ISOLATION OF CERTAIN CHEMICAL CONSTITUENTS FROM *AZADIRACHTA INDICA* AND *FICUS* SP. AND THEIR ASSESSMENT AS HEPATOPROTECTIVE AGENTS.

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Thesis

Submitted for the award of the degree of M. Sc. of Science (Organic Chemistry)

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INTRODUCTION

Liver is one of the largest and the most important organ in human body. It plays a surprising role in the maintenance, performance and regulating homeostasis of the body. The major functions of the liver are carbohydrate, protein and fat metabolism, detoxification, secretion of bile and storage of vitamin. Owing to the liver is involved with almost all biochemical process and continuously and variedly exposed to environmental toxins, poor eating habits, alcohol and different synthetic drugs, it is no wonder that there are many different diseases that will affect the liver **[Ward and Daly, 1999; Wolf, 1999]**.

Liver diseases (also called hepatic diseases) are some of the fatal diseases in the world today and they pore a serious challenge to international health. Liver problems include a wide range of diseases and some of them are temporary while the other problems still for a long time and led to serious complications. In Africa and Asia, their main causes are viral and parasitic infections while in Europe and America alcohol abuse is the major cause of liver diseases **[Wolf, 1999; Gutièrrez and Sohís, 2009; Muriel**

and Rivera-Espinoza, 2008; Subramoniam and Pushpangadan, 1999].

Liver fibrosis occurs when the liver is damaged as a result of many risk factors including chronic viral infection with hepatitis virus (types B or C), infection of *Schistosoma mansoni*, chemicals (e.g. some pharmaceuticals, excessive alcohol intake), and pesticides such as thioacetamide or due to autoimmune hepatitis. Also, fibrosis may be initiated by some metabolic disorders (e.g. lipid, glycogen or metal storage disorders) **[Poyrard *et al*., 2000; Friendman, 2003; Halton *et al*., 2001; Hessien *et al*., 2008]**. Advanced liver fibrosis results in cirrhosis, liver failure and portal hypertension and often require liver transplantation. Liver fibrosis and cirrhosis are generally the end and result of majority of chronic liver insults. The development of fibrosis and particularly cirrhosis are associated with a significant morbidity and mortality. Despite efforts to develop antifibrotic agents no drugs have been approved as antifibrotic agents in humans **[Gines *et al*., 2004; Friendman, 2003; Huseini *et al*., 2005]**.

Schistosomiasis (Bellarizia) is a parasitic disease caused by infection with helminth schistosoma species. Million of

people in subtropical countries is currently infected by *Schistosoma mansoni* which is the common human schistosome. Schistosoma worms live in the mesenteric and portal viens of their human host **[Mohamed *et al*., 2005; Al-Sharkawi *et al*., 2007]**. Eggs laid by *S.mansoni* adult females in the mesenteric veins after weeks of infection either exit through the feces to continue the life cycle or migrate to the liver and impacted in the liver where induce granulomatous inflammation. The egg cuticle composed of cross linked proteins, encloses a larvae which releases enzymes and antigens through multiple pores. The formed granuloma prevent the diffusion of the toxic and antigenic substance which release from the schistosome eggs into surrounding hepatic tissues and protect the liver from hepatotoxins. The accumulation of fibrotic tissues obstructs the blood flow through the liver led to portal hypertension, extended periporlal fibrosis and portal shunting **[Harvie *et al*., 2007; El-Shenawy *et al*., 2006]**.

The formed granuloma is principally composed of macrophages, eosinophils and lymphocytes as well as some other killer cells from different organs. The host reaction presumably involves reactive oxygen species (ROS). It has been reported that eosinophils kill *S.mansoni* eggs and