Autor(en) des Beitrags:

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) while 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

**Zeitschriftentitel:**
Digestive Diseases

**Jahr:**
2010

**Band:**
28

**Heft / Issue:**
6

**Seiten:**
792--798

**Volltext / DOI:**
http://doi.org/10.1159/000324287

**Verlag / Institution:**
S. Karger AG

**Verlagsort:**
Basel, Switzerland

**Print-ISSN:**
1421-9875

**E-ISSN:**
1421-9875

**Hinweise:**
Dieser Beitrag ist mit Zustimmung des Rechteinhabers aufgrund einer (DFG-geförderten) Allianz-bzw. Nationallizenz frei zugänglich. This publication is with permission of the rights owner freely accessible due to an Alliance licence and a national licence (funded by the DFG, German Research Foundation) respectively.

**Occurences:**
- Kollektionen > Open Access Publikationen > Verlage > Karger
- Kollektionen > Open Access Publikationen > 2010

**entries:**