

## **Regulation of p53-, Bcl-2- and Caspase-dependent Signaling Pathway in Xanthorrhizol-induced Apoptosis of HepG2 Hepatoma Cells**

### **Abstract**

Xanthorrhizol is a sesquiterpenoid compound extracted from the rhizome of *Curcuma xanthorrhiza*. This study investigated the antiproliferative effect and the mechanism of action of xanthorrhizol on human hepatoma cells, HepG2, and the mode of cell death. An antiproliferative assay using methylene blue staining revealed that xanthorrhizol inhibited the proliferation of the HepG2 cells with a 50% inhibition of cell growth (IC<sub>50</sub>) value of 4.17±0.053 µg/ml. The antiproliferative activity of xanthorrhizol was due to apoptosis induced in the HepG2 cells and not necrosis, which was confirmed by the Tdt-mediated dUTP nick end labeling (TUNEL) assay. The xanthorrhizol-treated HepG2 cells showed typical apoptotic morphology such as DNA fragmentation, cell shrinkage and elongated lamellipodia. The apoptosis mediated by xanthorrhizol in the HepG2 cells was associated with the activation of tumor suppressor p53 and down-regulation of antiapoptotic Bcl-2 protein expression, but not Bax. The levels of Bcl-2 protein expression decreased 24-h after treatment with xanthorrhizol and remained lower than controls throughout the experiment, resulting in a shift in the Bax to Bcl-2 ratio thus favouring apoptosis. The processing of the initiator procaspase-9 was detected. Caspase-3 was also found to be activated, but not caspase-7. Xanthorrhizol exerts antiproliferative effects on HepG2 cells by inducing apoptosis via the mitochondrial pathway.

**Keyword:** Xanthorrhizol, *Curcuma xanthorrhiza*, antiproliferative effect, apoptosis, p53, Bcl-2