CHAPTER V

CONCLUSIONS

Alcoholic liver disease (ALD) is one of major diseases that can cause death of patients in our country and worldwide [3]. Some studies reported that a patient with severe ALD has a 4-year mortality which is worse than many cancers or cardiovascular diseases [4]. The excessive of alcohol consumption leads to alcoholic liver disease [5]. The pathological changes of ALD are characterized by a progression from steatosis to chronic hepatitis, fibrosis and cirrhosis [7, 8, 9]. Nowadays, there is still no effective medicine for ALD. Moreover, the efficacies of the medicines used in ALD are inconsistent and have not been approved by FDA. The principles of treatments base on the reduction of pathological progression caused by the disease and a liver transplantation. The clinical treatments used for ALD are lifestyle modification, nutrition therapy, drug therapy, cytokine therapy and alternative medicines [6, 10]. Therefore, there is a potential to find alternative medicines to develop as a hepatoprotective agent from our herbal products.

Turmerics, ***Curcuma longa*** Linn are one of local herbal plants that has been used in traditional medicines for gastrointestinal disorders. Moreover, turmeric powder capsules are in the list of herbal products in the national of essential medicines. It has promoted to use widely in hospital. Major chemical constituents in turmeric comprise of volatile oil and the colouring compound, curcuminoids [16, 17, 18]. Curcuminoids have variety of pharmacological actions such as anti-inflammatory, anti-oxidant, anti-microbial and anti-cancer.

In this study, we proposed to determine the hepatoprotective effect of curcuminoids in ALD. We used the ethanol-induced hepatoxicity rats as animal model and also investigated the possible mechanism of action of curcuminoids on anti-oxidant properties in HepG2 cells.

The results from the long time-exposure ethanol stimulated hepatotoxicty in rats revealed that oral administration of curcuminoids at dose 500 and 750 mg/kg/day could alleviate the ethanol-induced liver damage significantly, by decreasing serum

AST and ALT levels. However, curcuminoids had minor effect on ALP and LDH enzyme levels. From the rat livers histological examination, curcuminoids promoted the liver cell recovery from the ethanol-induced liver injury, demonstrating by the decrease of fatty liver as well as inflammation lesion. In additions, the studies of acute toxicity of curcuminoids were carried in normal and ethanol induced hepatotoxicity rats. Our results have confirmed the safety of curcuminoids in both normal and hepatotoxicity animals at the high dose of testing (5000 mg/kg). There was no mortality or any signs of toxic observed which implies that curcuminoids treatment should be safe in ALD conditions.

We found the inhibitory effect of curcuminoids on lipid peroxidation which mainly impairs cell membrane and cause heptocytes injury in microsomal extraction from ethanol-induced toxicity rats. The antioxidant activity of curcumin in curcuminoids might be a major mechanism of action. However, there was no change in the hepatic SOD activity in our conditions. It is necessary to further investigate the effect of curcuminoids on the antioxidant enzyme such as glutathione peroxidase or catalase in this chronic ALD rat model. From the HepG2 cell study, we showed that ethanol was toxic to the cells by decreasing cell viability in dose and time dependent responses. The pre-incubation of curcuminoids trended to protect the hepatic membrane damages. Moreover, curcuminoids could decrease the lipid peroxidation in the ethanol-induced toxicity cells. These data might refer to the antioxidant effect of curcuminoids. However, the effect of curcuminoids on NO production in our study was indefinite. Curcuminoids at the lower concentration reduced NO production, on the other hand, the higher concentrations of curcuminoids had no effect or raise NO production in the ethanol stimulated toxicity.

The results of our study suggest that curcuminoids, the active compounds in turmeric may protect a progression of hepatic cell damages caused by chronic ethanol exposure, and curcuminoids are safe in hepatotoxicity. Therefore, curcuminoids could be potential substances to develop as the hepatoprotective agents to treat ALD. It is encouraging to promote the use of turmeric compound as one option for liver diseases. However, for further drug development and approval, the information of clinical study as well as the cellular mechanism of action of curcuminoids still needs to be done.