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The phytoalexin resveratrol ameliorates ochratoxin A toxicity in human embryonic kidney (HEK293) cells

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Ochratoxin A (OTA) is a nephrotoxic mycotoxin produced by *Aspergillus* and *Penicillium* fungi. It contaminates human and animal food products, and chronic exposure is associated with renal fibrosis in humans (Balkan endemic nephropathy). Resveratrol, a phytoalexin, possesses anti-cancer and antioxidant properties. We investigated the mechanism of cellular oxidative stress induced by OTA, and the effect of resveratrol in human embryonic kidney (HEK293) cells over 24 and 48 h. Cells were exposed to OTA [IC_{50} 1.5 μM (24 h) and 9.4 μM (48 h) determined using MTT assay] and 25 μM resveratrol. Glutathione was quantified by luminometry and gene expression of *Nrf2* and *OGG1* was determined by qPCR. Protein expression of Nrf2, LonP1, SIRT3, and pSIRT1 was assessed by Western blot, DNA damage (comet assay) and intracellular reactive oxygen species (flow cytometry). At 24 h, resveratrol increased mRNA expression of the DNA repair enzyme, OGG1 ($p<0.05$), whereas OTA and OTA+Resveratrol significantly decreased OGG1 expression ($p<0.05$). OGG1 expression increased during 48 h exposure to resveratrol and OTA+Resveratrol ($p<0.05$). Comet tail lengths doubled in 48 h OTA-treated cells, whereas at both time periods, OTA+Resveratrol yielded shorter comet tails ($p<0.0001$). During 24 and 48 h exposure, OTA, resveratrol, and OTA+Resveratrol significantly decreased mRNA expression of *Nrf2* ($p<0.05$). Luminometry analysis of GSH revealed an increase by OTA+Resveratrol for 24 and 48 h ($p<0.05$ and $p<0.001$, respectively). Western blot analysis showed decreased Nrf2 protein expression during 24 h exposure, but increased Nrf2 expression during 48 h. LonP1 protein expression increased during 24 h exposure to OTA ($p<0.05$), OTA+Resveratrol ($p<0.0011$) and during 48 h exposure to resveratrol ($p<0.0005$).

Biography

Shanel Raghubeer is currently a PhD student at the University of Kwazulu Natal. She has completed her undergraduate degree in Biomedical Sciences, Honors degree in Medical Biochemistry and Master's in Medical Science. Her research involves natural therapies for toxin-induced illnesses.

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