
Titel des Beitrags: Protective Role of HO-1 for Alcohol-Dependent Liver Damage

Abstract: Background/Aims: Alcoholic liver disease is continuously increasing in developed countries being a leading cause of death worldwide. Chronic ethanol consumption induces oxidative stress by accumulation of reactive oxygen intermediates (ROI) and reducing the cellular antioxidant defense. Induction of heme oxygenase-1 (HO-1) may protect primary human hepatocytes (hHeps) from such damage. Thus, the aim of this study was to investigate the potential of polyphenols to protect hHeps from ethanol-dependent oxidative damage. Methods: hHeps were isolated by collagenase perfusion. ROI and cellular glutathione (GSH) were measured by fluorescent-based assays. Cellular damage was determined by lactate dehydrogenase (LDH) leakage and staining for apoptosis and necrosis. Nuclear translocation of Nrf2 and HO-1 expression were analyzed by Western blot. Results: Ethanol and TGF-β rapidly increase ROI and reduce GSH in hHeps, causing apoptosis with a release of approximately 40% total LDH after 72 h. Similar to incubation with hemin preincubation and co-incubation of cells with nifedipine, verapamil and quercetin significantly reduce oxidative stress and resulting cellular damage, in a dose-dependent manner, by initiating nuclear translocation of Nrf2 which in turn induces HO-1 under the control of p38 and ERK. Blocking of HO-1 activity with ZNPP9 reverses the protective effect of all three substances. Conclusion: Our results suggest that increasing HO-1 activity
in hHeps protects them from oxidative stress-dependent damage. As polyphenols have great potential to induce HO-1 expression, they may play an important role for future therapeutic strategies to protect liver from oxidative stress-dependent damage observed during chronic alcohol consumption.

Stichworte: HO-1; Hepatocytes; Quercetin; Oxidative stress

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