Abstract

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The farnesoid X receptor (FXR) is a receptor of primary bile acids in the liver and intestine. FXR has been shown to be the master transcriptional regulator of several entero-hepatic metabolic pathways with relevance to the pathophysiology of cholestasis, metabolic syndrome and diabetes, fatty liver disease, cholesterol gallstone disease and intestinal inflammation. Furthermore, FXR plays an important role in the gut-liver axis feedbacks regulating lipid and glucose homeostasis. The apical sodium dependent bile acid transporter (ASBT; SLC10A2) is a bile acid transporter localized to the apical surface of the terminal ileal enterocytes. ASBT plays an important role in the reabsorption of bile acids in the ileum. In the liver, the hepatocytes take up the bile acids by the sinusoidal sodium-dependent taurocholate co-transporting polypeptide (NTCP; SLC10A1). ASBT and NTCP are regulated in the ileum and liver through FXR receptor by bile acids to control bile acids pool.

In the current study, we analyzed whether anthocyanins or anthocyanidins activate farnesoid X receptor (FXR), which controls key genes involved in bile acids synthesis, transport and their homeostasis in the body. We used gene reporter assays with pFXRE-luc2P reporter construct, FXR expression vector and the fusion expression construct containing the ligand binding domains of human FXR receptor fused to yeast GAL4 subunit to analyze interaction with human FXR. Experiments have been performed in HepG2 cells with the constructs treated for 24 h with increasing concentrations of natural polyphenolic compounds. We found interactions of these compounds with FXR in both experimental systems. We can therefore conclude that anthocyanidins might be weak ligands of FXR receptor which correlates with their choleretic effects in rats.