Food as Medicine for Inflammation in CKD

By Marcia Ribeiro and Denise Mafra

Chronic kidney disease (CKD), a noncommunicable metabolic and silent disease, is considered a serious public health problem affecting more than 37 million adults in the United States (1). Several factors are associated with kidney failure progression and complications in patients with CKD, such as oxidative stress, mitochondrial dysfunction, premature aging, gut dysbiosis, and endothelial dysfunction. The chronic inflammation that represents a pathological change and directly implies worsening CKD prognoses and cardiovascular outcomes should be highlighted (2). Diabetes mellitus, hypertension, obesity, physical inactivity, age, diet, anemia, metabolic acidosis, altered immune system, gut dysbiosis, and uremia per se can all contribute to inflammation. At the cellular level, oxidative stress, senescence cells, and mitochondrial dysfunction are directly involved in the inflammation observed in persons with CKD (3).

Corroborating this scenario, mitochondrial dysfunction with consequent overproduction of reactive oxygen species promotes increased inflammation through the activation of the nuclear transcription factor kappa B (NF-κB), which is related to the production of inflammatory cytokines, such as several interleukins (ILs) and tumor necrosis factor-alpha. In addition, inflammasome activation, mainly the nucleotide-binding oligomerization domain, leucine-rich repeat, and pyrin domain containing 3 (NLRP3), enormously exacerbates inflammation in patients with CKD since it releases IL-1β and IL-18 (4, 5). In contrast, the master of the antioxidant system, nuclear factor 2 related to erythroid 2 (NRF2), a transcription factor involved in synthesizing many antioxidant enzymes, seems to have reduced mRNA expression in patients with CKD. Thus, the expression of this transcription factor is inversely associated with inflammation (5).

All of these systems can be repressed or inducible, and nutrients play a crucial role in activating the NRF2 and repressing the NF-κB and NLRP3 signaling pathways, exerting therapeutic effects against inflammation. Current evidence indicates that many bioactive compounds found naturally in foods, such as isothiocyanates in cruciferous vegetables; catechins in dark chocolate; and polyphenols in fruits, propolis, and fermented food, can act as modulators of transcription factors involved in inflammation and oxidative stress, providing anti-inflammatory and antioxidant effects in individuals with CKD. Therefore, the concept of "food as medicine" becomes especially relevant for CKD (5).

Studies indicate that several bioactive compounds—such as curcumin, allicin, quercetin, sulforaphane, and catechins—can promote increased mRNA expression of NRF2 and antioxidant enzymes—such as heme oxygenase-1 (HO-1) and NADPH quinone dehydrogenase-1 (NQO-1)—in addition to attenuating the expression of the inflammasome and NF-κB. Also, they can inhibit essential proteins in the inflammatory cascade such as mitogen-activated protein kinase, inhibitory kappa B kinase alpha, and nuclear factor of kappa light polypeptide gene enhancer in B cells inhibitor alpha (6–8).

Given the above information, improving the quality of the diet of patients with CKD, including healthy foods rich in bioactive compounds such as fruits, vegetables, seeds, nuts, tea, cocoa, coffee, whole grains, and spices like turmeric and cinnamon, can be a potential strategy to prevent and treat inflammation in these individuals (Figure). ■

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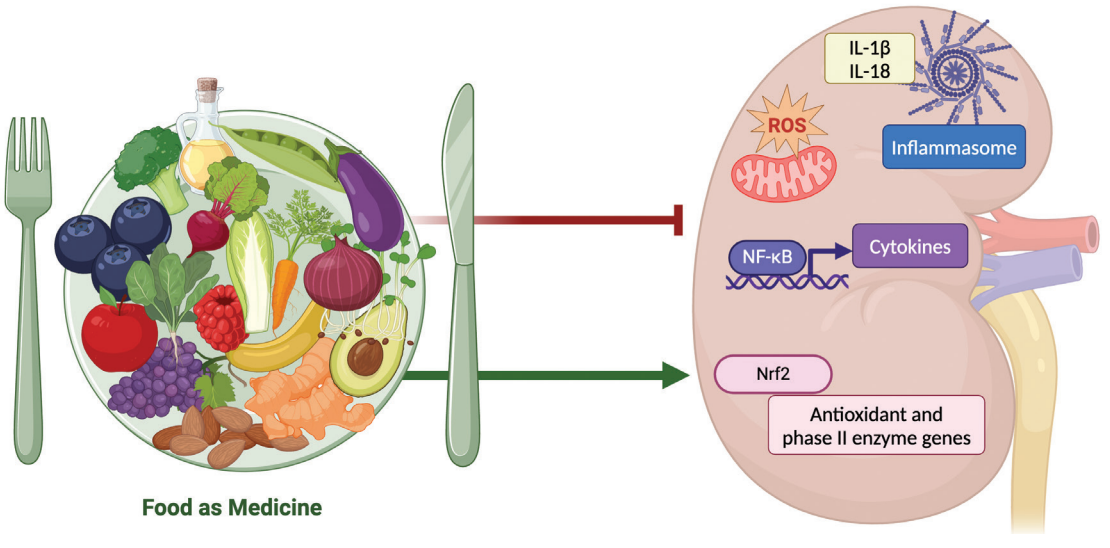
References

1. US Department of Health and Human Services, Centers for Disease Control and Prevention. Chronic kidney disease in the United States, 2021. https://nccd.cdc.gov/ckd/Documents/Chronic-Kidney-Disease-in-the-US-2021-h.pdf
2. Yan Z, Shao T. Chronic inflammation in chronic kidney disease. *Nephron* 2024; 148:143–151. doi: 10.1159/000534447
3. Lee DE, et al. Relative contribution of genetic and environmental factors in CKD. *S D Med* 2021; 74:306–309. PMID: 34449991
4. Alvarenga L, et al. Can nutritional interventions modulate the activation of the NLRP3 inflammasome in chronic kidney disease? *Food Res Int* 2020; 136:109306. doi: 10.1016/j.foodres.2020.109306
5. Mafra D, et al. Food as medicine: Targeting the uraemic phenotype in chronic kidney disease. *Nat Rev Nephrol* 2021; 17:153–171. doi: 10.1038/s41581-020-00345-8
6. Alvarenga LA, et al. Curcumin supplementation improves oxidative stress and inflammation biomarkers in patients undergoing hemodialysis: A secondary analysis of a randomized controlled trial. *Int Urol Nephrol* 2022; 54:1–7. doi: 10.1007/s11255-022-03182-9
7. Ribeiro M, et al. From the distinctive smell to therapeutic effects: Garlic for cardiovascular, hepatic, gut, diabetes and chronic kidney disease. *Clin Nutr* 2021; 40:4807–4819. doi: 10.1016/j.clnu.2021.03.005
8. Cardozo LFMF, et al. Cruciferous vegetables: Rationale for exploring potential salutary effects of sulforaphane-rich foods in patients with chronic kidney disease. *Nutr Rev* 2020; 79:1204–1224. doi: 10.1093/nutri/nuaa129

Figure. Mechanisms by which foods and nutrients exert anti-inflammatory and antioxidant effects in patients with CKD



Bioactive compounds, naturally present in foods, have anti-inflammatory properties and can inactivate the inflammasome by reducing the expression of IL-1β and IL-18 and the overproduction of reactive oxygen species (ROS) and attenuate the NF-κB pathway with a consequent reduction in the expression of inflammatory cytokines such as ILs and tumor necrosis factor-alpha, in addition to stimulating the NRF2 pathway, increasing the synthesis of phase II antioxidant enzymes. Created by BioRender.com.