Supplementary table 1 Selected antioxidant approaches with example substances and interventions in chronic kidney disease.

Approach	Example substance/ intervention	Mechanism of action	Ref.	Clinical effects	Ref.
nuclear factor erythroid 2-related factor (Nrf2) activation	*bardoxolone methyl*	• interaction with the Nrf2 repressor Keap1 (Kelch-like ECH-associated protein 1) -> facilitation of nuclear translocation of Nrf2 -> upregulation of antioxidant and cytoprotective target genes	[1]	• in patients with advanced CKD and type II diabetes mellitus improvement of estimated GFR • in patients with CKD stage 4 and type II diabetes mellitus no reduction of end-stage renal disease risk or of cardiovascular death; increased rate of cardiovascular events	[3] [4]
	dh404 (bardoxolone analog)	• as above, • dose-dependency (lower concentrations activate Nrf2 and target genes; higher concentrations suppress Nrf2 system)	[2]		
thiol (sulfhydryl) containing antioxidants	*N-acetylcysteine*	• free radical scavenger • maintenance of intracelluar glutathione • post-translational modification of protein cysteine residues *in vivo*	[5] [6] [7]	• in hemodialysis patients reduction of composite cardiovascular endpoints; no reduction of mortality • in peritoneal dialysis patients reduction of interleukin 6	[8] [9]
vitamin E supplementation	*alpha-tocopherol*	• incorporation into membrane bilayers -> interruption of lipid peroxidation chain reactions by free radical scavenging	[10]	• in hemodialysis patients with prevalent cardiovascular disease reduction of myocardial infarction and composite CVD endpoints, no effect on total mortality	[11]
	surface-modified cellulose dialysis membrane containing alpha-tocopherol	• manufactures *in vitro* testing shows favorable effect profile with respect to blood contact phase activation, interleukin 6 production and reactive oxygen production compared to selected other dialysis membranes	[12]		
				• in hemodialysis patients a meta-analysis that included studies comparing different types of vitamin E-modified dialysis membranes to control dialysis membranes suggested reduced oxidative stress and inflammation status	[13]
reducing gut-derived uremic toxins	*resistant starch*	• prebiotic, • amelioration of oxidative stress in kidney tissue (downregulation of reactive oxygen species-generating proteins, reduction of	[14]	• in hemodialysis patients reduction of gut-derived uremic toxins (significant for free concentrations of indoxyl sulfate in plasma)	[15]

		nitrotyrosine, upregulation of antioxidant proteins), • restoration of gut epithelial tight junctions			
	AST-120	• oral sorbent, • reduction of plasma indoxyl sulfate concentration, • reduction of superoxide production in skeletal muscle	[16]	• in patients with advanced CKD possible positive impact of > 6 month AST-120 treatment on left cardiac ventricle geometry (cross-sectional study) • in patients with CKD stage 3/4 no impact of AST-120 long-term treatment on renal disease progression or mortality (on top of RAAS inhibition and intended low protein diet)	[17] [18]
exercise training	*long-term aerobic exercise training*	• decrease of renal superoxide production and oxidative protein damage • increased activity of renal antioxidant enzymes	[19]	• in CKD patients with mild to moderately reduced eGFR reduction of serum lipid oxidation products and increase of the reduced form of glutathione • in CKD patients with mild to moderately reduced eGFR after 10 years less frequent occurrence of death or initiation of renal replacement therapy (group size n=7 and n=9)	[20] [21]
	long-term intradialytic exercise training			• in hemodialysis patients reduction of oxidative stress related parameters (alkaline phosphatase, thiobarbituric acid reactive substances) • in hemodialysis patients reduction of lipid peroxidation (15-F(2)alpha-isoprostanes)	[22] [23]

CKD chronic kidney disease
CVD cardiovascular disease
RAAS renin-angiotensin-aldosterone system

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