Abstract

Cholestasis is characterized by impaired bile flow. It can either be caused by malfunction of the transporters/proteins involved in bile acid homeostasis or by physical blockage of the bile duct. Regardless of cause, cholestasis leads to hepatic fibrosis, cirrhosis and ultimately liver failure. Uptill now, obeticholic acid and ursodeoxycholic acid are the only approved drugs for treatment of cholestatic related diseases. However the outcomes of these therapies are inconsistent. Therefore, there is a need to find out new therapeutic options for the management of cholestasis. As phytotherapy has been used for the treatment of various ailments, the current project is aimed to explore the anti-cholestatic potential of berberine. Twenty four mice were randomly divided into three groups: i. Control group, ii. DDC group iii. Treatment group. The mice of control group were given standard diet and water. DDC group served as cholestasis group. The mice of this group were fed with standard diet containing 0.1% 3,5-diethoxycarbonyl-1,4-dihydroxychollidine (DDC) for four weeks. In treatment group the mice were fed with standard diet containing 0.1% 3,5-diethoxycarbonyl-1,4-dihydroxychollidine (DDC) along with berberine (via oral gavage) for four weeks. After four weeks, all mice were sacrificed to obtain blood (for liver function tests) and liver samples (for histological studies). The results indicated that the serum levels of ALT, ALP, AST were significantly elevated in DDC group as compared to control group. This indicates that the liver of the mice of DDC group is damaged. However, the level of these parameters is significantly lower in treatment group as compared to DDC group indicating the protective role berberine. Furthermore, the liver hydroxyproline conent were assayed. Histological studies indicated that liver of mice of DDC group was severely damaged. However, in treatment group the liver architecture was intact. The underlying mechanism involves the activation of of Fernesoid X receptor (FXR) which ultimately regulates the transporters and proteins responsible for bile acid homeostasis. Berberine also attenuated liver damage by decreasing the hydroxyproline content. Altogether, our results indicate that berberine protects the liver from DDC induced cholestatic damages and regulates FXR expression . Therefore, berberine can be used as a potential candidate for the treatment of cholestasis. However, clinical study is required for its prescription as a medicine against cholestasis.