) and finally to minimise the risk of plaque erosion and ulceration. There is now a consensus about recommending the Mediterranean diet pattern for the secondary prevention of CHD because no other dietary pattern has been successfully tested so far in these patients. The most important aspect, in contrast with the pharmacological prevention of CHD (including cholesterol lowering), is that the Mediterranean diet results in a striking effect on survival.

Conclusions: The traditional Mediterranean diet is effective in reducing both coronary atherosclerosis/thrombosis and the risk of fatal complications such as SCD and heart failure.

Keywords
Sudden cardiac death
Chronic heart failure
Atherosclerosis
Thrombosis
n-3 fatty acids
Alpha-linolenic acid

The priority of secondary prevention is somewhat different from that of primary prevention. In the context of primary prevention, intervention focuses on traditional risk factors (e.g. lifestyle factors, diabetes, overweight or obesity, high blood pressure) and surrogate endpoints. In secondary prevention, it is critical to reduce the risk of severe and often fatal clinical complications such as sudden cardiac death (SCD) and chronic heart failure (CHF) (1,2). This does not mean that traditional risk factors of CHD should not be measured and, if necessary, corrected in secondary prevention, because they also play a role in the occurrence of CHD complications. It simply means that because complications such as SCD and associated syndromes are often unpredictable, occur out of hospital and far from any potential therapeutic resources in the majority of cases, and account for approximately 70% of cardiac mortality in secondary prevention, they should be the priority of any secondary prevention programme. For this reason, in the present text, we will focus our recommendations and comments specifically on clinical efficacy and not on surrogate efficacy (1,2).

Whatever the specific clinical aims of the programme, nutritional evaluation and counselling of each individual with CHD must be a key goal of the preventive intervention. Nutrition is, however, only one component of such a programme. Exercise training, behavioural interventions (particularly to help the patient abstain from smoking) and drug therapy – particularly antithrombotic drugs – also have important roles. The dietary prevention programme is commonly initiated during hospitalisation for a first CHD event. With the shortening of stay in the coronary care unit, the dietary intervention is initiated during the following days in hospital, and then continued in secondary prevention centres and included in cardiac rehabilitation programmes. An individualised dietary prevention programme should be developed under the guidance of a specialised dietician and in close collaboration with the patient’s cardiologist and primary care physician, so that there is no discontinuity or discrepancy in dietary counselling between the hospitalisation and post-hospitalisation phases of the rehabilitation programme (1,2).

The scientific concept of Mediterranean diet

There is now a consensus about recommending the Mediterranean diet pattern for the secondary prevention
of CHD because no other dietary pattern has been successfully tested so far in these patients\(^1,2\). The most important aspect, in contrast with the pharmacological prevention of CHD (including cholesterol lowering), is that the Mediterranean diet results in a striking effect on survival. The main explanation is that the Mediterranean diet is protective not only against CHD and CHD complications, but also against other chronic diseases including cancers\(^3,4\). Furthermore, the Mediterranean diet appears to be effective in reducing both coronary atherosclerosis/thrombosis and the risk of fatal complications (SCD and CHF) of atherosclerosis and thrombosis.

Finally, no harmful side effects have been reported following the adoption of this dietary pattern, unlike drug therapies\(^4,5\).

Prospective studies of the epidemiology of CHD have shown that mortality from CHD differs greatly among populations and that at least some of the differences are associated with differences in dietary habits\(^6\). Mediterranean populations have been relatively protected from CHD and certain cancers, and the particular composition of the traditional Mediterranean diet has been put forth to explain this\(^7,8\). However, epidemiological studies only provide associations between the risk factors and clinical endpoints, not causal relationships. Several confounding factors may play a part in these associations. The economic situation and the presence of extended social support systems, for instance, have been proposed to explain the low prevalence of CHD in some Mediterranean countries. Clearly, randomised trials are the only way to make sure that a given dietary pattern results in a significant protective effect against CHD complications.

Some dietary trials in primary or secondary prevention of CHD have reported an impressive reduction of CHD risk, especially in terms of mortality\(^9–11\).

In contrast, other dietary trials specifically aimed at reducing blood cholesterol failed to significantly improve the prognosis of the dieters\(^12–14\). The successful trials in general tested dietary patterns characterised by a low intake of total, saturated and \(\nu\)-6 polyunsaturated fats\(^9–11\) and an increased intake of \(\nu\)-3 fatty acids\(^9–11,15\). Their aim was not to primarily reduce blood cholesterol, but this is a critical issue.

Two of these trials\(^9,10\) also included a high intake of fresh fruits and vegetables, legumes and cereals containing large amounts of fibre, antioxidants, minerals, vegetable proteins and vitamins of the B group. The credibility of these trials was considerably reinforced by a number of studies showing protective effects of most of these foods and nutrients,\(^16–18\) with a particular emphasis on plant and marine \(\nu\)-3 fatty acids\(^5,10,11,15,19,20\).

The ‘Lyon Diet Heart Study’ was a randomised single-blind secondary prevention trial aimed at testing whether an experimental Mediterranean diet could reduce the risk of recurrence after a first myocardial infarction. A significant reduction of the rates of fatal and non-fatal cardiovascular complications was reported\(^5,10,21\), and no major bias was detected in the trial\(^5,22\). In addition, the trial suggested for the first time that patients following the Mediterranean diet were also relatively protected from cancer\(^23\). Although further controlled trials are warranted to confirm the cancer data, those obtained from the ‘Lyon Diet Heart Study’ are in line with several epidemiological observational studies suggesting that some dietary factors are very important in cancers and cancer prevention\(^5,25–26\).

In the ‘Lyon trial’, investigators advised patients to use either olive oil or rapeseed oil (or both oils together) because some French patients do not like the taste of olive oil and might have rejected the whole Mediterranean diet pattern. As rapeseed and olive oil have similar fatty acid compositions – very low saturated fatty acids and high oleic acid – the tested diet remains, on average, a very Mediterranean diet\(^5,10,21\).

In a recent and very large observational study about the health effects of the Mediterranean diet\(^27\), the authors concluded that their results provide strong evidence for a beneficial effect of higher conformity with the Mediterranean dietary pattern on risk of death from all causes, including deaths due to CVD and cancer, in a US population. They base their conclusions on previous epidemiological studies conducted in non-US populations and reporting similar data about the effect of the Mediterranean diet on longevity\(^28\).

Thus, epidemiological studies\(^3,27,28\) confirmed the results of the ‘Lyon Diet Heart Study’, now a reference trial in the field\(^29\). Interestingly, in that trial, there was no difference between groups for the main conventional risk factors, including blood cholesterol and blood pressure. This suggested that protection was largely independent from these traditional (conventional) factors.

In contrast, it is noteworthy that a recent meta-analysis involving 534,906 individuals reported that the Mediterranean diet was associated with a significant reduction of metabolic syndrome, a pre-diabetes state\(^30\).

All these data are of considerable relevance for public health. No other dietary pattern is apparently as effective in reducing the risks of both diabetes and cardiovascular complications. It is therefore surprising that when defining dietary recommendations to prevent chronic diseases, experts forget to mention the Mediterranean diet\(^31\), sometimes distort the published data to discredit the concept, and put forward treatments that increase the risk of diabetes\(^32,33\).

**The Mediterranean diet in practical terms**

The diet score usually used to assess conformity with the Mediterranean dietary pattern in epidemiological studies\(^27,28,30\) is rather simplistic and does not capture the various practical aspects of the real and various traditional Mediterranean diets.

Briefly, what must clinicians (and their patients) know?
The Mediterranean diet is characterised by the consumption of:

1. A wide variety of raw, sometimes cooked, seasonal vegetables throughout the year, often large amounts of onions, garlic, parsley, rosemary, oregano, thyme and other aromatic herbs.
2. Fruit throughout the year, both fresh and dried (during the summer, for consumption in winter, e.g. apricots, figs and grapes).
3. Various nuts (almonds, hazelnut), particularly walnuts, which are rich in alpha-linolenic acid (ALA), the main plant n-3 and a major characteristic of traditional Mediterranean diets. There are many other sources of ALA in Mediterranean diets, including salads such as purslane and products from animals fed with ALA-rich feed such as linseed (rabbit, eggs and chicken, dairy products).
4. Grains, preferably whole, especially wheat in the form of bread, fermented with natural leaven and sometimes flavoured with ALA-rich linseed. The wheat used in traditional Mediterranean diets (like the vegetables and fruit) is rustic and does not contain pesticides as it is not a product of industrial agriculture.
5. Fatty fish, including anchovy, sardine, mackerel, sea bream and red tuna, all rich in very-long chain (marine) n-3 fatty acids. Another source of indispensable marine n-3 fatty acids may be the eggs of linseed-fed chicken, as well as the ‘fish-like effect of moderate wine drinking’.
6. Olive oil, the main edible oil used in the Mediterranean area, low saturated and rich monounsaturated. However, the monounsaturated fat/saturated fat ratio used by epidemiologists does not capture one major lipid characteristic of the Mediterranean diet, which is low in n-6 and rich in n-3 fatty acids. The n-6/n-3 ratio has been proposed as a major component of a healthy diet.
7. In contradiction with many experts, Mediterranean populations do traditionally eat dairy products, though made of goat and ewe milk and not cow milk. Importantly, these are consumed in the fermented forms of cheese and yoghurt, and almost never as milk, butter or cream.
8. Mediterranean populations are not vegetarian. They eat ALA-rich eggs and small amounts of meat, mainly lean meat such as rabbit, chicken and duck. Beef and/or pork are also on the menu in the North of the area, while mutton is the preferred meat for festive meals in the South. It is also important to note that everywhere in the Mediterranean area the diet includes a large number of legumes and is therefore rich in vegetable proteins.
9. Moderate alcohol drinking, essentially during meals, is a major characteristic of the Mediterranean diet. The main alcoholic beverage is wine, particularly red wine, a major source of various polyphenols. Wine is a mix of ethanol and polyphenols. South of the Mediterranean Sea, the main source of healthy polyphenols is not wine but fermented black tea (a mix of water and polyphenols). Thus, most people living in the Mediterranean area are high consumers of various polyphenols whose health effects are still considerably underestimated by scientists and physicians. This is another major item not included in the Mediterranean diet score used by epidemiologists.

The wine drinking issue

The medical and scientific literature shows that moderate drinking (one to two drinks per day for women and two to four drinks per day for men) is usually associated with a better life expectancy in the general population, as well as in patients with established CHD. In the absence of a controlled trial, which is neither technically nor ethically feasible, the main question for physicians remains whether the inverse association between moderate drinking and CHD complications is a cause–effect relationship.

Although prospective studies with light drinkers (rather than non-drinkers) as the referent group have shown that the ‘sick quitter bias’ is not the main explanation for the protective effect of moderate drinking, a recent study, in which former drinkers were examined separately from long-term abstainers, confirmed that protection is still present when only long-term abstainers are included in the referent group. This was an important finding because it strongly supports the cause–effect relationship between moderate drinking and better survival.

In meta-analyses, moderate drinking generally results in approximately 30% lower cardiac mortality and a 20% reduction of all-cause mortality, which is considerable when compared with the effect of drug treatment and in terms of public health. In addition to the strong epidemiological evidence (and in the absence of clinical trials), another way of evaluating the relationship between moderate drinking and survival is to examine the biological mechanisms by which moderate drinking may reduce the risk of cardiac death and improve survival. In addition to the well-known effects of alcohol on haemostasis (through reduced platelet function and fibrinogen levels) and insulin resistance, recent data indicate that moderate drinking may have a direct protective effect on the ischaemic myocardium, and may positively interact with n-3 fatty acids known to be highly protective in secondary prevention, especially against SCD.

These two mechanisms are important to know because they may partly explain why moderate drinking was shown to reduce the risk of SCD, a complication that accounts for 65–75% of all cardiac deaths in the US population. Thus, epidemiological and biological studies strongly suggest that moderate drinking results in
reduced mortality and better life expectancy in patients with established CHD.

Finally, regarding alcohol consumption in secondary prevention, it is important to:

1. identify those at very high risk of cardiac death, for whom there is a clear indication for an implantable cardiac defibrillator (ICD);
2. identify binge and heavy drinkers and explain to them a better way of drinking to protect their lives;
3. identify non-drinkers (and respect their choice), but also those who abstain because they wrongly believe that even light drinking is bad for their health;
4. explain to all patients (with or without ICD) that moderate drinking, especially (but not only) in the form of wine in the context of the traditional Mediterranean diet, may be the most effective way to prevent both fatal and nonfatal complications of CHD, even in Northern Europe and in old age.

Further studies are needed to fully understand the mechanisms of this protection. Finally, coming back to the Mediterranean diet and to the specific consumption of wine, the next question is whether wine drinking (the preferred beverage of Mediterranean populations) is superior to other alcoholic beverages for the prevention of CHD complications. Recent observational data and meta-analysis suggest that wine is more protective than beer and spirits.

Conclusion

The traditional Mediterranean diet is effective in reducing both coronary atherosclerosis/thrombosis and the risk of fatal complications such as SCD and CHF.

Acknowledgements

The authors declare that they have no conflict of interest.

References


Comparison and evaluation of the reliability of indexes of adherence to the Mediterranean diet

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Abstract
Objective: To compare and evaluate the reliability of several indexes of adherence to the Mediterranean diet.
Design: The ten indexes included in the analysis were: Mediterranean Diet Score (MDS), Mediterranean Score (MS), Dietary Score (DS), Mediterranean-Dietary Quality Index (Med-DQI), Mediterranean Dietary Pattern adherence index (MDP), Mediterranean Adequacy Index (MAI), Mediterranean Style Dietary Pattern Score (MSDPS), Mediterranean food pattern PREDIMED Study (MeDiet-PREDIMED), relative Mediterranean diet (rMED) and Cardioprotective Mediterranean diet index.
Factor analysis using the correlations between indexes was applied. The correlation with factors and the reliability coefficient were calculated.
Setting: A total of 324 healthy undergraduates at the University of Barcelona, Spain, were surveyed.
Results: The highest correlations were observed between MDP adherence index and MAI (0.82); MAI and MSDPS (0.80); and MDS and rMED (0.77). Factor analysis showed a hidden common factor that explained over 70 % of the variability (71.03 %). This factor is understood as ‘adherence to the Mediterranean diet’. The indexes that showed the highest correlation with this factor were Med-DQI (0.85), MDS (0.84), rMED (0.80) and MAI (0.80). These indexes showed acceptable performance in measuring the adherence to the Mediterranean diet. The components that correlated strongly with this factor were monounsaturated-to-saturated fatty acid ratio (MS ratio), fruit and vegetables. Furthermore, a second common factor was found explaining 18 % of the variability. This second factor is highly positive related to dairy products and lean meat, and negative related to MS ratio.
Conclusions: The indexes showed satisfactory performance in assessing adherence to the Mediterranean diet. However, in order to improve the reliability and concordance between the indexes, further studies are required to select the components, the number of components, and the scoring criteria of the indexes to improve their internal consistency.

Keywords
Mediterranean diet indexes
Mediterranean diet scores
Factor analysis
Mediterranean diet

Keys and Grande Covian(1) introduced the concept of the Mediterranean diet in the 1950s. Initially describing eating habits in the Mediterranean area, this concept has further been referred to as the traditional dietary pattern found in the olive-growing regions along the Mediterranean coastline in the late 1950s and early 1960s(13). The traditional Mediterranean diet is characterised by a high intake of vegetables, legumes, fruits and nuts, unrefined cereals and olive oil (but a low intake of saturated lipids); a moderate intake of fish; a low-to-moderate intake of dairy products; a low intake of meat and poultry and a regular but moderate intake of ethanol, mainly in the form of wine and generally during meals(22). However, this diet is not homogeneous as there are regional variations, influenced by various factors, such as sociocultural, religious and economic determinants(3,4).

The Mediterranean dietary pattern has consistently been shown to provide a degree of protection against CVD and major chronic degenerative diseases(5,6). Research in this field over recent years has focused on estimating adherence to the Mediterranean diet rather than analysing the individual components of the diet in

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Reliability of Mediterranean diet indexes

Material and methods

Subjects
The survey was carried out on 336 healthy undergraduates. Students were invited to participate in the study during their degree course. Data were collected over four consecutive academic years (2003–2007) from students registered in the third year of Human and Dietetics Studies at the University of Barcelona, Spain. After exclusion of errors or inconsistencies in data and incomplete questionnaires, the final sample included 324 subjects. Information on food consumption was collected through a quantitative FFQ.

FFQ
Nutrient and food intake was estimated using an adaptation of the quantitative FFQ used in the Catalonian nutritional survey (25). This form includes approximately fifty-one commonly consumed food and beverage items. The questionnaire was administered in person by trained interviewers. Standard portion sizes were used to estimate the amounts consumed, and nutrient and ethanol intakes were calculated using the food composition database of the Centre for Superior Studies on Nutrition and Dietetics (CESID; University of Barcelona) (24). For each participant, we calculated intake in g/d of various food groups and nutrients, as well as total energy intake.

We focused on each food and nutrient variable included in general indexes used to assess observance of the Mediterranean diet. The most common food groups used were as follows: pulses; cereals; potatoes; fruit; vegetables; fish and seafood; olive oil; alcohol; red meat; dairy products; cereals; monounsaturated-to-saturated fatty acid ratio (MS ratio); and lean meat (poultry and rabbit).

Indexes of adherence to the Mediterranean diet
For the purpose of the present study, ten indexes were included in the analysis: Mediterranean Diet Score (MDS) (25), Mediterranean Score (MS) (26), Dietary Score (DS) (27), Mediterranean-Dietary Quality Index (Med-DQI) (28), Mediterranean Dietary Pattern adherence index (MDP) (29), Mediterranean Adequacy Index (MAI) (30), Mediterranean Style Dietary Pattern Score (MSDPS) (31), Mediterranean food pattern PREDIMED Study (McDiet-PREDIMED) (32), relative Mediterranean diet (rMED) (33) and Cardioprotective Mediterranean diet index (Cardio) (34).

Statistical analyses
To describe the data, mean values and standard deviation were calculated and, on the basis of their quartile values, indexes were classified into four groups. As the indexes differ in the scales used to assess adherence, the association between them was evaluated by means of Spearman’s coefficient of correlation.

Given that the attribute ‘adherence to the Mediterranean diet’ cannot be measured directly (latent attribute), it is necessary to use indirect measures obtained from the indexes. It was therefore assumed that all the indexes were designed to measure this attribute, although they may differ in the definition of the Mediterranean dietary pattern. Thus, we performed a factor analysis (35) using the correlations between indexes as data. We used the goodness-of-fit index (GIF) (35) to assess the degree of relationship between factors and indexes. The GIF can be interpreted as the percentage of variability of indexes explained by the model. The factor model that better fit the data was selected using the Akaike Information Criterion (AIC). The correlation with factors and the reliability coefficient are provided for each index. All analyses were performed using the SAS statistical software package version 9.1 (SAS Institute, Cary, NC, USA).

Results
A total of 324 FFQ were used to calculate the ten adherence indexes. The mean, minimum, maximum and percentile (25th, 50th and 75th) values of each index are shown in Table 1. The DS index showed the highest value of adherence to the Mediterranean diet, whereas the other indexes centred on the average value.
A first comparison of indexes was made by grouping them into four categories on the basis of their theoretical range of scores and comparing the frequencies of each category. Most indexes accumulated the highest scores in central values, and the second and third categories (54% and 25%, respectively), except DS and MSDPS, which resulted in more extreme values (Fig. 1). Most of the values from the MSDPS index fell in the first two ranges, with 159 (49.1%) and 165 (50.9%) subjects in ranges 1 and 2, respectively. In contrast, the values from the DS index concentrated in the ranges 3 and 4, but especially in the latter (78%; 253 subjects).

Table 2 shows the correlations among indexes. Only three correlations were high. The highest correlations (dark grey) were observed between MDP adherence index and MAI (0.82); MAI and MSDPS (0.80); and MDS and rMED (0.77). The remaining correlations were fair (0.5–0.7; light grey) or poor (<0.5; white). More than half of the indexes show poor correlation.

Factor analysis showed a common factor 1, which explained more than 70% of the variability (GIF: 71.03%; AIC: 512.43; Table 3). Thus, this would be the main common factor between indexes and can be understood as ‘adherence to the Mediterranean diet’. The indexes that most correlated with this factor were Med-DQI (0.85), MDS (0.83), rMED (0.80) and MAI (0.83), all of which showed satisfactory performance in measuring adherence to the Mediterranean diet. However, 30% of the variability was attributed to measurement error, that is, variability between indexes that is not caused by the ‘adherence to the Mediterranean diet’ factor. The MS, DS and Cardio indexes showed less accuracy in measuring this factor, with correlations of 0.67, 0.64 and 0.67, respectively.

We next fitted a model with two factors. This model showed an increase in explained variance and a better fit of data (GIF: 88.97%; AIC: 160.08). Thus, a second common factor was observed to explain 18% of the variability.

Table 1

<table>
<thead>
<tr>
<th>Indexes</th>
<th>Mean</th>
<th>Min</th>
<th>Max</th>
<th>Pctl25</th>
<th>Pctl50</th>
<th>Pctl75</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDS</td>
<td>4.75</td>
<td>0.00</td>
<td>9.00</td>
<td>3.00</td>
<td>5.00</td>
<td>6.00</td>
</tr>
<tr>
<td>MS</td>
<td>18.82</td>
<td>6.00</td>
<td>36.00</td>
<td>17.00</td>
<td>19.00</td>
<td>21.00</td>
</tr>
<tr>
<td>DS</td>
<td>43.78</td>
<td>8.00</td>
<td>100.00</td>
<td>7.00</td>
<td>12.00</td>
<td>16.00</td>
</tr>
<tr>
<td>Med-DQI</td>
<td>7.33</td>
<td>2.00</td>
<td>12.00</td>
<td>6.00</td>
<td>7.00</td>
<td>9.00</td>
</tr>
<tr>
<td>MAI</td>
<td>1.67</td>
<td>0.29</td>
<td>7.36</td>
<td>1.04</td>
<td>1.48</td>
<td>1.95</td>
</tr>
<tr>
<td>MDP</td>
<td>40.95</td>
<td>0.00</td>
<td>100.00</td>
<td>33.38</td>
<td>40.87</td>
<td>48.39</td>
</tr>
<tr>
<td>rMED</td>
<td>8.06</td>
<td>2.00</td>
<td>16.00</td>
<td>6.00</td>
<td>8.00</td>
<td>10.00</td>
</tr>
<tr>
<td>MSDPS</td>
<td>25.17</td>
<td>7.94</td>
<td>44.61</td>
<td>19.82</td>
<td>25.33</td>
<td>30.58</td>
</tr>
<tr>
<td>PREDIMED</td>
<td>5.93</td>
<td>2.00</td>
<td>10.00</td>
<td>5.00</td>
<td>6.00</td>
<td>7.00</td>
</tr>
<tr>
<td>Cardio</td>
<td>4.16</td>
<td>1.00</td>
<td>7.00</td>
<td>3.00</td>
<td>5.00</td>
<td>6.00</td>
</tr>
</tbody>
</table>

Min, minimum; Max, maximum; Pctl25, 25th percentile; Pctl50, 50th percentile; Pctl75, 75th percentile; MDS, Mediterranean Diet Score; MS, Mediterranean Score; DS, Dietary Score; Med-DQI, Mediterranean-Dietary Quality Index; MAI, Mediterranean Adequacy Index; MDP, Mediterranean Dietary Pattern adherence index; rMED, relative Mediterranean diet; MSDPS, Mediterranean Style Dietary Pattern Score; PREDIMED, Mediterranean food pattern PREDIMED Study; Cardio, Cardioprotective Mediterranean diet index.

Fig. 1 Comparison of indexes according to the frequencies of each category. The reference values used were: Mediterranean Adequacy Index (MAI): 1 (<0.5), 2 (0.5–1), 3 (>1–2) and 4 (>2); relative Mediterranean diet (rMED): 1 (0–4), 2 (5–9), 3 (10–14) and 4 (15–18); Mediterranean-Dietary Quality Index (Med-DQI): 1 (0–3), 2 (4–7), 3 (8–11) and 4 (11–14); Mediterranean Score (MS): 1 (0–11), 2 (12–22), 3 (23–33) and 4 (34–44); Mediterranean Style Dietary Pattern Score (MSDPS): 1 (0–25), 2 (>25–50), 3 (>50–75) and 4 (>75–100); Dietary Score (DS): 1 (0–13), 2 (14–27), 3 (28–41) and 4 (42–55); Mediterranean Dietary Pattern adherence index (MDP): 1 (0–25), 2 (>25–50), 3 (>50–75) and 4 (>75–100); Mediterranean Diet Score (MDS): 1 (0–2), 2 (3–5), 3 (6–8) and 4 (9–10); Mediterranean food pattern PREDIMED Study (MeDiet-PREDIMED): 1 (0–3), 2 (4–7), 3 (8–10) and 4 (11–14); Cardioprotective Mediterranean diet index (Cardio): 1 (0–2), 2 (3–5), 3 (6–7) and 4 (8–9)
Table 2 Correlation among indexes of adherence to the Mediterranean diet

<table>
<thead>
<tr>
<th>Indexes</th>
<th>MS</th>
<th>DS</th>
<th>Med-DQI</th>
<th>MAI</th>
<th>MDP</th>
<th>rMED</th>
<th>MSDPS</th>
<th>PREDIMED</th>
<th>Cardio</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Correlation coefficient 95 % CI</strong></td>
<td>0.52 0.44-0.60</td>
<td>0.64-0.70</td>
<td>0.67 0.53-0.67</td>
<td>0.66 0.53-0.67</td>
<td>0.77 0.53-0.67</td>
<td>0.55 0.46-0.62</td>
<td>0.63 0.55-0.69</td>
<td>0.58 0.50-0.66</td>
<td>0.58 0.50-0.66</td>
</tr>
<tr>
<td><strong>Correlation coefficient 95 % CI</strong></td>
<td>0.67 0.53-0.73</td>
<td>0.59 0.52-0.66</td>
<td>0.66 0.53-0.67</td>
<td>0.77 0.53-0.67</td>
<td>0.55 0.47-0.62</td>
<td>0.56 0.48-0.63</td>
<td>0.53 0.44-0.60</td>
<td>0.48 0.39-0.56</td>
<td>0.63 0.55-0.69</td>
</tr>
<tr>
<td><strong>Correlation coefficient 95 % CI</strong></td>
<td>0.58 0.50-0.66</td>
<td>0.3 0.09-0.39</td>
<td>0.34 0.24-0.43</td>
<td>0.49 0.40-0.56</td>
<td>0.49 0.40-0.56</td>
<td>0.26 0.16-0.36</td>
<td>0.53 0.44-0.60</td>
<td>0.48 0.39-0.56</td>
<td>0.67 0.53-0.67</td>
</tr>
<tr>
<td><strong>Correlation coefficient 95 % CI</strong></td>
<td>0.7 0.64-0.75</td>
<td>0.61 0.53-0.67</td>
<td>0.61 0.53-0.67</td>
<td>0.82 0.78-0.85</td>
<td>0.61 0.53-0.67</td>
<td>0.8 0.76-0.83</td>
<td>0.54 0.46-0.62</td>
<td>0.4 0.30-0.49</td>
<td>0.63 0.55-0.69</td>
</tr>
<tr>
<td><strong>Correlation coefficient 95 % CI</strong></td>
<td>0.68 0.62-0.74</td>
<td>0.68 0.62-0.74</td>
<td>0.68 0.62-0.74</td>
<td>0.68 0.62-0.74</td>
<td>0.45 0.36-0.53</td>
<td>0.45 0.36-0.53</td>
<td>0.45 0.36-0.53</td>
<td>0.45 0.36-0.53</td>
<td>0.56 0.52-0.66</td>
</tr>
<tr>
<td><strong>Correlation coefficient 95 % CI</strong></td>
<td>0.5 0.41-0.58</td>
<td>0.5 0.41-0.58</td>
<td>0.5 0.41-0.58</td>
<td>0.5 0.41-0.58</td>
<td>0.5 0.41-0.58</td>
<td>0.5 0.41-0.58</td>
<td>0.5 0.41-0.58</td>
<td>0.5 0.41-0.58</td>
<td>0.5 0.41-0.58</td>
</tr>
</tbody>
</table>

MS, Mediterranean Score; DS, Dietary Score; Med-DQI, Mediterranean-Dietary Quality Index; MAI, Mediterranean Adequacy Index; MDP, Mediterranean Dietary Pattern adherence index; rMED, relative Mediterranean diet; MSDPS, Mediterranean Style Dietary Pattern Score; PREDIMED, Mediterranean food pattern PREDIMED Study; Cardio, Cardioprotective Mediterranean diet index; MDS, Mediterranean Diet Score.

A: The remaining indexes showed correlations from 0.28 to 0.52 (MSDPS) and 0.45 (DS). The correlation coefficients between the groups of indexes (Table 3). This factor allowed us to identify three groups of indexes: group 1 (MSDPS, MDS, and MDP); group 2 (MAI, MDP, and MDS); and group 3 (DS, MAI, MDP, and MDS). In order to interpret the meaning of this second factor except for MSDPS and MDS, which were independent indexes and the second factor ranged from 0.28 to 0.37 (MSDPS) and 0.45 (DS). The remaining indexes showed correlations from 0.28 to 0.37 (MSDPS) and 0.45 (DS). The remaining indexes showed correlations from 0.28 to 0.37 (MSDPS) and 0.45 (DS).
The indexes included in the present study measure the same concept: the degree of adherence to a dietary pattern based on consumption of certain foods that are characteristic of the Mediterranean area. Hence, in theory, the correlations between these indexes should be strong; however, we found that they were weak. This weakness is probably explained by how these indexes have been developed.

For example, the indexes vary in the components included, the weight given to each and the score used.

To identify the main factors explaining this variability, we carried out an exploratory factor analysis. Much of the variability shown by the indexes was explained by two factors. The first factor explained approximately 71% of the variability, so that there was a main common factor to all indexes. Because the indexes were designed to assess the degree of adherence to the Mediterranean diet, the main factor was understood as the Mediterranean dietary pattern.

Most indexes showed correlations above 0.75 with this latent attribute (Mediterranean diet; Table 3), although it should be noted that the measurement error ranged from 28% to 59% (1 – R²; Table 3) of the variability of the measurements, thus indicating weak to fair reliability.

The second factor explained almost 18% of the variability. Thus, reducing the dimensionality of the indexes to these two factors explained 89% of the variability, so that the model fits the data excellently.

However, the correlation between the indexes and the second factor was uneven: indexes such as MAI, MSDPS or MDP had a strong negative correlation, whereas others had a low or null correlation (rMED, MedDQI) and DS had a high positive correlation. As the first factor grouped most of the indexes into a single group because they all shared a common factor, this second factor is a divergence element between indexes because it separates indexes into three differentiated groups: negative correlation (MAI, MSDPS and MDP), low or null correlation (rMED, MedDQI, MDS, PREDIMED) and high positive correlation (DS, Cardio and MS; Table 3). The most plausible hypothesis is that this second factor is related to the way in which components are treated in the index: weight or plus/minus sign of the effect of components in the score, for example.

To identify the components that are related to the second factor, we extracted factor scores for each subject and analysed the correlation between Mediterranean and non-Mediterranean components of the MAI index with

### Table 3 Correlation among factors (1 and 2) and indexes of adherence to the Mediterranean diet

<table>
<thead>
<tr>
<th>Index</th>
<th>Factor 1 β</th>
<th>Factor 1 SE</th>
<th>Factor 1 R² (%)</th>
<th>Factor 2 β</th>
<th>Factor 2 SE</th>
<th>Factor 2 R² (%)</th>
<th>Variance error</th>
<th>SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDS</td>
<td>0.83</td>
<td>0.048</td>
<td>69</td>
<td>0.17</td>
<td>0.033</td>
<td>3</td>
<td>0.25</td>
<td>0.028</td>
</tr>
<tr>
<td>MS</td>
<td>0.67</td>
<td>0.049</td>
<td>45</td>
<td>0.19</td>
<td>0.038</td>
<td>4</td>
<td>0.51</td>
<td>0.044</td>
</tr>
<tr>
<td>DS</td>
<td>0.64</td>
<td>0.049</td>
<td>41</td>
<td>0.45</td>
<td>0.039</td>
<td>20</td>
<td>0.39</td>
<td>0.041</td>
</tr>
<tr>
<td>Med-DQI</td>
<td>0.85</td>
<td>0.045</td>
<td>72</td>
<td>0.02</td>
<td>0.028</td>
<td>0.04</td>
<td>0.27</td>
<td>0.025</td>
</tr>
<tr>
<td>MAI</td>
<td>0.83</td>
<td>0.043</td>
<td>69</td>
<td>-0.52</td>
<td>0.027</td>
<td>27</td>
<td>0.04</td>
<td>0.025</td>
</tr>
<tr>
<td>MDP</td>
<td>0.76</td>
<td>0.046</td>
<td>58</td>
<td>-0.35</td>
<td>0.031</td>
<td>12</td>
<td>0.30</td>
<td>0.027</td>
</tr>
<tr>
<td>rMED</td>
<td>0.80</td>
<td>0.046</td>
<td>64</td>
<td>0.09</td>
<td>0.030</td>
<td>0.8</td>
<td>0.35</td>
<td>0.031</td>
</tr>
<tr>
<td>MSDPS</td>
<td>0.76</td>
<td>0.046</td>
<td>53</td>
<td>-0.37</td>
<td>0.032</td>
<td>14</td>
<td>0.67</td>
<td>0.030</td>
</tr>
<tr>
<td>PREDIMED</td>
<td>0.76</td>
<td>0.047</td>
<td>58</td>
<td>0.17</td>
<td>0.032</td>
<td>3</td>
<td>0.39</td>
<td>0.036</td>
</tr>
<tr>
<td>Cardio</td>
<td>0.67</td>
<td>0.049</td>
<td>45</td>
<td>0.28</td>
<td>0.037</td>
<td>8</td>
<td>0.47</td>
<td>0.043</td>
</tr>
</tbody>
</table>

β, standardised coefficient; R², reliability coefficient; variance error, standardised about measurement error; MDS, Mediterranean Diet Score; MS, Mediterranean Score; DS, Dietary Score; Med-DQI, Mediterranean-Diet Quality Index; MAI, Mediterranean Adequacy index; MDP, Mediterranean Dietary Pattern adherence index; rMED, relative Mediterranean diet; MSDPS, Mediterranean Style Dietary Pattern Score; PREDIMED, Mediterranean food pattern PREDIMED Study; Cardio, Cardioprotective Mediterranean diet index.

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![Factor chart](image)

**Fig. 2** Factor chart Mediterranean diet indexes (1: Mediterranean Diet Score; 2: Mediterranean Score; 3: Dietary Score; 4: Mediterranean-Dietary Quality Index; 5: Mediterranean Adequacy Index; 6: Mediterranean Dietary Pattern adherence index; 7: relative Mediterranean diet; 8: Mediterranean Style Dietary Pattern Score; 9: Mediterranean food pattern PREDIMED Study; 0: Cardioprotective Mediterranean diet index).
Table 4 Correlations among factors and common food components in Mediterranean adherence indexes

<table>
<thead>
<tr>
<th></th>
<th>Pulses</th>
<th>Cereals</th>
<th>Potatoes</th>
<th>Fruit</th>
<th>Vegetables</th>
<th>Fish</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Correlation</td>
<td>Coefficient</td>
<td>95% CI</td>
<td>Correlation</td>
<td>Coefficient</td>
<td>95% CI</td>
</tr>
<tr>
<td>Factor 1</td>
<td>0.24</td>
<td>0.13, 0.34</td>
<td>0.32</td>
<td>0.22, 0.41</td>
<td>0.16</td>
<td>0.06, 0.27</td>
</tr>
<tr>
<td>Factor 2</td>
<td>0.12</td>
<td>0.02, 0.23</td>
<td>-0.08</td>
<td>-0.19, 0.03</td>
<td>0.03</td>
<td>-0.08, 0.14</td>
</tr>
<tr>
<td>Olive oil</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Alcohol</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Red meat</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Dairy products</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Fatty acids ratio</td>
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<tr>
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In general, the indexes performed satisfactorily in measuring adherence to the Mediterranean diet. However, the lack of high correlation between them indicates that these indexes are not equally valid and reliable. The results reported here suggest that further validation and refinement of these indexes are needed. Additionally, the lack of agreement on the criteria for defining the Mediterranean dietary pattern remains a challenge, as evidenced by the variability in factor scores among different studies. Thus, the development of a standardized approach for defining adherence to the Mediterranean diet becomes crucial for improving the reliability and comparability of the indexes.
the need to reach a consensus on the components included in the Mediterranean diet indexes, specifically the dairy products, MS ratio and lean meat.

On the basis of the correlations observed between the main factor and the components, we conclude that, in addition to the MS ratio, fruit and vegetables are the most correlated components of indexes designed to assess adherence to the Mediterranean diet. In addition, as expected, we also found strong positive correlations between adherence to the Mediterranean diet and olive oil, pulses, cereals and fish components; on the other hand, a strong negative correlation was found with red meat. Thus, these components should be included in a reliable index to assess adherence to the Mediterranean diet, so that the index would make easy the discrimination of the consumption among subjects increasing the internal consistency. Conversely, weak correlations were found between the adherence to the Mediterranean diet and potatoes, alcohol, dairy products and lean meat.

However, given that different correlations between components and the adherence to the Mediterranean diet have been found, the weights of the components in such indexes should be adjusted accordingly.

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References

Reliability of Mediterranean diet indexes

2345


Food consumption and civil society: Mediterranean diet as a sustainable resource for the Mediterranean area

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Abstract

Objective: To define the Mediterranean diet model inside a Mediterranean social and cultural food framework and from the perspective of a local model of consumption.

Design: Reflection and review of literature available in relation to the Mediterranean diet, locality and proximity.

Setting and subjects: Mediterranean region and its populations.

Results: The Mediterranean local food system under the term Mediterranean diet encourages local production and local consumption. From this perspective, this model takes part of every local Mediterranean lifestyles and encourages sustainability.

Conclusions: From a local Mediterranean point of view and as a proximity model of consumption, Mediterranean food and diet can be a sustainable resource for the Mediterranean area.

Keywords
Mediterranean diet
Sustainability
Tradition
Trust
Naturalness

During almost the whole twentieth century, but especially in the second half, transformations in the food field have been increasing. In societies with a higher socio-economic development, with local markets well provided with food, this has, in general terms, involved a larger production and distribution of products at an industrial level and more fluid access to a large variety of food by the public, at much more accessible prices.

In developing countries, with home economies – and not only home economies – very attached to small production and subsistence agriculture, this process has had very different effects, and not always positive. The reality is that, as the FAO points out(1), one billion people live in chronic hunger globally.

Food knowledge is social and industrial trust

In developed countries, very well provided, the argument, however, is to the contrary. On the other hand, we find that such production, nowadays more massified and industrialised than ever, has likewise seen itself affected in a different way: by different health problems (diseases, infections, etc.) related to industrial production as well as, and consequently, by a growing mistrust among the population towards the food they consume(2).

In this context, it should also be noted that systems for representing citizens evolve more slowly than production and distribution systems, with technological innovations in products and packaging, places of production and transport, storage and distribution, as well as in relation to other individuals. Consumers have only a partial understanding of these developments, which span the entire period from what might be termed the ‘traditional’ or ‘pre-industrial’ situation to the present-day era of ‘cracking’ and ‘assembly’. In this pattern of evolution, the role of food manufacturers has changed and food itself is now presented in two ways: on the one hand, it has become more artificial, and on the other, it must retain a certain ‘natural’ status, as this is the sole tangible nexus with nature for the consumer.

Moreover, given that consumers today now have a much wider range of food flavours to choose from, it is important to consider the fact that they can have no more than a partial knowledge of the variety of tastes and aromas of foods whose organoleptic and microbiological qualities have improved and continue to do so. The time lag between one experience of a particular foodstuff and the next occasion when it is eaten makes it more difficult for people to build up a personal memory bank of different food tastes(3).

On the other hand, changes in food come up against a degree of dissatisfaction on the part of the consumer, who is faced, for example, with ‘industrial’ foods that he finds bland, lacking in the taste and aroma these foods used to have, and perhaps even dangerous. Thus, nowadays it is impossible not to emphasise the doubts and the feeling of danger connected to the impossibility of control over...
industrial production processes by a broad strata of consumers. In the same way, we are living in times in which urban people – most of the population in industrialised countries – have contact with only end elements of the chain, that is, final points of distribution and products.

This implies that, concerning food, consumers' trust is taken for granted in phases of the process that are absolutely unknown by them, leaving out the ignorance of the processes undertaken by experts, who are entrusted with the control of the different phases of the process that extend from the earliest stages of production to the table, through the factory and the supermarket. The consumer, in short, gets further and further from the food production process and loses control over it as well as information about it. In view of this situation, the public opinion manifests its fears and concerns widely and in different ways. In the words of the North American anthropologist Sydney Mintz(4), ‘recent history and mass media are preparing us for an environmental catastrophe. We are willing to discover impurity at every step, willing to be threatened by impurity at every moment’. Unawareness of the mentioned production procedures, of food transformation, makes consumers mistrust the industrial processes and the mediators who create, transform, pack, transport them, etc. One of the most important consequences of this is the increasing attempts by consumers to recover control, to go back, even mentally, to those stages in which things were ‘pure’, ‘healthy’, ‘authentic’ and handmade, made with time… In a ‘traditional’ way, in short. Much of our longing for what is pure – water, air, vegetables, fruits – looks back yearning for a past more and more on its way to extinction(4). A past that brings in ‘quality’ and ‘naturalness’ to an uncertain present. It is not strange, then, that publicity has decided to exploit these aspects broadly, offering ‘traditional’, ‘old style’, ‘homemade’, ‘grandmother’s’ dishes, etc.

Consumers usually sum up their perception of this entire panorama by mentioning notions to do with authenticity and quality, which implies perfect adaptation to their culture and representational system. Food cannot be observed as an isolated element from their cultural framework. Otherwise it can lose all meaning to the extent that it does not seem to be ‘real food’.

New strategies

This trend, this ‘search’ by consumers for what is natural, hand-crafted, has not gone unnoticed by the different social actors involved in this process: public and private institutions, producers, industrialists, traders, publicists, editors, restaurateurs, tourism promoters… At the same time that users try to recover control over what they eat, from the other side of the commercial barrier this trend towards what is ‘traditional’ and ‘natural’ is reaffirmed. But we cannot forget that, as with every other aspect of cultures, nothing is static, everything is ductile and is in continuous re-élaboration, re-creation. Thus, ‘tradition’ is built; it is ‘created’ and ‘re-created’ every day(5). Hence, for example, a strategy that fast-food chains have taken into account in order to guarantee themselves future customers has precisely been that of building customers’ loyalty from the time they are children, making them integrate fast-food taste and smell as part of their past, of their personal food tradition. As the North American writer Eric Schlosser(6) points out in relation to fast-food establishments in the USA, ‘the flavours of food during childhood seem to leave a permanent mark, and adults usually go back to them without knowing why most of the time. This “soothing food” of childhood becomes a source of pleasure and calmness, an increasing attempt to provide the public in general with broader information about the offered product, information that takes us to its origin’, and that points out the ‘traditional’ and ‘hand-crafted’ elements of it. This is an element that fast-food chains strongly try to provide.

The search for ‘traditional’, ‘authentic’ dishes, the appreciation of ‘family cooking’, old cookbooks, orally transmitted recipes, etc. takes place, very particularly, in a social and historical moment in which the industrial transformation of food increasingly moves consumers of industrialised countries away from the control and knowledge of its production procedures. Going back to what is ‘traditional’, to the old cooking ‘teachings’, to things the origin of which is known – including the growth of the importance and of the search for ‘bio’ products or for ecological products – to those whose transformation procedures are trusted, then becomes a value intimately linked to the enjoyment of cooking as well as to nutrition in general terms. Such an appreciation involves a social demand for these types of products, which has an effect on different social, cultural and economic environments – such as the case of individuals and families, especially those who can afford to place quality before price; ‘gourmets’ and gastronomic critics and their influence face to face to the media; the publicity and editorial fields, cooks and restaurateurs, touristic operators, etc. – who, from their own professional spheres, have contributed and still contribute to this fact as well, inside a general social process that does not seem to be, at least in the near future, drawing to an end.
Mediterranean diet is an outstanding resource, yet it has been neglected in favour of intensification and industrialisation of agricultural systems. More recently, the growing concern over food safety has motivated a renewed interest in organic foods and locally produced and sustainable foods, particularly in the Mediterranean area. Movements like ‘Slow Food’, born in Turin (Italy), are based on the defence of local productions, biodiversity and sustainability, where both socio-cultural and biological aspects are included:

'Slow Food is a non-profit, eco-gastronomic member-supported organization that was founded in 1989 to counteract fast food and fast life, the disappearance of local food traditions and people's dwindling interest in the food they eat, where it comes from, how it tastes and how our food choices affect the rest of the world. To do that, Slow Food brings together pleasure and responsibility, and makes them inseparable.'

As every food system in its own biosocial context, the Mediterranean diet is an outstanding resource, yet it has not been fully acknowledged and enhanced within the Euro-Mediterranean partnership, for the achievement of effective sustainable development in the Mediterranean, as was pointed out in the report Mediterranean Strategy on Sustainable Development, issued in 2005 by the United Nations Environment Programme:

‘Mediterranean agricultural and rural models, which are at the origins of Mediterranean identity, are under increasing threat from the predominance of imported consumption patterns. This trend is illustrated in particular by the decline of the Mediterranean dietary model despite the recognized positive effects on health. The prospective scenario for the expected impacts of trade liberalization, climate change and the lack of efficient rural policies offers a gloomy picture in some southern and eastern Mediterranean countries, with the prospect of aggravated regional imbalances, deeper ecological degradation and persistent or accrued social instability... . Create a conducive regional environment to help countries develop policies and efficient procedures for the labelling and quality certification of Mediterranean food products and to promote the Mediterranean diet.'

In this sense, and as Akkelidou points out regarding the Mediterranean area, 'Current agricultural and trade policies are inappropriate (...). Thus, it is imperative to reform them to ensure the quality, safety and availability of food, as well as the sustainability of production, resources and the environment'.

Conclusions

In short, the consumer is moving further and further away from the processes used to produce the food he eats, foodstuffs that are treated in industrial processes that are beyond his influence and in many cases his understanding. Consumers are becoming increasingly unhappy with such processes and are looking instead for produce they believe to be ‘natural’, ‘healthy’ and ‘traditional’. In doing so, they are trying to regain their control over and confidence in the food they eat.

In this context (and as every food system in its own biosocial context), the Mediterranean diet is an outstanding resource – locally produced in culturally coherent contexts – for the Mediterranean area.

While good nutrition should be a goal of agriculture, it is imperative that concerns over sustainability are not lost in the process. Many dietary patterns can be healthy, but they can vary substantially in terms of their resource cost. The Mediterranean diet has been characterised, analysed and promoted through a variety of methods within a number of scientific and applied disciplines (Burlingame and Dernini, unpublished results). It continues to be recognised and appreciated as a sustainable and culturally coherent diet in the Mediterranean region. In this framework, the recent recognition in November 2010 of the Mediterranean diet as a World Immaterial Heritage by UNESCO can be an important future challenge for Mediterranean local food production and manufacture. However, this major challenge involves a strong commitment to safeguarding and promotion that cannot be neglected. In this framework, the active role of the public sector is absolutely necessary.

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