

CHAPTER I

INTRODUCTION

Herpes simplex viruses are the first of human herpesviruses. Infections of these viruses occur worldwide and have been reported in both developed and developing countries. Consequently, the infection has been recognized as a public health concern. In addition, herpes simplex viruses (HSV) are intensely human pathogens and responsible for a broad range of human diseases. The clinical specimens of HSV-induced disease have been recognized as eczema herpeticum, vulvovaginitis, keratoconjunctivitis, encephalitis and meningitis. The existence of two distinct antigenic types of HSV was revealed in the early 1960s, and, under the formal designation of the International Conference for Taxonomy of Viruses (ICTV), they are now designated as human herpesviruses 1 (HHV-1) and human herpesviruses 2 (HHV-2) (Ginsberg, 1988). Type 1 and 2 herpes simplex viruses differ significantly in their pathogenic potential. Infection with HSV-1 generally is limited to the oropharynx and is transmitted by direct contact of a susceptible individual with infected secretions. Thus, initial replication of virus will occur in the oropharyngeal mucosa. The trigeminal ganglion becomes colonized and harbors latent virus. Acquisition of HSV-2 infection is usually the consequence of transmission by genital contact. Virus replicates in the genital, perigenital, or anal skin sites with seeding of the sacral ganglia. Changes in sexual mores, however, have somewhat altered these common patterns: occasionally, type 2 viruses are isolated from oral lesions and type 1 viruses from genital lesions.

In various populations, the range of 60% and more than 95% are infected with HSV-1, and between 6% and 50% with HSV-2. Recurrences of both oral labial and genital herpes simplex virus infections in human occur frequently. For more than 60% of patients with initial HSV-2 infection, the infection recurs within 6 months, and patients with recurrent genital disease have a median of five recurrences per year. The disease is often painful, sometimes debilitating, and causes considerable social and psychological stress. Moreover, a number of clinical and epidemiological studies have

shown a significant correlation between genital HSV-2 infections and a higher incidence of cervical carcinoma. In Thailand, HSV infections have been frequently found in various populations and it is an important public health problem. Investigators from virus research institute, Department of Medical Sciences, Ministry of Public Health had surveyed HSV-1 and HSV-2 antibodies of the people in Bangkok and Chainart provinces (ประเสริฐ ทองเจริญ 2528). They concluded that (1) 10-17% of young people ever had symptomatic herpes and 5% of them were genital herpes; (2) 0.21-0.35% (4-7 cases per 2,000 people) had HSV infection in vagina and cervix, and this had increased in the past years; (3) HSV infection incidence had increased in the women with genital infections; (4) In Bangkok, almost upward 30-year old people had HSV-1 infections and had a little lower HSV-2 infection incidence. In Chainart where the population density is lower than Bangkok, there were also lower incidences of HSV infection. It was reported that herpes simplex viruses were isolated from 40.8 to 56.0 percent of the patients with genital herpes. (Yoosook et al., 1989) The frequencies of recovery from HSV diseases seemed to be higher in female than in male, particularly during the first episode of infection. Asymptomatic shedding of the viruses from female genitalias was approximately 0.7 percent. Herpes simplex virus type 2 represented 98.4 percent of all isolates and the remaining isolates were type 1..

In the treatment of HSV-infections, many antiviral agents are available such as idoxuridine, trifluridine, vidarabine which are toxic and poorly effective, whereas acyclovir (ACV) is efficient but expensive. However, Leung and Sacks (2000) reported that acyclovir in topical, oral or intravenous forms was highly effective only at first episode of herpes simplex infection and ineffective with latent infection. Resistances of HSV to ACV were reported in many parts of the world (Pottage and Kessler, 1995; Shin et al., 2001). Trisodium phosphonoformate (PFA, foscarnet), an antiviral agent which inhibits HSV-DNA polymerase, was used to treat ACV-resistant virus, but it showed strong side effect. So, foscarnet is recommended for only severe infection treatment (Hasegawa and Kaeagushi, 1994). In addition, the development of clinical resistance to foscarnet and the isolation of foscarnet-resistant virus after several courses of the drug had been reported (Birch et al., 1990). Therefore, a new approach to explore of

alternative drugs, especially constituents from medicinal plants, is very interesting worldwide.

Medicinal plants have a long history of use and their use is widespread in both developing and developed countries. Herbal medicines provide rational means for the treatment of many diseases including viral infections. These are gaining popularity because of several advantages such as often fewer side effects, better patient tolerance, relatively less expensive and acceptance due to long history of use. Plants also continue to be a major source of new lead compounds. Many Thai medicinal plants have been preliminary reported to have antiviral activities and can be the good candidates for the development of antiviral agents.

Therefore, the purpose of this study was to investigate the antiviral activities of the extracts from three Thai medicinal plants, *Glycosmis pentaphylla* (Retz) DC., *Ipomoea maxima* (Linn.) F. and *Willughbeia edulis* Roxb, against HSV-1 strain KOS and HSV-2 strain Baylor 186 . The antiviral activity assay was performed by inactivation, prophylactic and plaque reduction assay. The most active fraction from each plant was selected for preliminary mechanism study by post binding assay, penetration assay and virus yield inhibition assay.

The results from this study could provide a preliminary information on the *in vitro* anti-HSV-1 and HSV-2 activities of extracts from. *Glycosmis pentaphylla*, *Ipomoea maxima* and *Willughbeia edulis* Furthermore, effective medicinal plant(s) would be interesting candidate(s) for the anti-HSV-1 and HSV-2 drug development in the future.