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REVIEW ARTICLE

Olive Oil as a Source of Bioactive Compounds: The Role of Polyphenols, Antioxidants, and Other Constituents in Its Health-Related Effects

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ABSTRACT

Olive oil has been used for nutritional, medicinal, cosmetic, and cultural purposes for millennia. Contemporary research indicates that its health-related properties are associated not only with its high content of monounsaturated fatty acids, particularly oleic acid, but also with a complex fraction of bioactive constituents. This review integrates historical perspectives with current evidence on the chemical composition, major bioactive compounds, mechanisms of action, and potential health-related effects of olive oil and other Olea europaea L-derived products. It focuses on hydroxytyrosol, tyrosol, oleuropein and ligstroside derivatives, oleacein, oleocanthal, and other minor constituents. Experimental, epidemiological, and clinical evidence suggests that these compounds may influence oxidative stress, inflammatory signaling, lipid metabolism, endothelial function, and other pathways relevant to chronic disease. The most consistent clinical evidence supports olive oil consumption, particularly within a Mediterranean dietary pattern, for cardiovascular and overall health.

In contrast, evidence for neuroprotective, cancer-related, and wound-healing effects remains heterogeneous. Olive leaves and olive-processing by-products also represent promising sources of bioactive phenolic compounds. Further standardized clinical studies are required to clarify their bioavailability, dose-response relationships, long-term safety, and clinical relevance.

Keywords. Antioxidant activity; Extra-virgin olive oil; Hydroxytyrosol; Olea europaea; Oleocanthal; Olive oil; Phenolic compounds.

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INTRODUCTION

Olive oil has been an integral component of Mediterranean nutrition, culture, and traditional practices for millennia. Archaeological, palaeobotanical, and historical evidence indicates that olive domestication and early olive oil production developed in the eastern Mediterranean and Near East and subsequently became closely associated with the economic and cultural traditions of Mediterranean civilizations.[1] Beyond its nutritional value, olive oil was also used in religious practices, cosmetics, body care, and medicinal preparations in the ancient Mediterranean world.[1,2]

The long-standing use of olive oil has acquired renewed scientific relevance with advances in nutritional science, biochemistry, and molecular medicine. Contemporary research has identified a complex chemical composition that may contribute to its biological properties. Olive oil is characterized by a lipid fraction dominated by monounsaturated fatty acids, particularly oleic acid, together with a quantitatively smaller but biologically important fraction containing phenolic compounds, tocopherols, phytosterols, squalene, and other bioactive constituents. Extra-virgin olive oil (EVOO) is of particular interest because mechanical extraction and limited processing favor preserving these minor components.[3]

Among the bioactive constituents of olive oil and olive-derived products, hydroxytyrosol, tyrosol, oleuropein and its derivatives, oleacein, and oleocanthal have attracted considerable scientific interest.[3,4] Experimental, epidemiological, and clinical research has investigated the antioxidant and anti-inflammatory activities of olive phenolics and their potential effects on lipid metabolism, endothelial function, oxidative stress, cellular signaling, and other mechanisms relevant to chronic disease.[4,5] These findings provide a biological framework for evaluating the potential contribution of olive oil and its constituents to human health, while highlighting the need to distinguish mechanistic and preclinical findings from clinically established effects.[5]

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Accordingly, this review integrates the historical perspective of olive oil with contemporary evidence on its chemical composition, principal bioactive constituents, mechanisms of action, and health-related effects. Attention is given to olive-derived phenolic compounds and the evidence concerning their potential roles in oxidative stress and inflammation, cardiovascular and metabolic health, neuroprotective mechanisms, cancer-related biological pathways, and tissue repair and wound healing. The review also considers olive leaf extracts and phenolic-rich olive processing by-products as additional sources of bioactive compounds with potential biomedical applications.

Interpretive evidence hierarchy

For clarity, evidence is classified descriptively: A, randomized trials reporting clinical events; B, randomized trials reporting intermediate risk factors or biomarkers; C, prospective observational studies; D, human pharmacokinetic or mechanistic investigations; E, animal experiments; and F, in vitro studies. These labels identify study design, not formal GRADE certainty or an overall quality score. Small trials, inconsistent formulations, confounding, and indirectness may substantially reduce confidence within any category.

Methods of literature identification and critical appraisal

This article is a narrative, clinically oriented review rather than a systematic review or meta-analysis. The initial manuscript synthesized the cited historical, chemical, mechanistic, epidemiological, and interventional publications. For this revision, priority is given to landmark randomized outcome trials, human intervention studies, prospective cohorts, and systematic syntheses, with experimental findings used to explain biological plausibility. Evidence is interpreted by study design, route of exposure, comparator, and outcome type. No exhaustive database search, independent dual screening, formal risk-of-bias assessment, or quantitative pooling was performed; therefore, completeness of retrieval and formal certainty grading cannot be claimed. The authors should document and verify the actual databases, Boolean search strings, search dates and language restrictions before submission; these cannot be reconstructed reliably from the manuscript alone. The SANRA principles of transparent aims, scientific reasoning and balanced referencing inform the presentation, without claiming a formal SANRA assessment.

REVIEW

Historical perspectives on the medicinal use of olive oil

Olive oil occupied an important place in ancient Mediterranean traditions. In ancient Greek and Roman societies, its nutritional and cultural significance was accompanied by medicinal uses, both in its natural form and as a component of preparations used for a variety of health-related purposes.[6]

Ancient Egyptian medicine also employed plant-derived substances, oils, fats, and ointments for medicinal, hygienic, and cosmetic purposes. The *Ebers Papyrus*, dating to approximately 1500 BCE, is among the most important surviving records of ancient Egyptian medicine and contains numerous therapeutic formulations, illustrating the extensive use of natural substances in ancient medical practice.[7] During the Greek and Roman periods, olive oil was widely used in both culinary and medicinal contexts and was incorporated into preparations used for a range of health-related purposes.[6]

Olive-derived products also featured in Persian and Islamic medicine. Avicenna (Ibn Sina, 980–1037), in *The Canon of Medicine (Al-Qanun fi al-Tibb)*, described numerous natural substances and herbal remedies, including preparations containing olive oil for topical use in managing burns and wounds.[8] The *Canon of Medicine* became an influential medical text across several regions and contributed to the transmission of earlier medical knowledge into medieval medical practice.[8]

The Georgian scientific tradition provides an additional historical perspective on the study and practical use of natural substances. Relevant is the eighteenth-century work of King Vakhtang VI (1675–1737), whose intellectual and educational activities contributed to the development and dissemination of scientific knowledge in Georgia, including chemistry and practical chemical methods.[9]

Vakhtang VI's book on mixing oils and making chemistry (*Ts'igni zetebis shezavebisa da kimiisa kmnisa*) describes chemical procedures and practical methods for preparing and transforming various substances. Importantly, the historical concept of "oil" used in this work was broader than its contemporary chemical definition: the term could refer to liquids composed of different ingredients, not exclusively lipid-based oils.[9]

From the perspective of the history of medicine, pharmacy, and chemistry, this work illustrates the interaction between empirical knowledge and the scientific traditions available in eighteenth-century Georgia. Although it should not be interpreted as evidence specifically concerning the biomedical properties of modern olive oil, it complements the broader historical discussion of natural substances. It provides a distinctive Georgian context for the

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development of chemical and practical scientific knowledge.[9]

Clinical scope and exposure categories

Dietary olive oil, extra-virgin olive oil (EVOO), purified phenolic compounds, olive leaf extract, topical formulations and olive-processing by-products represent distinct exposures. Their routes, concentrations, and pharmacokinetics differ; evidence for one cannot establish efficacy for another. This review primarily focuses on dietary olive oil within Mediterranean-style dietary patterns. Concentrated extracts, topical formulations, and by-products are discussed separately as adjunctive or emerging areas. Historical observations are contextual and do not establish clinical efficacy.

Chemical composition and major Bioactive constituents of olive oil

Olive oil consists predominantly of a lipid fraction (approximately 98–99%), mainly triacylglycerols, together with a quantitatively smaller but biologically important fraction of minor constituents. Its fatty acid profile is characterized by a predominance of oleic acid (C18:1 n-9), a monounsaturated fatty acid (MUFA), with smaller proportions of saturated and polyunsaturated fatty acids, including palmitic (C16:0), linoleic (C18:2 n-6), and α-linolenic (C18:3 n-3) acids. The precise composition varies according to cultivar, geographical and environmental conditions, fruit ripeness, processing, and storage.[3]

The high oleic acid content represents an important nutritional characteristic of olive oil. Evidence from dietary studies indicates that replacing saturated fats with unsaturated fats, including MUFAs, may favorably influence plasma lipid profiles and cardiovascular risk factors; however, these effects depend on the overall dietary pattern and the nutrients being replaced and should not be attributed to oleic acid in isolation.[10,11] In addition, randomized clinical evidence indicates that the phenolic fraction of olive oil may contribute independently to some cardiovascular risk markers: in the EUROLIVE randomized crossover trial, olive oils with increasing phenolic content produced graded improvements in HDL cholesterol and markers of lipid oxidative damage.[11]

The minor fraction of olive oil includes phenolic compounds, tocopherols, phytosterols, squalene, pigments, and other bioactive constituents. These compounds are particularly relevant in virgin and extra-virgin olive oil (EVOO), where mechanical extraction and limited processing favor preserving naturally occurring minor constituents compared with extensive refining. Principal olive-derived phenolics include hydroxytyrosol, tyrosol, oleuropein and ligstroside derivatives, oleacein, and oleocanthal.[13]

Phenolic compounds contribute to the oxidative stability and biological properties of EVOO. 3,4-Hydroxytyrosol and related phenolics exhibit antioxidant activity and have been investigated for their potential modulation of endogenous antioxidant defenses and signaling pathways involved in oxidative stress and inflammation. oleocanthal, a secoiridoid phenolic compound, has attracted particular attention because experimental evidence demonstrates inhibition of cyclooxygenase enzymes involved in prostaglandin biosynthesis.[12] However, these mechanistic findings should not be interpreted as evidence of clinical or pharmacological equivalence to established anti-inflammatory drugs.[5,12]

Tocopherols, particularly α-tocopherol, contribute to antioxidant activity and oxidative stability, while phytosterols may influence intestinal cholesterol absorption. Squalene, a naturally occurring triterpene involved in sterol biosynthesis, has also been investigated for potential biological effects. Overall, the health-related properties of olive oil likely reflect the combined contribution of its MUFA-rich lipid fraction and minor bioactive constituents rather than the action of any single component.[3]

Olive oil phenolic compounds and their biological activities

Phenolic compounds constitute a quantitatively minor but biologically important fraction of virgin and extra-virgin olive oil (EVOO), contributing to its oxidative stability, sensory characteristics, and potential health-related properties.[3,4] Among the principal olive-derived phenolics are hydroxytyrosol, tyrosol, oleuropein and ligstroside derivatives, oleacein, and oleocanthal.[3,4] Their concentrations vary according to cultivar, fruit ripeness, environmental conditions, extraction technology, processing, and storage.[13]

Hydroxytyrosol and tyrosol are phenolic alcohols present in olive-derived products and may also arise from the degradation and metabolism of more complex secoiridoids.[4] hydroxytyrosol has been extensively investigated for its antioxidant and anti-inflammatory properties and its potential effects on lipid oxidation, endothelial function, and cardiometabolic pathways.[4,5] oleuropein, found predominantly in olive leaves and fruit, gives rise to several phenolic derivatives during maturation and processing.[3,4] Importantly, the biological relevance of these compounds depends not only on their intrinsic activity but also on their absorption, metabolism, tissue exposure, and concentrations achieved in vivo.[5,14] Human evidence

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demonstrates that tyrosol and hydroxytyrosol are absorbed following consumption of realistic doses of virgin olive oil.[15]

Oleacein and oleocanthal are secoiridoid derivatives characteristic of virgin olive oils.[4] oleocanthal has received particular attention because experimental evidence demonstrates its ability to inhibit cyclooxygenase (COX) enzymes, a mechanism that shares features with the action of nonsteroidal anti-inflammatory drugs.[12] However, this mechanistic similarity does not imply pharmacological equivalence or established therapeutic efficacy in humans.[5,12]

The biological activity of olive phenolics extends beyond direct antioxidant effects. Experimental evidence suggests modulation of endogenous antioxidant defenses, inflammatory signaling, endothelial and mitochondrial function, lipid metabolism, and cellular stress responses.[5,16] Selected olive-derived phenolics have also been linked to signaling pathways involved in cellular metabolism, proliferation, and stress responses, including the mechanistic target of rapamycin (mTOR) pathway.[16]

Overall, the biological effects of olive oil phenolics are likely to result from interactions among multiple compounds and their metabolites rather than from a single constituent.[5,14] Variability in phenolic composition, absorption, metabolism, and bioavailability should therefore be considered when extrapolating experimental findings to human health outcomes.[13,14]

An emerging area of research concerns the interaction between olive-derived phenolics and the intestinal microbiota. Phenolic compounds undergo gastrointestinal biotransformation, including microbial metabolism, which may influence their bioavailability and systemic activity. Conversely, olive phenolics and dietary patterns rich in EVOO may influence gut microbial composition and metabolic activity.[14,17] Although available evidence suggests a potentially bidirectional interaction between olive phenolics and the gut microbiota, human evidence remains limited, and its clinical significance has not yet been established.[17]

Diabetes, neurocognitive and cancer outcomes

Mediterranean dietary patterns have been associated with favorable metabolic outcomes, including incident type 2 diabetes in some randomized and observational analyses, but individual contributions of EVOO and phenolic constituents remain uncertain. Neurocognitive outcomes are less consistently studied with sufficiently powered, prespecified clinical endpoints; proposed antioxidant or neuroprotective mechanisms alone do not establish prevention of dementia. Similarly, epidemiologic associations between olive oil and cancer outcomes are vulnerable to residual confounding and dietary-pattern effects. Antiangiogenic and antiproliferative findings from isolated extracts or cell lines are experimental oncology evidence, not evidence of anticancer treatment in humans.

Cardiovascular events and intermediate outcome

PREDIMED evaluated Mediterranean dietary patterns supplemented with extra-virgin olive oil or nuts against advice to reduce dietary fat in people at high cardiovascular risk. In its reanalysis, the EVOO-supplemented arm had fewer major cardiovascular events than control (adjusted hazard ratio 0.69; 95% CI 0.53–0.91). Important randomization and protocol deviations prompted republication; therefore, the findings require careful interpretation. Crucially, the trial tested a whole dietary strategy, not isolated EVOO. CORDIOPREV randomized 1,002 patients with established coronary heart disease to Mediterranean or low-fat diets and reported fewer major cardiovascular events with the Mediterranean dietary pattern over seven years; this likewise does not isolate an olive-oil effect. By contrast, EUROLIVE assessed intermediate lipid and oxidative markers across oils of differing phenolic content. Biomarker improvements cannot be represented as direct evidence of fewer myocardial infarctions, strokes or deaths.

Human exposure and translation limitations

The pharmacological relevance of hydroxytyrosol, tyrosol and secoiridoid metabolites depends on the ingested oil mass, phenolic concentration (mg/kg oil), metabolic conjugation, circulating exposure and tissue distribution. Free aglycones measured in cell assays should not be equated with conjugated metabolites present after food intake. Human absorption has been demonstrated, but most cell-based concentrations have not been shown to reproduce sustained target engagement after ordinary dietary EVOO consumption. Oleocanthal-associated cyclooxygenase inhibition is mechanistically interesting; it does not justify using EVOO in place of nonsteroidal anti-inflammatory drugs. When primary reports do not provide dose-normalized plasma concentrations or metabolite profiles, quantitative exposure comparisons remain unresolved.

Olive oil in wound healing

In an assessor-blind randomized controlled trial involving 60 patients with type 2 diabetes and grade 1 or 2 diabetic foot ulcers, standard wound care supplemented with daily topical olive oil dressing was associated with significantly improved wound-healing parameters and a higher proportion of complete wound healing over four weeks compared with standard care alone.[18] Although clinically relevant, these findings should be interpreted cautiously because of the

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relatively small sample size, short follow-up period, and restriction of the study population to patients with grade 1 or 2 diabetic foot ulcers.[18]

Overall, the available clinical evidence remains limited and heterogeneous. A separate randomized controlled trial in women undergoing cesarean section also reported improved wound-healing scores following topical application of an olive-containing cream.[19] However, differences in wound type, study population, and topical preparation limit direct comparison between these studies. Larger controlled trials using standardized preparations, clearly defined wound types, and validated outcomes are required before topical olive oil can be considered an established intervention in routine wound care.[18,19]

Olive-processing by-products as sources of bioactive compounds

Recovering phenolic compounds from olive-processing by-products may reduce the environmental burden associated with olive-industry waste while providing value-added compounds for potential food, nutraceutical, and biomedical applications.[3,20]

Polyphenol-rich extracts derived from olive mill wastewater (OMWW) have demonstrated biological activities of potential biomedical interest in experimental models.[20-22] In particular, the polyphenol-rich OMWW extract A009 has been shown to inhibit endothelial cell proliferation, migration, and capillary-like structure formation and to exert antiangiogenic activity in vitro and in vivo.[21] In prostate cancer cell models, A009 inhibited cell proliferation, adhesion, migration, and invasion and modulated pro-inflammatory and pro-angiogenic signaling pathways, including NF-κB, VEGF, CXCL8, CXCL12, and the IL-6/STAT3 axis.[22] These findings suggest that the biological activity of OMWW-derived phenolic extracts may involve multiple cellular and molecular targets; however, their relevance to clinical cancer prevention or treatment remains unestablished.[21,22]

Preclinical studies have also investigated A009 in combination with chemotherapeutic agents. In experimental breast cancer models, A009 enhanced the anticancer activity of doxorubicin and 5-fluorouracil while reducing chemotherapy-associated toxicity in cardiomyocyte models.[23] These findings suggest potential research applications of OMWW-derived polyphenols in oncology and cardio-oncology; however, the available evidence remains preclinical. Their efficacy, pharmacokinetics, optimal composition, dosing, and safety in humans require evaluation in appropriately designed clinical studies.[23]

Topical preparations: route-specific evidence

The wound-care studies discussed below concern locally applied olive-derived preparations, not oral dietary intake. The diabetic-foot study included 60 patients with grade 1–2 ulcers and assessor blinding, with short follow-up; the cesarean-wound study used an olive-containing cream in a different clinical setting. Differences in formulation, comparator, wound biology and endpoints preclude pooling or generalization to routine care. Concentration, effect estimates and full trial risk-of-bias details require checking against the original reports before a quantitative comparison can be published.

Olive oil consumption and long-term health outcomes

Evidence from two large prospective U.S. cohorts supports an association between higher olive oil consumption and favorable long-term health outcomes. Among 60,582 women and 31,801 men followed for up to 28 years, consumption of more than 7 g/day of olive oil was associated with a 19% lower risk of all-cause mortality and lower risks of cardiovascular (19%), cancer (17%), neurodegenerative (29%), and respiratory (18%) mortality compared with no or rare olive oil consumption.[24]

Substitution analyses further showed that replacing 10 g/day of margarine, butter, mayonnaise, or dairy fat with an equivalent amount of olive oil was associated with an 8–34% lower risk of total and cause-specific mortality. In contrast, substitution of other vegetable oils with olive oil was not associated with significant reductions in mortality risk.[24] These findings emphasize that the observed health associations of olive oil may depend partly on the dietary fat it replaces.

Because these data are observational, they demonstrate associations rather than causality. Overall, the findings support higher olive oil consumption as part of a health-promoting dietary pattern but should not be interpreted as evidence that olive oil itself is a therapeutic intervention.[24]

Interpreting observational mortality findings

Associations with mortality do not establish causation. Confounding may arise from total dietary quality, socioeconomic status, exercise, smoking, baseline health, and differential use of animal fats. Substitution analyses are particularly informative: replacing butter or other animal-derived fats with olive oil is a different intervention from adding oil to an otherwise unchanged, energy-balanced diet. Prospective cohorts generally cannot determine whether observed associations are caused by EVOO phenolics specifically.

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Olive leaf extracts: biological and clinical evidence

Olive leaves (*Olea europaea L.*) represent an additional source of bioactive phenolic compounds. Oleuropein is one of their principal secoiridoids, accompanied by hydroxytyrosol, tyrosol, verbascoside, caffeic acid, luteolin derivatives, and other phenolics. Their concentrations vary according to cultivar, environmental conditions, harvesting period, leaf maturity, extraction method, and storage.[25]

Experimental studies of olive leaf extracts (OLEs) have reported antioxidant, anti-inflammatory, antimicrobial, cardiometabolic, neuroprotective, and antiproliferative activities. Oleuropein and hydroxytyrosol have been investigated in particular for their roles in oxidative stress and inflammatory signaling. However, much of this evidence derives from in vitro and preclinical studies and should not be interpreted as demonstrating therapeutic efficacy in humans.[25,26]

Clinical studies have investigated the effects of OLEs on blood pressure, glucose metabolism, insulin sensitivity, lipid parameters, and other cardiometabolic outcomes.[27] In a randomized, double-blind, controlled crossover trial involving 60 prehypertensive men, daily consumption of a phenolic-rich OLE for six weeks significantly reduced daytime and 24-hour systolic and diastolic blood pressure. It reduced total cholesterol, LDL cholesterol, and triglycerides compared with a polyphenol-free control. However, other vascular, inflammatory, and metabolic outcomes were not consistently affected.[28] A systematic review and meta-analysis of randomized controlled trials subsequently found significant reductions in systolic blood pressure and triglyceride concentrations but not consistent improvements across all assessed cardiometabolic outcomes.[27]

Overall, the clinical evidence remains limited and heterogeneous, with variability in extract composition, phenolic content, dosage, treatment duration, study design, and participant characteristics.[27] Importantly, evidence concerning OLEs should be distinguished from that concerning olive oil consumption because the two differ substantially in composition, bioactive-compound concentrations, and exposure.[25,27]Further adequately powered clinical trials using chemically characterized and standardized preparations are required to clarify efficacy, dose-response relationships, bioavailability, safety, and potential drug interactions.[25,27]

Olive leaf extract as a distinct nutraceutical exposure

Olive leaf extracts may deliver oleuropein and related constituents in amounts and proportions unlike food-level olive oil. Small controlled trials and meta-analyses suggest possible changes in blood pressure or triglycerides, but variable standardization, doses, durations, and participant characteristics limit general recommendations. Extract-specific daily dose, oleuropein/hydroxytyrosol content, adverse events, and concomitant antihypertensive or glucose-lowering therapy should be reported when available. No indication to replace established treatment follows from these preliminary findings.

Safety considerations and clinical limitations

Olive oil is widely consumed as a food and is generally considered safe when incorporated into a balanced dietary pattern. Because olive oil is energy-dense, however, its contribution to total energy intake should be considered, particularly when it is added to the diet rather than used to replace other dietary fats.[24]

Dietary olive oil should be distinguished from concentrated olive-derived extracts and supplements, which may provide substantially different exposures to individual phenolic compounds. The absorption, metabolism, distribution, and elimination of olive-derived phenolics are influenced by the compound's chemical form, dose, and food matrix.[14] Clinical studies of olive leaf extracts have generally been short-term, and the available evidence is insufficient to establish the long-term safety of concentrated phenolic preparations across different populations and doses.[27]

Similarly, the use of olive oil or olive-derived preparations for specific clinical conditions should be supported by condition-specific evidence. Findings from nutritional, observational, or experimental studies should not be extrapolated directly to therapeutic indications. In particular, the currently available evidence does not justify replacing established medical or wound-care interventions with olive oil or olive-derived products.[18,19,27]

Research priorities

Priorities include adequately powered head-to-head dietary trials reporting hard clinical outcomes; chemically characterized EVOO interventions reporting g/day and mg phenolics/day; human pharmacokinetic studies distinguishing free from conjugated metabolites; standardized extract trials with systematic adverse-event collection; and independently replicated topical trials using validated wound endpoints. The emerging olive-mill wastewater literature should remain explicitly preclinical until human safety and efficacy studies are available.

Safety, certainty and clinical implications

Dietary olive oil is energy dense and should generally replace, rather than supplement, less favorable dietary fats when total energy intake matters. Sensory

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deterioration, oxidation, adulteration, and variability in phenolic content complicate exposure assessment. Food allergy or intolerance may occur, although uncommon. Concentrated supplements require separate evaluation for batch quality, gastrointestinal tolerability, potential blood-pressure or glucose-lowering effects, and interactions with relevant medicines; pregnancy and lactation safety data are inadequate for routine high-dose use. Clinical implications are strongest for Mediterranean dietary patterns containing EVOO; isolated phenolics, olive leaf extracts, topical products, and industrial extracts lack equivalent outcome evidence.

CONCLUSIONS

Olive oil represents a complex bioactive food whose health-related properties reflect the combined contribution of its monounsaturated fatty acid profile and minor constituents, particularly phenolic compounds. Contemporary research provides a biological basis for several effects historically attributed to olive-derived products while emphasizing the need to distinguish traditional use and mechanistic findings from clinically established effects.

Current epidemiological and clinical evidence most consistently supports olive oil consumption, particularly within a Mediterranean dietary pattern, in relation to cardiovascular, cardiometabolic, and overall health. Although experimental and observational studies suggest additional potential roles in neuroprotection, cancer-related pathways, tissue repair, and wound healing, the clinical evidence for these applications remains limited or heterogeneous. Olive oil should therefore primarily be regarded as a bioactive component of a healthy dietary pattern rather than as a pharmaceutical intervention.

Olive leaves and olive-processing by-products also represent promising sources of bioactive phenolic compounds. They may have biomedical, nutraceutical, and biotechnological potential while supporting the sustainable valorization of olive-industry waste. However, variability in composition, bioavailability, formulation, dose, and study design limits direct comparison across studies. Further standardized and adequately powered clinical studies are required to establish dose-response relationships, long-term safety, and the clinical relevance of olive-derived phenolics and concentrated extracts.

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