CHAPTER I

INTRODUCTION

The hepatitis B virus (HBV), a hepadnavirus, is a 42 nm partially double stranded circular DNA virus, composed of a 27 nm nucleocapsid core, hepatitis B core antigen (HBcAg), surrounded by an outer lipoprotein coat called envelope, containing the hepatitis B surface antigen (HBsAg) (Robinson, 1995).

HBV, discovered in 1966, infected more than 350 million people worldwide (Purcell, 1993). HBV is a leading cause of chronic hepatitis, cirrhosis, and hepatocellular carcinoma, accounting for 1 million deaths annually. In addition, chronic infection with HBV is the most important risk factor which lead to liver cancer (World Health Organization International Agency for Research on Cancer [IARC], 1994). The distribution of hepatitis B infection varies greatly throughout the world, and can be divided into three areas where the prevalence of chronic HBV infection is high (>8%), intermediate (2-8%), and low (<2%) (Plotkin and Orenstein, 1999). In areas where the prevalence is high, such as Southeast Asia, China, and Africa, more than half of the population is infected at some time in their lives, and more than 8 percent are chronic carriers of the virus (William and Lee, 1997)

HBV can cause hepatitis by interfering with the function of the liver while replicating in hepatocyte. The immune system is then activated to produce a specific reaction to combat and possibly eradicate the infectious agent. As a consequence of pathological damage, the liver becomes inflamed.

HBV is transmitted through percutaneous or parenteral contact with infected blood, body fluids, and sexual intercourse. The virus cannot penetrate the skin or the mucous membrane barrier. Rupture of this barrier, eventhough minimal and insignificant, can lead to transmission.

Usually, the detection of HBV can be done by using markers such as HBsAg, HBV DNA or HBeAg (hepatitis B e antigen). Although all of these markers can be found in patient's sera infected by HBV. However the most reliable diagnosis is to use HBsAg marker (สิริฤกษ์ ทรงศิวไล, 2000).

Treatment of chronic hepatitis B is aimed at eliminating infectivity to prevent transmission and spread of HBV, halting the progression of liver disease and improving the clinical feature, and preventing hepatocellular carcinoma (HCC) from developing by losing markers of HBV replication in serum and liver like HBV DNA, HBeAg, and HBcAg. Normalization of alanine aminotransferase (ALT) activity, resolution of hepatic inflammation and the improvement of a patients' symptoms usually accompany these virological changes. Antiviral agents and immunomodulators are two main classes of treatment, aimed at suppressing HBV by interfering with viral replication and help the human immune system to defense and eradicate the virus.

For immunomodulators, interferon alfa-2a and interferon alfa-2b are approved to use for treatment hepatitis B. However, interferon therapy is effective about 30 percent to 40 percent of the patients with chronic HBV infection. The study in USA shows that interferon treatment for chronic hepatitis B in 35-year-old man increase life expectancy by 3.1 year, an average cost is $6,000 (Dusheiko and Roberts, 1995).

In case of nucleoside analogue, such as lamivudine, these antiviral demonstrated the clearance of HBV DNA from serum during treatment in virtually 100 percent of the patients, but sustained remissions in 19 percent (Dienstag, 1995) (Lai, Ching, and Tung, 1997). With prolonged treatment, escape mutants develop in approximately 16 percent of patients at one year because of base pair substitutions at specific sites of the DNA polymerase gene (Lai, Liaw, and Leung, 1997) (Honkoop, 1997).

Interferon therapy is successful only in some patients, the results are still unpredictable, and a cost in treatment is not so cheap. Lamivudine therapy, yet founded a remission of HBV DNA and resistances. Thus research for a new alternative agent is required. A new approach to explore of alternative drugs, especially constituents from medicinal plants, is very interesting worldwide. Consequently, several plant extracts were screened for anti-HBsAg activity as shown in Table 1.

The purpose of this study was to screen for anti HBV activity of some medicinal plant extracts by detection the inhibition of HBsAg secretion from PLC/PRF/5 cells. In this study, thirteen medicinal plants were investigated including *Caesalpinia sappan*

(ฝาง), *Derris scandens* (เถาวัลย์เปรียง), *Duranta repens* (เทียนหยด), *Homalomena aromatica* (เต่าเกียด), *Houttuynia cordata* (พลูคาว), *Litchi chinensis* (ลิ้นจี่), *Loranthus pentandrus* (กาฝากมะม่วง), *Santalum album* (แก่นจันทน์), *Phyllanthus emblica* (มะขามป้อม), *Phyllanthus amarus* (ลูกใต้ใบ), *Rhinacanthus nasutus* (ทองพันชั่ง), *Saussurea lappa* (โกฐกระดูก).

Table 1. List of medicinal plants with anti-HBsAg activity

Plant	Family	Reference
Andrographis paniculata	Acanthaceae	Mehrotra, 1990
Anemone hupehensis	Ranunculaceae	Zheng and Zhang, 1990
Caesalpinia sappan	Caesalpiniaceae	Zheng and Zhang, 1990
Cudrania cochinochinensis	Moraceae	Zheng and Zhang, 1990
Evodia rutaecarpa	Rutaceae	Zheng and Zhang, 1990
Glycyrrhiza uralensis	Fabaceae	Terumi, 1994
Gossypium herbaceum	Malvaceae	Zheng and Zhang, 1990
Litchi chinensis	Sapindaceae	Zheng and Zhang, 1990
Oldenlandia tenelliflora	Rubiaceae	Zheng and Zhang, 1990
Phyllanthus amarus	Euphorbiaceae	Yeh et al,. 1993 Liu, Lin, and Mcintosh, 2001
Phyllanthus ninuri	Euphorbiaceae	Ji et al., 1993
Picrorrhiza kurroa	Scrophilariaceae	Mehrotra, 1990

Table 1. (continued)

Plant	Family	Reference
Portulaca grandiflora	Portulacaceae	Zheng and Zhang, 1990
Prunella vulgaris	Lamiaceae	Zheng and Zhang, 1990
Saussurea lappa	Asteraceae	Chen et al., 1995