Abstract

Charles University in Prague

Faculty of Pharmacy in Hradec Králové

Department of Pharmacology & Toxicology

Student:	Jana Jeřábková
Supervisor:	Doc. PharmDr. Petr Pávek, Ph.D.
Title of diploma thesis:	Interaction of selected anthocyanidins with farnesoid X receptor

Human farnesoid X receptor (FXR) is a member of nuclear receptor superfamily that act as ligand-activated transcription factors. FXR binds to specific regulatory DNA regions and induces expression of many target genes. These regulated genes are involved in bile acid metabolism and transport, maintaining blood lipids, liporoteins and glucose homeostasis and also contribute to maintain intestinal bacterial balance, hepatoprotection and liver regeneration. The interest of recent studies is to test the range of FXR ligands for treatment and prevention of many diseases such as cholestais, cholesterol gallstone disease, steato-hepatitis, dyslipidemia, atherosclerosis, type 2 diabetes mellitus, metabolic syndrome, liver cancer and other forms of cancer such as breast cancer. In this experimental diploma thesis we are focused on testing of potencial ligands of human farnesoid X receptor from the group of natural plant pigments anthocyanidins (cyanidin, delphinidin, malvidin, pelargonidin, peonidin and petunidin) using the human hepatoma cell line HepG2. The cytotoxic effect of anthocyanidins was tested using the CellTiter 96® AQ_{ueous} One Solution Cell Proliferation Assay, negative effects on cellular activity has not been observed. To demonstrate the interaction of the studied compounds with human farnesoid X receptor we used molecular biological methods gene reporter assay and one hybrid assay. Based on our results, we assume that peonidin, delphinidin and cyanidin are the ligands-agonists of human farnesoid X receptor. These our results could outline the potencial importance of peonidin, delphinidin and cyanidin in the treatment and prevention of many diseases.