Annals of Research in Antioxidants

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Mechanistic impact of renal tubular cell protection by antioxidants

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Received: 28 December 2015
Accepted: 10 January 2016
ePublished: 18 January 2016

Keywords: Tubular cell, Recovery process, Antioxidants, Bioactive components

Citation: Dehghan Shahreza F. Mechanistic impact of renal tubular cell protection by antioxidants. Ann Res Antioxid. 2016;1(1):e11.

Core tip

Toxins, infections, radiocontrast and dehydration are main reasons of acute tubular cell injury that induce ischemic/hypoxic damages. In hypoxic renal condition, mitochondrial ATP, reactive nitrosative and oxygenated species generation is disrupted and leads to disturb homeostatic kidney function.

Toxins, infections, radiocontrast and dehydration are main reasons of acute tubular cell injury that induce ischemic/hypoxic damages. In hypoxic renal condition, mitochondrial ATP, reactive nitrosative and oxygenated species generation is disrupted and leads to disturb homeostatic kidney function. Over production of radicals trigger pro-inflammatory processes by endothelial cell injury and glycocalyx alterations promoted leukocytes adhesion and infiltration. Up-regulating transforming growth factor (TGF)-β and downregulating vascular endothelial growth factor (VEGF) decrease peritubular capillary density which finally leads to aggravate primary injury (1). In epithelial tubular cells, post-ischemic recovery processes are activated to adapt cell to short-term oxidative condition through preventing proteins translation and increasing protein degradation in endoplasmic reticulum network. In addition, these recovery processes protect mitochondrial structure, normal ATP generation and enhancement of transcription factors PPARα, Nrf2 and Nrf1 which induce endogenous production of antioxidant enzymes and mitochondrial biogenesis, result in accelerating improvement of renal oxidative damage. Conversely, prolonged stress activates maladaptive responses by enhancing endoplasmic reticulum stress induced atrophic, apoptotic and fibrosis mediators (2).

None of therapeutic applications for acute kidney damage are efficient to limit injury progression or accelerate tubular regeneration. Recently many efforts are directed to recognize components that regulate cellular recovery processes to prevent acute kidney injury. Interestingly, some bioactive components of medicinal plants and fruits have potential to be promising therapeutic alternative for renal tubular damage.

Isoflavones are polyphenolic components which have biological actions. It has been determined these components are activator of sirtuin 1, a protein coding gene that increases peroxisome proliferator-activated receptor gamma coactivator1α (PGC-1α) expression, regulates mitochondrial function and biogenesis. Renal proximal tubular cells depend on aerobic metabolism, and then they are more susceptible to ischemic injury. These natural components ameliorate tubular damage by preventing mitochondrial dysfunction and increasing mitochondrial biogenesis (3). Likewise, it was indicated polyphenolic components of green tae such as catechin, epigallocatechin gallate, epicatechin and epigallocatechin are able to prevent cyclosporine A induced renal failure by stimulating mitochondrial biogenesis in tubular cells. Also, they have antioxidant and anti-inflammatory properties that attenuate overexpression of pro-inflammatory mediators through inhibiting NF-κB pathway (4,5). Furthermore, resveratrol is natural polyphenolic constituent that exists abundantly in grape, berries and peanut. It can exert renoprotective impacts through scavenging reactive species, activating SIRT1 that contributes to various cellular functions such as mitochondrial biogenesis, promoting Nrf2 activity that leads to prevent NF-κB activity induced oxidative stress and increase antioxidant enzymes. In addition, it was shown resveratrol is potential inhibitor of hedgehog signaling pathway that suppresses TGF-β1 expression and fibrotic pathways (6,7).

Ellagic acid is other bioactive component

that is found in berries, nuts and pomegranate peel. There are numerous studies that examine renoprotective effects of ellagic acid against nephrotoxins, metabolic disorders, ischemic and infectious conditions. It prevents hemeoxygenase (HO)-1 activity, lipid peroxidation, apoptotic and fibrotic cytokines. Also, it is capable to normalize glucose and lipid metabolism and prevent glucose abnormality associated renal tubular cell damage (8).

In conclusion, all mentioned phytochemical components are potential agents to activate cellular recovery processes to keep renal tubular cell homeostasis.

Author's contribution

FDS was the single author of the paper.

Conflicts of interest

The author declared no competing interests.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the author.

Funding/Support

None.

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