

## **Cytoprotective effects of phlorofucofuroeckol A isolated from *Ecklonia stolonifera* against tacrine-treated HepG2 cells.**

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### **Abstract**

We have recently reported that phlorofucofuroeckol A isolated from *Ecklonia stolonifera* showed potential antioxidative and anti-inflammatory properties in LPS-stimulated macrophages. This study aims to investigate the cytoprotective effect of phlorofucofuroeckol A and to characterize its molecular mechanisms using tacrine-treated HepG2 cells. Phlorofucofuroeckol A showed a cytoprotective effect against tacrine-treated HepG2 cells in a dose-dependent manner (EC(50):  $5.7 \pm 0.5 \mu\text{M}$ ). Increased intracellular reactive oxygen species (ROS) by tacrine were decreased by phlorofucofuroeckol A. The cytotoxicity of tacrine to HepG2 cells was associated with upregulations of Fas and JNK phosphorylation resulted in the caspase activations and apoptosis. Phlorofucofuroeckol A inhibited the phosphorylation of JNK and the expression of Fas-mediated apoptotic proteins including Fas ligand, cleaved caspase-8, cleaved caspase-3, and poly (ADP-ribose) polymerase. In addition, treatment of phlorofucofuroeckol A regulated the release of cytochrome c from mitochondria to cytosol in a dose-dependent manner in tacrine-treated HepG2 cells. Furthermore, pretreatment of an inhibitor of JNK, SP600125, downregulated Fas and cleaved caspase-3 without change of ROS productions in tacrine-treated HepG2 cells. In conclusion, our study demonstrated that phlorofucofuroeckol A regulates Fas-mediated apoptosis via inhibition of ROS productions and inhibition of JNK phosphorylation in tacrine-treated HepG2 cells.