Introduction: Acute kidney injury (AKI) is associated with a high mortality rate especially in patients admitted to intensive care. Oxidative stress (OS) is implicated in the development and progression of AKI which involves oxidant injury to proximal tubular and other renal cells. Dietary constituents such as hydroxycinnamates and resveratrol are potent antioxidants in vitro which have the potential to reduce renal OS and oxidant injury.

Objective: The aim of this study was to investigate and compare the effects of these dietary antioxidants on oxidant injury in rat renal proximal tubular cells.

Methods: An in vitro model of nephrotoxic AKI was developed using paraquat (PQ) to generate OS and oxidant injury in the NRK-52E rat renal proximal tubular cell-line. Both time (3mM, over 24 hours) and concentration (0-5mM) dependent profiles of protection by hydroxycinnamates and resveratrol against PQ-mediated oxidant injury were determined. NRK-52E cells were co-incubated with 3mM PQ and increasing concentrations of hydroxycinnamates or resveratrol. For pre-incubation experiments, cells were incubated with either incubation medium or 10 microM hydroxycinnamate or resveratrol for 24 hours followed by up to 24 hours PQ incubation. Cell viability and death were measured using the MTT and lactate dehydrogenase (LDH) assays, respectively. Furthermore, the antioxidant capacities of the hydroxycinnamates and resveratrol were investigated using the ABTS radical scavenging assay and their internalization into renal cells over 24 hours was measured using LC-MS.

Results: Hydroxycinnamates and resveratrol demonstrated minimal toxicity up to 5mM after 24 hours. No significant protection was observed when NRK-52E cells were co-incubated with hydroxycinnamates or resveratrol and PQ together for 24 hours. In contrast, significant protection against PQ toxicity was demonstrated after 24 hour pre-incubation with a protective hierarchy of (1) ferulic acid, (2) meta-coumaric and (3) resveratrol after 24 hours when cell viability was measured (Table 1). A similar profile of protection was observed for cell death. Furthermore, these effects were paralleled by radical scavenging activity and internalization data.

Conclusions: This in vitro investigation demonstrates that pre-treatment of proximal tubular cells with hydroxycinnamates or resveratrol provides significant protection against nephrotoxic oxidant injury with the hydroxycinnamate ferulic acid providing the greatest protection.