

Extra Virgin Olive Oil and the Mediterranean Diet:

A Bioactive and Bioethic Alliance for Health

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The connection between diet and disease is one of the oldest and most persistent questions in the field of medicine and public health. For centuries, physicians and researchers have observed how dietary habits influence the onset and progression of chronic illnesses. As early as 1908, scientists found that rats fed animal-based diets high in eggs, milk, and meat developed arterial lesions that closely resembled those found in human cases of atherosclerosis. These early experiments suggested a direct link between certain types of food and cardiovascular disease, laying the groundwork for future research into diet-related health risks.¹

This contrast in dietary effects became even more pronounced in the mid-20th century.

American researchers studying global health patterns observed that populations living in Mediterranean countries, such as Greece, Italy, and parts of Spain, exhibited significantly lower rates of cardiovascular diseases, heart attacks, and certain types of cancer, despite consuming diets that were relatively high in fats. This observation, often referred to as the "Mediterranean paradox," challenged the prevailing assumption that all high-fat diets were inherently harmful.

Further investigation revealed that the fats consumed in these regions primarily came from sources such as olive oil, nuts, and fish, rather than from processed foods or red meat. Moreover, the Mediterranean diet was characterized by an abundance of fruits, vegetables, legumes, whole grains, and moderate consumption of wine, usually during meals. Physical activity and strong social bonds around food and mealtimes also appeared to contribute to these populations' overall well-being.²

This paradox catalyzed an international interest in understanding the protective benefits of the Mediterranean way of eating. Over time, numerous epidemiological studies and clinical trials have supported the health advantages of this diet, linking it to reduced inflammation, improved lipid profiles, and better metabolic health.

Today, the Mediterranean diet is globally recognized not only for its cardiovascular benefits but also for its role in promoting longevity and preventing a range of chronic diseases, from diabetes to neurodegenerative disorders.

1. The Mediterranean Diet and its Scientific Foundations

The Mediterranean diet, rich in vegetables, fruits, legumes, whole grains, and particularly extra virgin olive oil (EVOO), has proven to be far more than a cultural tradition, it represents a scientifically validated model for healthy living. Its benefits extend well beyond basic nutrition, offering protection against a wide array of chronic diseases, including cardiovascular disease, type 2 diabetes, certain cancers, and neurodegenerative disorders. Recognized in 2013 by UNESCO as part of the Intangible Cultural Heritage of Humanity, the Mediterranean diet is a testament to the enduring wisdom of regional food practices that prioritize both nourishment and enjoyment.

At the heart of this dietary pattern lies a harmonious balance of macronutrients, a high intake of antioxidants and anti-inflammatory compounds, and a culinary philosophy that values simplicity, seasonality, and quality. But the Mediterranean diet is not solely defined by what is consumed, it is deeply embedded in how food is prepared, shared, and experienced. Meals are often communal, slow-paced, and centered around fresh, locally sourced ingredients. There is a respect for tradition, for the land that produces the food, and for the act of eating as a ritual that nourishes both body and spirit. This holistic approach is increasingly seen as essential to its health-promoting effects.

One of the most fascinating developments in recent years is the emerging field of nutritional epigenetics, which has begun to shed light on how the foods we eat can influence gene expression. Epigenetics refers to changes in gene activity that do not involve alterations to the underlying DNA sequence. These changes can be triggered by a range of external factors, including diet, physical activity, stress, exposure to toxins, and the gut microbiome, and can significantly impact an individual's health trajectory.

This dynamic interplay between environment and genes suggests that food is not merely fuel but an active participant in shaping our biological destiny. Components of the Mediterranean diet, particularly bioactive compounds found in extra virgin olive oil, such as polyphenols, have been shown to modulate epigenetic mechanisms. These compounds may help regulate inflammation, oxidative stress, and even cancer-related gene pathways, thereby influencing disease susceptibility and progression.

In this context, the Mediterranean diet emerges not only as a preventive health strategy but also as a powerful tool for personalized medicine. It bridges the gap between traditional wisdom and cutting-edge science, illustrating how time-honored food choices can influence genetic expression and long-term health in ways we are only beginning to understand. As research continues to explore the connections between diet, genes, and disease, the Mediterranean model offers both inspiration and guidance for a healthier future rooted in sustainable, culturally rich practices.³

2. The Composition of EVOO: A Functional Biocomplex

Extra virgin olive oil (EVOO) is far from being merely a source of dietary fat. It represents a highly complex and biologically active matrix, rich in a wide variety of compounds that collectively contribute to its well-documented health benefits. Unlike refined oils, EVOO is obtained through mechanical pressing without the use of heat or chemical processing, thereby preserving its delicate chemical profile and enhancing its nutritional value.

At the core of EVOO's lipid composition are monounsaturated fatty acids (MUFA), with oleic acid being the most abundant. Oleic acid plays a central role in cardiovascular protection, helping to improve lipid profiles by increasing HDL (good cholesterol) and reducing LDL (bad cholesterol) oxidation. In addition to MUFA, EVOO contains polyunsaturated fatty acids (PUFA) such as linoleic acid, which contribute to essential cellular functions and support the integrity of cell membranes. Saturated fatty acids (SFA), including palmitic and stearic acids, are present in lower amounts and are structured in a way that mitigates their potential negative impact.

However, the most compelling evidence for EVOO's health-promoting properties stems not from its fat content alone, but from its rich and diverse array of phenolic compounds. These bioactive molecules, present in much higher concentrations in extra virgin varieties compared to refined oils, exhibit potent antioxidant, anti-inflammatory, and even anti-carcinogenic activities. Notably, compounds such as oleuropein, hydroxytyrosol, and tyrosol have attracted significant scientific interest for their ability to influence key cellular processes.

Oleuropein, found in the olive leaf and unripe olives, is a powerful phenolic with demonstrated effects in reducing oxidative stress, modulating inflammatory responses, and inhibiting LDL oxidation, an early step in the development of atherosclerosis. Tyrosol and its derivative hydroxytyrosol are particularly effective at neutralizing reactive oxygen species (ROS) and improving endothelial function, which is vital for maintaining healthy blood vessels and reducing the risk of cardiovascular disease. Moreover, the specific structural arrangement of fatty acids within the triglyceride molecules in EVOO plays a crucial role in their digestion, absorption, and metabolic impact. This molecular architecture influences how fats are broken down and transported in the body, enhancing their availability and efficacy in modulating processes such as insulin sensitivity, lipid metabolism, and inflammation regulation.⁴

3. Cardiovascular Protection and Anti-inflammatory Activity

The protective role of extra virgin olive oil (EVOO) in cardiovascular disease (CVD) prevention is supported by a robust and steadily growing body of scientific evidence, encompassing epidemiological data, clinical trials, and molecular research. Its complex composition, rich in

monounsaturated fats and phenolic compounds, confers a unique set of biological properties that act synergistically to promote cardiovascular health and reduce the risk of atherosclerosis, hypertension, and related complications.

Among its well-documented cardiovascular effects, EVOO has been shown to:

- **Reduce total and LDL cholesterol levels**, thereby lowering the risk of lipid accumulation in arterial walls.
- **Improve endothelial function** by enhancing nitric oxide (NO) bioavailability, which facilitates vasodilation and supports vascular homeostasis.
- **Inhibit the proliferation and migration of vascular smooth muscle cells (VSMCs)**, a key event in plaque formation and arterial remodeling.
- **Stabilize blood glucose levels and attenuate postprandial metabolic responses**, contributing to improved insulin sensitivity and reduced glycemic variability.

Beyond these metabolic effects, the phenolic compounds in EVOO exhibit powerful anti-inflammatory and antioxidant actions. Chronic inflammation and oxidative stress are central drivers in the pathogenesis of CVD, particularly in the initiation and progression of endothelial dysfunction, arterial stiffness, and plaque instability. EVOO polyphenols, such as hydroxytyrosol, oleuropein, and apigenin, target these mechanisms at the molecular level.

One of the primary molecular pathways modulated by EVOO polyphenols is NF- κ B (nuclear factor kappa-light-chain-enhancer of activated B cells), a critical transcription factor involved in the expression of pro-inflammatory cytokines, adhesion molecules, and enzymes like COX-2 and iNOS. By inhibiting NF- κ B activation, EVOO components can significantly reduce vascular inflammation and oxidative damage. Additionally, they influence the MAPK (mitogen-activated protein kinase) signaling pathway, which plays a role in cellular stress responses and inflammatory gene expression. Experimental studies have further highlighted the therapeutic potential of individual phenolic compounds. For instance, apigenin, a flavonoid found in olive leaves and derivatives, has demonstrated the ability to suppress endothelial inflammation induced by tumor necrosis factor-alpha (TNF- α). It downregulates the expression of endothelial nitric oxide synthase (eNOS) and matrix metalloproteinase-9 (MMP-9), enzymes involved in vascular remodeling and inflammation.

Remarkably, even by-products of olive oil production, such as olive pomace, have been shown to possess significant bioactivity. Extracts from olive pomace have been found to protect endothelial cells under anoxic (low oxygen) conditions, mimicking ischemic stress. These extracts reduce the expression of key inflammatory mediators including COX-2, inducible nitric oxide synthase (iNOS), and TNF- α , suggesting that the cardioprotective properties of the olive tree extend far beyond the oil itself and could be harnessed for sustainable health interventions.⁵

4. From Inflammation to Cancer: Broader Protective Effects

The health benefits of extra virgin olive oil (EVOO) and its phenolic compounds extend well beyond cardiovascular protection. Increasingly, scientific research is uncovering their role in modulating chronic inflammatory processes throughout the body, most notably within the gastrointestinal tract, where sustained inflammation is a known contributor to both inflammatory bowel diseases (IBD) and colorectal cancer.

The modern diet, particularly one rich in processed foods and oxidized lipids such as oxysterols (formed during the heating or oxidation of cholesterol-containing foods), has been implicated in disrupting intestinal homeostasis. These compounds can compromise the intestinal epithelial barrier, trigger immune activation, and induce oxidative stress, factors that contribute to the onset and progression of chronic inflammatory conditions like Crohn's disease, ulcerative colitis, and ultimately, colorectal carcinogenesis.

In this context, EVOO emerges as a potent dietary ally. Its phenolic constituents, such as hydroxytyrosol, oleuropein, and verbascoside, have demonstrated the capacity to preserve the integrity of the intestinal epithelial layer, a critical defense against microbial translocation and immune dysregulation. These compounds enhance tight junction protein expression, reduce intestinal permeability ("leaky gut"), and inhibit the recruitment of immune cells that drive mucosal inflammation.

In vitro and ex vivo studies offer compelling evidence for these protective effects. When intestinal epithelial cells are exposed to oxidative stress or inflammatory stimuli, EVOO polyphenols help mitigate cellular damage by reducing the production of pro-inflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF- α), and interleukin-1 β (IL-1 β). They also act as direct scavengers of reactive oxygen species (ROS), thereby restoring redox balance and preventing DNA damage, one of the early events in cancer initiation.

Moreover, EVOO's polyphenols have shown potential to influence gut microbiota composition, another critical factor in inflammation and cancer risk. By promoting the growth of beneficial bacterial strains (such as *Lactobacillus* and *Bifidobacterium*) and suppressing pathogenic microbes, EVOO helps maintain a favorable microbial balance that supports immune tolerance and reduces mucosal inflammation.

Emerging research also suggests that EVOO may play a role in epigenetic regulation within the gastrointestinal tract. Some of its bioactive compounds are capable of influencing gene expression involved in detoxification, apoptosis, and cell cycle regulation, mechanisms that are fundamental to cancer prevention.

Taken together, these findings support the hypothesis that regular consumption of high-quality EVOO, especially as part of a Mediterranean-style diet, can serve as a nutritional intervention to modulate both systemic and localized inflammation. This not only reduces the risk of IBD and colorectal cancer but may also have broader implications in preventing other inflammation-associated cancers, including breast and prostate cancer.

As we deepen our understanding of the diet-inflammation-cancer axis, EVOO stands out as a powerful example of how traditional, plant-based dietary elements can provide targeted, multi-level protection against some of the most pressing chronic diseases of our time.⁶

5. EVOO and the Gut Microbiota: A Symbiotic Relationship

One of the most compelling frontiers in modern nutritional science is the dynamic, bidirectional relationship between diet and the gut microbiota, the vast, diverse community of microorganisms including bacteria, archaea, fungi, and viruses that reside primarily in the colon. Far from being passive inhabitants, these microbes actively participate in essential physiological processes such as digestion, immune modulation, vitamin synthesis, neurotransmitter production, and the regulation of inflammation. Maintaining a healthy and balanced microbiota is now recognized as a cornerstone of overall well-being.

Extra virgin olive oil (EVOO), with its rich profile of polyphenols and monounsaturated fats, plays a pivotal role in shaping the gut microbial environment. Unlike simple nutrients that are fully absorbed in the upper gastrointestinal tract, many of EVOO's polyphenolic compounds, such as oleuropein, hydroxytyrosol, and tyrosol, resist digestion in the small intestine. They reach the colon largely intact, where they serve as substrates for microbial fermentation.

Once in the colon, these polyphenols undergo biotransformation by specific microbial enzymes, yielding a variety of low-molecular-weight metabolites with enhanced bioactivity. This interaction functions similarly to a prebiotic effect, stimulating the growth and metabolic activity of beneficial bacteria such as *Lactobacillus*, *Bifidobacterium*, and *Faecalibacterium prausnitzii*. These microbes are known to produce short-chain fatty acids (SCFAs) like butyrate, which nourish colonocytes, strengthen the intestinal barrier, reduce local inflammation, and have protective effects against colorectal cancer.

At the same time, EVOO polyphenols exhibit antimicrobial properties against pathogenic and pro-inflammatory microbes including *Escherichia coli*, *Clostridium perfringens*, and *Helicobacter pylori*. This selective modulation helps maintain microbial diversity and equilibrium, a key factor in preventing dysbiosis, a condition linked to numerous diseases, from metabolic syndrome to autoimmune disorders.

Beyond local gut effects, the systemic impact of these interactions is increasingly evident. Polyphenol-derived microbial metabolites can enter the bloodstream and exert physiological effects on distant organs. For example:

- **In the liver**, these metabolites can reduce lipid accumulation, improve insulin sensitivity, and modulate detoxification pathways.
- **In the brain**, they may influence the gut-brain axis by affecting neurotransmitter levels, reducing neuroinflammation, and supporting cognitive function.
- **In the cardiovascular system**, they contribute to improved endothelial function, reduced oxidative stress, and lower blood pressure.

This gut-mediated extension of EVOO's benefits aligns with the emerging concept of "food as medicine," in which dietary choices are recognized not only for their nutritive value but also for their ability to influence the microbiome and, through it, systemic health. The intimate relationship between EVOO and the gut microbiota represents a symbiotic alliance, one in which EVOO nourishes beneficial microbes, and in return, these microbes transform its compounds into potent health-promoting agents.

In the broader context of the Mediterranean diet, EVOO thus plays a dual role: it acts both directly, via its bioactive constituents, and indirectly, through its favorable modulation of the gut microbiota. This synergy underscores the importance of whole-diet approaches to health, and points to the microbiome as a key mediator in the complex interaction between nutrition, immunity, and chronic disease prevention.⁷

6. Ethical Reflections on Health, Food, and Knowledge in the Era of Nutritional Transition

As the scientific consensus grows around the health benefits of extra virgin olive oil (EVOO) and the Mediterranean diet, we find ourselves at a crucial ethical crossroads. Nutritional science, once focused narrowly on biological mechanisms, is increasingly forced to reckon with questions of equity, sustainability, culture, and communication. In this broader framework, nutrition becomes not just a matter of physiology, but of justice, stewardship, and collective well-being.

6.1. Access and Nutritional Inequality

While EVOO is celebrated as a pillar of preventive nutrition, particularly due to its rich content of monounsaturated fats and polyphenols, it remains inaccessible to many. Premium EVOO varieties, those most densely packed with health-promoting compounds, are often priced beyond the reach of lower-income populations. This creates a paradox: the very groups most at risk of diet-related diseases

(such as type 2 diabetes, obesity, and cardiovascular conditions) are the least likely to access these preventive resources.

In many global regions, and even within Mediterranean countries themselves, cheaper, highly processed vegetable oils dominate the shelves of supermarkets and school cafeterias. This discrepancy is not merely an economic issue, it is an ethical failing of public policy, agriculture, and food systems.

Public health responses must go beyond individual education. They must include structural interventions: government subsidies for health-promoting foods, nutritional assistance programs that prioritize quality over quantity, policies supporting small-scale producers, and school-based meal programs rooted in traditional dietary patterns. Without such systemic efforts, the “health gap” will continue to widen, reinforcing cycles of disease and poverty.⁸

6.2. Commodification of Tradition and Cultural Ethics

The Mediterranean diet, officially recognized by UNESCO as Intangible Cultural Heritage, represents a living system: rooted in seasonal rhythms, biodiversity, intergenerational knowledge, and communal eating practices. However, in the global marketplace, this holistic food culture is increasingly fragmented and commodified.

Functional compounds such as oleuropein, hydroxytyrosol, and tyrosol are extracted, isolated, and repackaged into capsules, drinks, and supplements—often stripped of their cultural and ecological contexts. While nutraceuticals may offer convenience or concentrated therapeutic potential, this biomedical reductionism risks turning ancestral knowledge into a proprietary commodity.

It also raises questions of intellectual and economic justice. Who owns the right to market a molecule embedded in centuries of collective culinary wisdom? Are smallholder olive growers, traditional farmers, and regional communities benefitting from this commercialization? Or are they being bypassed in favor of global pharmaceutical and biotech players?

An ethical path forward must ensure fair recognition, compensation, and partnership with local stakeholders. It must safeguard the cultural integrity of traditional food systems, resist the erosion of identity and meaning in the name of industrial efficiency or scientific validation.⁹

6.3. Sustainability and Intergenerational Responsibility

As the global demand for EVOO grows, fueled by its health halo and expanding markets, the environmental impact of olive oil production becomes a central ethical concern. Monoculture expansion, water overuse, soil degradation, and pesticide reliance can threaten the ecological health of Mediterranean landscapes.

Sustainability, in this context, is not a marketing label, it is an intergenerational obligation. Ethical nutrition must ask not only what foods support human longevity, but also what agricultural systems can endure for generations without compromising planetary boundaries.

Encouragingly, innovations in circular agriculture, such as repurposing olive pomace, pits, and leaves into valuable products, offer ways to reduce waste and maximize resource efficiency. However, even these initiatives must be evaluated critically to ensure they do not become vehicles for greenwashing or excuses for unchecked industrial expansion.

True sustainability demands a balance between ecological limits, cultural values, and economic livelihoods. It involves supporting diversified farms, respecting local ecosystems, and ensuring fair labor practices across the supply chain.¹⁰

6.4. Ethics of Scientific Communication and Consumer Autonomy

In an era of health influencers, viral trends, and commercial health claims, how scientific knowledge is communicated to the public becomes a moral issue. EVOO is now frequently branded as a "superfood," but such labels risk oversimplifying science, distorting expectations, and undermining consumer trust. Ethical communication demands clarity, humility, and respect for complexity. Scientists, journalists, and health professionals have a duty to inform without sensationalizing, presenting evidence with its limitations, contextualizing health claims, and avoiding deterministic narratives that reduce wellness to single ingredients.

Consumer autonomy hinges on access to truthful, nuanced information. This includes helping individuals understand how EVOO fits into a broader dietary and lifestyle pattern, what kinds of EVOO retain the most bioactive compounds, and how environmental or cultural factors shape nutritional outcomes. Moreover, special care must be taken with vulnerable populations, those living with chronic illnesses, dietary restrictions, or limited health literacy. The promise of "miracle foods" may create false hope or unhelpful guilt, when in fact health is shaped by many intersecting determinants.¹¹

7. Ethics at the Crossroads of Food, Science, and Society

Ultimately, extra virgin olive oil, and by extension, the Mediterranean diet, is more than a sum of its nutrients. It is a cultural, ecological, and ethical expression of how humans relate to food, to one another, and to the planet. Treating food merely as a tool for disease prevention reduces it to a pharmaceutical model, efficient, measurable, and alienated from meaning.¹²

A more ethical and holistic vision of nutrition asks deeper questions:

- What kind of food system supports collective well-being, not just individual health?

- How do we align scientific progress with cultural preservation and environmental justice?
- What would it look like to build a world where eating well is not a privilege, but a right?

For food systems to be truly transformative, they must be:

- **Just:** ensuring equitable access to nutritious, culturally relevant food for all
- Transparent – offering clear, evidence-based information free from manipulation
- **Sustainable:** respecting planetary boundaries and supporting regenerative practices
- **Culturally respectful:** honoring traditional knowledge and local food sovereignty
- **Inclusive:** centering the voices and experiences of diverse communities

This ethical horizon invites us to move beyond the question, “What should we eat to live longer?” toward a more profound inquiry: How should we eat to live better, together, fairly, and sustainably?

Conclusions

Extra virgin olive oil is more than a staple of Mediterranean cuisine, it is a functional food with proven capacity to reduce the risk of cardiovascular, inflammatory, and metabolic diseases. Its effects are not isolated to the vascular system but extend to the gut, brain, and beyond, thanks to its complex composition of bioactive lipids and polyphenols.

Understanding and harnessing these properties requires a multidisciplinary approach, bridging nutritional science, molecular biology, epigenetics, and microbiology. At the same time, it demands ethical consideration of how such knowledge is translated into practice, ensuring health promotion is both effective and equitable.

In an age where lifestyle-related diseases are surging, revisiting traditional diets through the lens of modern science reveals a simple yet profound truth: food, when thoughtfully cultivated and wisely consumed, is not only nourishment, it is medicine.

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