CHAPTER VI

DISCUSSION

The main findings of this study were administration of curcuma 80 mg/day following cigarettes smoke exposure for 10 and 13 weeks have significantly reduce liver cells change. Its mean Curcuma L has reparative effect on liver cell change induced by long term cigarette smoke exposure. Furthermore this study also showed administration of Curcuma L for 13 weeks also significantly reduce liver tissue TNF-α expression. On the other side the administration of the curcuma L dident have potency to reduce up-regulation of liver tissue TNF-α expression due to cigarette smoke exposure for 10 weeks may give suggest that with increasing time using of *curcuma L* inhance the regenirative role aganist the expusore effect of passive cigarette smoke

Base on above findings the hypothesis in the tow variable given suggest that the regenireative role of the administration of curcuma L on the liver cell change is more potency reduction than regenirative role on the TNF-α expression may be because the curcuma longa extract act as antioxidant much more than act as anti-inflammatory production and also may be because curcuma longa extract can be regenirative & reparative role much more against early stage of liver damage like liver cell change than than serious liver cell damage like TNF-α expression as

inflamation procces inside liver cell at the same period of the curcuma longa administration

Smoking has been associated with several disease such as cardiovascular disease, respiratory disease, cancer, infertility, hearing loss and recently gastrointestinal disease including hepatotoxicity.[54]

Adverse effect of smoking to liver tissue has been reported on several studies. Watanabe, et al reported exposure cigarette smoke for 27 days on rats may cause increase of blood level of liver enzymes. This study also found an increased of blood level of malondialdehyde (MDA) on rats exposed to cigarette smoke. These findings suggest the mechanism of cigarette smoke-induced liver injury is through lipid peroxidation.[55] Study by Yuan, et.al. also found exposure of cigarette smoke for 19 weeks cause lipid accumulation on mice liver tissue.[56] Recent study also reported cigarette smoking is an independent risk factor for hepatocellulare carcinoma.[57] Cigarette smoking also has been reported enhance progression of chronic liver disease such as non-alcoholic fatty liver disease (NAFLD) through it effect on insulin resistance, stress oxidative and increase liver cell appotosis.[58,59]

Smoking causes a variety of adverse effects on organs that have no direct contact with the smoke itself such as the liver. It induces three major adverse effects on the liver: direct or indirect toxic effects, immunological effects and oncogenic effects. Smoking yields chemical substances with cytotoxic potential which increase necroinflammation and fibrosis. In addition, smoking increases the production of proinflammatory cytokines such as IL-1, IL-6 and TNF-α that would be involved in

liver cell injury. It contributes to the development of secondary polycythemia and in turn to increased red cell mass and turnover which might be a contributing factor to secondary iron overload disease promoting oxidative stress of hepatocytes. Increased red cell mass and turnover are associated with increased purine catabolism which promotes excessive production of uric acid. Smoking affects both cell-mediated and humoral immune responses by blocking lymphocyte proliferation and inducing apoptosis of lymphocytes. Smoking also increases serum and hepatic iron which induce oxidative stress and lipid peroxidation that lead to activation of stellate cells and development of fibrosis. Smoking yields chemicals with oncogenic potential that increase the risk of hepatocellular carcinoma (HCC) in patients with viral hepatitis and are independent of viral infection as well. Tobacco smoking has been associated with supression of p53 a tumor suppressor gene. In addition, smoking causes suppression of T-cell responses and is associated with decreased surveillance for tumor cells.

In this study, SD rats that received oral administration of Curcuma L. extract have significantly lower liver cells change and TNF-α expression compare to without administration of Curcuma L. extract. This study is the first evidence that Curcuma L has reparative of on smoking-induced liver injury. This findings is consistent with previous study reported Curcuma L has hepatoprotective effects from a variety of hepatotoxic agent including carbon tetrachloride (CCl4)[60], galactosamine, acetaminophen (paracetamol), and Aspergillus aflatoxin[61]. The protective of

Curcuma is through antioxidant property that inhibit stress oxidative and free radical scavengers. [62,63]

The increased of TNF-α expression play central mechanism on liver cell injury due to cigarette smoke exposure. As mentioned previously, the adverse effect of cigarette smoking can be direct or indirect to cells. Direct effect is through nicotine toxin to cells especially cells of oral cavity and respiratory pathway. Indirect effect is through increase of stress oxidative and proinflammatory cytokine production. This study showed Curcuma L inhibit liver tissue TNF-α expressions. Previous study by Mouzaoui et all reported Curcuma L attenuate curcumin TNF-α induced oxidative stress hepatotoxicity in mice. Curcula L treatments significantly attenuated the markers of oxidative stress, neutrophils influx and ROS-related cellular and histological damages.[64]

The degenerative changes of liver cells could be attributed to oxidative stress, which is generally correlated with cellular damage.[65] In this study the cellular changes were shown as liver cells change characterized as odeama, karyolysis and picnosys. This finding is supported by recent study that reported antioxidant property of Curcuma L can inhibit liver cell damage due to aflatoxin and carbon tetrachloride.[60,61]

V. Limitations of the Study

Limitations of this study is difficult to make sure that every rats got the same dose of the passive cigarette smoke exposure one and another since can't control the air cerculation.