Highlight report: overview of hepatoprotective compounds

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Published online: 27 November 2015
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Recently, Robert Domitrović and Iva Potočnjak from Rijeka University in Croatia have published a comprehensive review article about the mechanisms of action and clinical perspectives of hepatoprotective natural compounds (Domitrović and Potočnjak 2015). Key evidence of the 27 most promising and most intensively studied phytochemicals has been summarized and critically discussed. Since the mode of action of most hepatotoxic compounds often includes generation of oxidative stress (Godoy et al. 2013; Tolosa et al. 2013; Lu and Cederbaum 2010; Reif 2010; Chang and Abbott 2006), it is not surprising that antioxidant properties often play a key role. However, recently, antifibrotic effects have been shown to be due to immune cell–stellate cell interactions (Puche et al. 2013; Gressner and Weiskirchen 2006; Baeck and Tacke 2014). Particularly, natural killer cells have been shown to induce killing of activated stellate cells (Tian et al. 2013; Zimmermann and Tacke 2011). Therefore, it is plausible that hepatoprotective phytochemicals act by inducing apoptosis of stellate cells or stimulation of matrix degradation (Domitrović and Potočnjak 2015). Further mechanisms include binding to pro- or antiapoptotic proteins, inhibition of tyrosine protein kinases, interaction with signal transduction pathways, such as PI3 K, IKK and COX-2, as well as modification of the DNA-binding activity of transcriptional regulators (Peck et al. 2006; Domitrović and Potočnjak 2015).

Currently, mechanisms of hepatotoxicity represent a cutting-edge topic in toxicological research (Hwang et al.

2014; Hammad 2014; Campos et al. 2014; Vitins et al. 2014; Liu et al. 2014; Dias da Silva et al. 2013; Schyschka et al. 2013; Rodrigues et al. 2013; Driessen et al. 2013). Moreover, liver in vitro systems (Chen et al. 2014; Vinken et al. 2014; Godoy et al. 2013; 2015; Ghallab 2014; Reif 2014; Godoy 2011; Ilkavets 2013; Messner et al. 2013) have been intensively applied and systems biology approaches (Schliess et al. 2014; Drasdo et al. 2014a, b; Hoehme et al. 2010) have been introduced to gain a deeper understanding of the mechanisms of hepatotoxicity. Considering this background, the present review of Domitrović and Potočnjak is a must read for anyone interested in how protective compounds can interfere with hepatotoxic mechanisms.

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