ABSTRACT:

Cholestasis is a liver disorder resulting from impairment in the secretion of bile and its flow to duodenum. The maintenance of normal of bile flow is accomplished by several hepatocyte and enterocyte localized transporters. Malfunction of these transporters or blockage of the bile duct impairs the bile flow thus leading to its accumulation the liver. Ursodeoxycholic acid and obelticholic acid are the only approved therapy for cholestatic related liver injury. However, several studies indicated that outcomes of these drugs are not satisfactory. Therefore, the exploration of new treatment for cholestasis is required. Being safer and cost-effective, the phytonutrients have occupied the central stage in modern medicines. Berberine, one of such compounds, has been used to treat various liver related disorders. The aim of this study was to investigate the therapeutic effects of berberine against cholestasis mouse models. For that, cholestasis was induced by diethoxycarbonyl-1,4-dihydroxychollidine(DDC) in mice which were then treated with berberine (300mg/kg/day). Serological and histological results indicated that berberine protects liver from DDC induced cholestasis. Furthermore, we also performed the docking studies to find out the interaction of berberine with farnesoid X receptor (FXR), which is a transcriptional regulator of the genes involved in bile homeostasis. The docking results indicated that berberine binds with FXR and its interaction is comparable to GW4064 (an agonist of FXR). Our data indicate that as berberine binds with FXR, it activated FXR which ultimately bind with DNA to alter the transcription of target genes. This transcriptional regulation of genes involved in bile homeostasis ultimately protect the liver from bile acid induced injury.