

Background & Purpose

Chronic kidney disease (CKD) affects approximately 37 million Americans and is considered the ninth-leading cause of death in the United States.¹ The most common causes of CKD are hypertension and diabetes mellitus, which are widely prevalent conditions in the developed world. Although advances have been made in conventional nephrology such as diagnostic classification, goal-oriented management, and renal replacement therapies, persistent problems remain without updated solutions. Out of all the major medical specialties, nephrology has the lowest number of clinical trials and only a few treatments have been shown to improve clinical outcomes.^{2,3}

A 2019 executive order from the President launched the Advancing American Kidney Health Initiative, which directs the Department of Health and Human Services to emphasize early identification and adopt new treatments focused on delaying the rate of CKD progression. This has created a unique opportunity for integrative and multidisciplinary approaches to take lead and offer solutions. An integrative health approach offers diagnostic and treatment options that have traditionally not been widely considered when treating and managing patients with CKD. A review of literature has demonstrated clinically relevant options for the treatment and management of CKD while addressing underlying mechanisms and thereby decreasing the rate of disease progression.

Questions & Knowledge Gaps

1. What is the integrative health approach?
2. Are there integrative treatment approaches to CKD?
3. Can the integrative health approach delay or prevent CKD progression?

A growing body of evidence is beginning to demonstrate the effectiveness of complementary and integrative treatments in treating and managing patients with CKD. While treatments are often aimed at addressing comorbidities which we know accelerate CKD progression, many more studies are taking a closer look at the effect of nutrients and botanical constituents on the underlying mechanisms that drive CKD pathophysiology. This is an opportune time for integrative health to apply itself to the problem of CKD.

Methods

Peer-reviewed literature were search in PubMed, Medline and Embase with specific Medical subject headings (MeSH) and studies dated up to 2003 were considered. The following MeSH terms were used alone and together: chronic kidney disease, glomerular filtration rate, creatinine, cystatin C, albuminuria, nephropathy, microangiopathy, oxidative stress, inflammation, microbiome, toxins, dysbiosis, endothelial, vascular, mitochondria, botanical, herb, nutrient, nutraceutical, and nutrition. Both preclinical and clinical studies were considered.

Results

Based on the evaluated studies, three main underlying disease mechanisms have been identified that contribute to the rate of CKD progression – *oxidative stress*,^{4,7} *chronic inflammation*,^{4,5,10-12} and *vascular changes*.⁷⁻¹⁰ Additional studies demonstrated important relationships in support of emerging concepts in CKD management, including the relationship between the kidneys and the microbiome,^{11,12} the liver and toxic burden,¹³⁻¹⁵ as well as the role of mitochondria⁶ and metabolic resilience. Treatment and strategies were examined and evaluated, with promising evidence in support of an integrative, whole-person approach for the treatment of patients with CKD. Both direct and indirect effects of various treatments were noted and considered.

Figure 1. Interrelationship between the underlying mechanisms in CKD progression.

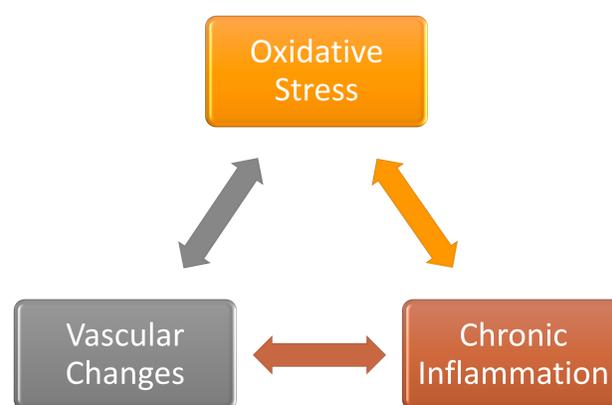


Figure 2. Extrarenal influences on CKD progression.

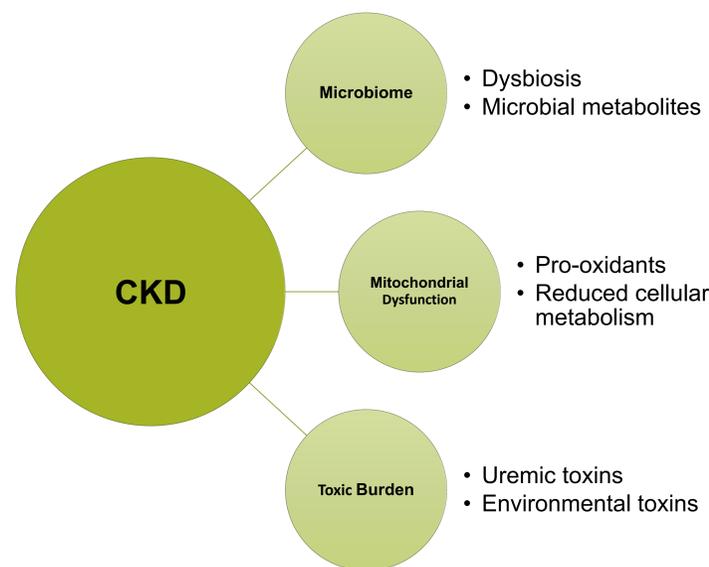


Table 1. Proposed Integrative Treatment Strategies.

Intervention	Disease Mechanism	Kidney Parameters	SORT*
Coenzyme Q10	Oxidative Stress, ^{21,23} Vascular Changes ²⁰	Reduce SCr and BUN ¹⁷	B
Omega-3 fatty acids	Oxidative Stress, ^{22,23} Chronic Inflammation ¹⁹	Reduce proteinuria ¹⁸	B
<i>Astragalus membranaceus</i>	Oxidative Stress, ³² Chronic Inflammation ^{28,30}	Increase CrCl, reduce proteinuria ^{28,29}	B
<i>Cordyceps sinensis</i>	Oxidative Stress, Chronic Inflammation ³¹⁻³³	Reduce SCr, increase CrCl, reduce proteinuria ^{31,34}	B
Green tea polyphenols	Oxidative Stress, ²³⁻²⁵ Chronic Inflammation ²⁶	Limited to animal models	C
Alpha lipoic acid	Oxidative Stress ^{23,24,27}	Limited to animal models	C

*Strength-of-Recommendation Taxonomy (SORT)¹⁶:
A – Consistent, good-quality patient-oriented evidence
B – Inconsistent or limited-quality patient-oriented evidence
C – Consensus, disease-oriented evidence, usual practice, expert opinion, or case series for studies of diagnosis, treatment, prevention, or screening

Discussion

An integrative health approach to the treatment of CKD offers possible solutions to delay or prevent CKD progression by targeting the main mechanisms that drive the disease process while also protecting the kidneys by increasing metabolic and organ resilience. It is important to note that the proposed model of care using integrative modalities does not replace current treatment guidelines, but rather enhances and optimizes outcomes. The current body of evidence largely supports the use of integrative treatments to decrease risk of CKD progression. However studies are limited and focus on various elements of treatment, rather than an integrative, multi-modal treatment protocol. Additional studies are needed to explore the therapeutic value of specific nutrients, vitamins, and botanical medicines both as isolated constituents and in more complex, controlled trials as part of an integrative strategy. Overall, the collective safety profile of the studied interventions is safe and future research can primarily focus on assessing clinical effectiveness.

Conclusions & Future Directions

Both preclinical and clinical studies evaluating the effectiveness of integrative therapies demonstrate preliminary evidence of enhanced clinical outcomes in CKD patients, irrespective of primary etiologies and contributing comorbidities. Additionally, future disease management models for CKD must include an integrative, multidisciplinary, and whole-person approach in order to address the broader determinants of health and target mechanisms that drive the disease, while protecting the kidneys and preventing CKD progression to end-stage renal failure and delay the need for renal replacement therapies.

References

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