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PII: S0300-483X(15)30018-4
DOI: http://dx.doi.org/doi:10.1016/j.tox.2015.07.012
Reference: TOX 51572

To appear in: *Toxicology*

Received date: 16-5-2015
Revised date: 14-7-2015
Accepted date: 15-7-2015

Please cite this article as: Zenger, Katharina, Dutta, Subhajit, Wolff, Horst, Genton, Marc G., Kraus, Birgit, In vitro structure-toxicity relationship of chalcones in human hepatic stellate cells.Toxicology http://dx.doi.org/10.1016/j.tox.2015.07.012

In vitro structure-toxicity relationship of chalcones in human hepatic stellate cells

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Abstract

Xanthohumol (XN), the major prenylated chalcone from hops (*Humulus lupulus* L.), has received much attention within the last years, due to its multiple pharmacological activities including anti-proliferative, anti-inflammatory, antioxidant, pro-apoptotic, anti-bacterial and anti-adhesive effects. However, there exists a huge number of metabolites and structurally-related chalcones, which can be expected, or are already known, to exhibit various effects on cells. We have therefore analyzed the effects of XN and 18 other chalcones in a panel, consisting of multiple cell-based assays. Readouts of these assays addressed distinct aspects of cell-toxicity, like proliferation, mitochondrial health, cell cycle and other cellular features. Besides known active structural elements of chalcones, like the Michael system, we have identified several moieties that seem to have an impact on specific effects and toxicity in human liver cells *in vitro*. Based on these observations, we present a structure-toxicity model, which will be crucial to understand the molecular mechanisms of wanted effects and unwanted side-effects of chalcones.