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Short Article

Omega-3 Fatty Acids and Renal Health: Mechanisms, Protective Effects and Clinical Implications – A Narrative Review

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Abstract

Background: Chronic kidney disease (CKD) is a major global health problem associated with increased cardiovascular risk, progressive renal function decline, and high mortality. Despite advances in pharmacological therapy, disease progression often persists, highlighting the need for supportive, lifestyle-based interventions. Omega-3 polyunsaturated fatty acids (PUFAs) have gained interest in nephrology due to their anti-inflammatory, anti-oxidative, and endothelial-protective properties.

Aim of the study: This narrative review aimed to summarize current evidence on the role of omega-3 PUFAs, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA),

in renal health, with emphasis on mechanistic pathways and clinical implications in chronic kidney disease and inflammation-related renal injury.

Materials and methods: A narrative literature review was conducted using PubMed, Scopus, and Google Scholar. Publications from 2020–2025 were prioritized, including randomized controlled trials, systematic reviews, meta-analyses, and experimental studies. Search terms included omega-3 fatty acids, EPA, DHA, chronic kidney disease, proteinuria, renal inflammation, and fibrosis.

Current stage of knowledge: Omega-3 fatty acids exert pleiotropic effects relevant to renal protection, including modulation of inflammatory signaling, oxidative stress, mitochondrial dysfunction, endothelial function, and fibrotic pathways. Clinical data suggest modest but consistent reductions in proteinuria, particularly in IgA nephropathy and early-stage CKD, while effects on long-term renal function decline remain inconsistent.

Conclusions: Omega-3 fatty acids may offer supportive renoprotective benefits, especially in proteinuric and inflammation-mediated kidney diseases. They should be considered an adjunct to established therapies. Further long-term studies are needed to identify optimal dosing and patient populations most likely to benefit.

Keywords: omega-3 fatty acids; EPA; DHA; chronic kidney disease; proteinuria; renal inflammation; nephrology

1. Introduction

Chronic kidney disease (CKD) represents a major global public health challenge, affecting approximately 10% of the adult population worldwide and substantially increasing cardiovascular morbidity and mortality [1]. Despite advances in pharmacological management, including renin–angiotensin–aldosterone system blockade and sodium–glucose cotransporter-2 inhibitors, progression of renal dysfunction frequently persists, highlighting the need for complementary preventive and supportive strategies.

Omega-3 fatty acids are essential polyunsaturated fatty acids that cannot be synthesized endogenously in sufficient quantities and must be obtained through diet or supplementation. Beyond their established cardiovascular benefits, omega-3 PUFAs have attracted increasing attention in nephrology due to their immunomodulatory, anti-inflammatory, and anti-fibrotic properties [2]. Renal tissue is particularly vulnerable to chronic inflammation, oxidative stress, and microvascular dysfunction—processes that omega-3 fatty acids may attenuate through multiple biological mechanisms.

The aim of this narrative review is to provide a comprehensive overview of current evidence regarding the role of omega-3 fatty acids in renal health, integrating mechanistic data, experimental findings, and clinical outcomes relevant to CKD prevention and management.

2. Materials and Methods

A narrative literature review was conducted using PubMed, Scopus, and Google Scholar. Search terms included *omega-3 fatty acids*, *EPA*, *DHA*, *chronic kidney disease*, *proteinuria*, *renal inflammation*, and *fibrosis*. Publications from January 2020 to May 2025 were prioritized, including randomized controlled trials, systematic reviews, meta-analyses, and relevant experimental studies. Earlier landmark publications were selectively included to provide mechanistic context. Due to heterogeneity in study design, dosing regimens, and outcome measures, a qualitative synthesis approach was applied.

3. Biological Mechanisms Linking Omega-3 Fatty Acids to Renal Protection

3.1 Anti-inflammatory and Immunomodulatory Effects

Chronic inflammation is a central driver of CKD progression. Omega-3 fatty acids compete with arachidonic acid for incorporation into cell membranes, resulting in the production of less pro-inflammatory eicosanoids and the generation of specialized pro-resolving mediators, including resolvins, protectins, and maresins [3,4]. These mediators reduce leukocyte recruitment, suppress pro-inflammatory cytokines such as tumor necrosis factor-α and interleukin-6, and promote resolution of chronic inflammation within renal tissue.

3.2 Oxidative Stress and Mitochondrial Protection

Oxidative stress contributes to tubular injury, endothelial dysfunction, and progressive nephron loss. EPA and DHA enhance antioxidant defenses by modulating nuclear factor erythroid 2–related factor 2 (Nrf2) signaling and reducing reactive oxygen species production [5]. Improvements in mitochondrial membrane stability and bioenergetic efficiency further protect renal cells from apoptosis and metabolic failure.

3.3 Anti-fibrotic Pathways

Progressive renal fibrosis represents a final common pathway in CKD. Experimental models demonstrate that omega-3 fatty acids attenuate transforming growth factor-β signaling, inhibit fibroblast activation, and reduce extracellular matrix deposition [6]. These effects translate into reduced collagen accumulation and slower progression of interstitial fibrosis in animal models of kidney disease.

3.4 Endothelial Function and Renal Hemodynamics

Renal microvascular dysfunction accelerates nephron loss and contributes to proteinuria. Omega-3 fatty acids improve endothelial nitric oxide bioavailability, reduce vascular stiffness, and modulate intraglomerular pressure [7]. These mechanisms may underlie reductions in proteinuria and stabilization of glomerular filtration rate observed in selected clinical studies.

The principal biological mechanisms underlying omega-3–mediated renal protection are summarized in Table 1.

Table 1. Biological mechanisms linking omega-3 fatty acids to renal protection

Mechanism	**Molecular pathways**	**Renal effects**
Anti-inflammatory	Resolvins, cytokine suppression	Reduced immune-mediated injury
Anti-oxidative	Nrf2 activation	Protection of tubular cells
Anti-fibrotic	TGF-β inhibition	Reduced interstitial fibrosis
Endothelial support	NO bioavailability	Improved hemodynamics

4. Clinical Evidence in Kidney Disease

4.1 Chronic Kidney Disease and Proteinuria

Several randomized trials and meta-analyses report modest but consistent reductions in proteinuria with omega-3 supplementation, particularly in IgA nephropathy and early-stage CKD [8,9]. While effects on estimated glomerular filtration rate decline remain variable, reductions in urinary protein excretion and inflammatory markers suggest potential renoprotective benefits.

4.2 Inflammation-Driven Renal Injury

In conditions characterized by heightened systemic inflammation—such as diabetic kidney disease and obesity-related nephropathy—omega-3 fatty acids may provide adjunctive benefits by attenuating low-grade inflammation, improving lipid profiles, and modulating endothelial function [10].

4.3 Safety and Tolerability

Omega-3 fatty acids are generally well tolerated. Gastrointestinal symptoms represent the most commonly reported adverse effects. Available evidence suggests minimal bleeding risk at standard therapeutic doses, including in patients with impaired renal function [11].

Clinical evidence regarding omega-3 supplementation in kidney disease is summarized in Table 2.

Table 2. Clinical evidence for omega-3 fatty acids in kidney disease

Clinical context	Population	Main outcomes	Clinical relevance
CKD (early stages)	Adults with CKD	Reduced proteinuria	Adjunctive therapy
IgA nephropathy	Proteinuric patients	Lower urinary protein	Disease modulation
Diabetic kidney disease	Metabolic CKD	Reduced inflammation	Supportive benefit
Advanced CKD	Mixed populations	Neutral GFR effects	Safety preserved

5. Discussion

The available evidence supports a biologically plausible role for omega-3 fatty acids in renal protection, mediated through anti-inflammatory, anti-oxidative, anti-fibrotic, and endothelial-stabilizing mechanisms. Clinical studies suggest modest benefits, particularly in proteinuric and inflammation-driven renal disorders, though effects on long-term renal outcomes remain inconsistent. Variability in dosing, formulation, study duration, and patient populations complicates interpretation.

From a clinical perspective, omega-3 supplementation should be considered an adjunct rather than a replacement for established renoprotective therapies. Identification of patient subgroups most likely to benefit remains a key research priority.

6. Limitations and Future Directions

Most clinical trials are limited by small sample sizes and relatively short follow-up periods. Heterogeneity in omega-3 formulations and dosing regimens further limits comparability across studies. Large, well-designed randomized trials focusing on hard renal endpoints are required to clarify the therapeutic role of omega-3 fatty acids in CKD management.

7. Conclusions

Omega-3 fatty acids exert multiple biological effects that may support renal health and attenuate progression of kidney disease. Current evidence suggests modest clinical benefits, particularly in proteinuric and inflammatory renal disorders. Incorporation of omega-3 fatty

acids as part of a comprehensive, lifestyle-oriented approach to renal protection appears justified, pending further high-quality evidence.

Disclosure

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