

## CHAPTER I

### INTRODUCTION

Natural products are chemical compounds produced by plants, animals or microorganisms. The term of natural products in commercial is generally used for cosmetics, medicines, dye, dietary supplements, and foods produced from natural sources that are minimally processed or do not contain any artificial ingredients. While in the field of organic chemistry, the definition of natural products are particularly organic compounds derived and isolated from natural sources that are produced by the bio-synthetic pathways of primary or secondary metabolism. Within the field of medicinal chemistry, the definition is always further restricted to secondary metabolites, small molecules (mol wt <2000 amu) that are not necessary for the survival of the organism [1].

Primary metabolites are organic compounds that are essential for growth, development, reproduction and survival such as nucleic acids, amino acids, proteins, carbohydrates, and various energetic compounds involved in the primary metabolic pathways of all living organism. Unlike primary metabolites, secondary metabolites are found in only specific organisms and are expression of the individuality of species. Secondary metabolites are organic compounds that are not directly involved in the normal growth, development, or reproduction of an organism, but the living produces them for evolutionary advantage such as poison agent to defense themselves against predators, as volatile attractants towards the same or other species, or as coloring agents to attract or warn other species, so it is logical that most of natural products always have pharmacological or biological activities that can be of therapeutic benefit in treating diseases [2].

For thousands of years natural products, especially from higher plant, have been served mankind through the use of traditional medicines as an important source of therapeutic agents to treat or prevent disease and improve quality of life. According to report of the World Health Organization (WHO), 80% of the world population still relies on plant-based traditional medicines for their primary health care [3]. Higher plants with ethnomedicinal properties have been regarded as primary sources of medicines for early drug discovery. Clinical, pharmacological, and chemical studies of medicinal plants base on the knowledge of traditional medicine had led to the isolation of many natural products that have become well known

pharmaceutical drugs such as aspirin, digitoxin, morphine, quinine, and pilocarpine [4]. The success of natural products and synthetically modified natural product derivatives in drugs discovery are play a major role in the treatment of human diseases and cover almost all therapeutic areas in the range of anti-cancer agents [3, 5], anti-fungal agents [6], anti-bacterial agents [7], anti-viral agents [8] and anti-diabetic agents [9].

Since natural products are chemical compounds derived from the phenomenon of biodiversity which are always stereochemically complex molecules, less than 10% of the world's biodiversity has been evaluated for potential biological activity. Many more useful natural lead compounds still await discovery with the challenge of how to access this natural chemical diversity [10, 11].

The family Apocynaceae consists of approximately 250 genera and 2000 species of tropical trees, shrubs, woody climbers, and herbs. The characteristic botanical features of the family are an abundant milky latex [12, 13]. In traditional medicine, the latex of Apocynaceae species are used to treat gastrointestinal ailments, combat fever and pain, malaria and treat diabetes and infectious diseases. Non-medicinal uses include food, poisons, fodder, wood, ornamentals, dye and perfume. Many members of Apocynaceae have been reported to be rich sources of indole alkaloids, steroidal glycosides, steroidal alkaloids and iridoid glycosides, especially in the seeds and latex [14, 15]. The most well-known indole alkaloids with therapeutic usefulness are vinblastine and vincristine, from Madagascar periwinkle, *Catharanthus roeueus*. They are antimicrotubule drug included in combination with other chemotherapeutic agents for the treatment of a variety of cancers such as leukemia, lymphoma, breast and lung cancers. Vinblastine (Velbe ®) is particularly useful in treating Hodgkin's disease whereas vincristine sulphate (Oncovi ®) is used to treat acute leukemia in children. Ibogaine from *Tabernanthe iboga* is another example of active indole alkaloid used as a therapeutic agent for the treatment of Alzheimer's disease, Huntington chorea and other brain damages [14].

The genus *Gymnema* belongs to the Apocynaceae family. There are about 119 known species in the genera *Gymnema*, at least 4 species found in Thailand, and they are distributed in tropical or subtropical Asia, South Africa and Oceania [16]. Several species in the *Gymnema* genus are in the list of Indian and Chinese traditional medicine used for treatment of diabetes, rheumatism, blood-vessel inflammation and snakebites [13, 17]. Additionally, extracts of various species have shown anti-sweetening [18], antidiabetic [19], hypoglycemic [20], anti  $\alpha$ -glucosidase

and  $\alpha$ -amylase [21] and antioxidant activities [22]. Previous phytochemical investigations of plants in the genus *Gymnema* have led to the isolation of steroidal glycosides [23, 24] and triterpenoid saponins, especially olenane type saponins [25-29] with a wide range of biological activities, particularly cytotoxic [30] and anti-diabetic activities [31].

*Holarrhena* is a genus belongs to the Apocynaceae family consisting of 4 species. They are native to Africa and Asia [32], only *H. pubescens* and *H. curtisii* found in Thailand. *Holarrhena* genus has been reported to possess antihelminthic, appetising, antidiarrhoeal, antibiotic and astringent properties [17, 33]. In Indian traditional medicine, *Holarrhena* genus has been considered a popular remedy for the treatment of dysentery, diarrhea and intestinal worms. In addition, the seeds of this genus are also used as an anti-diabetic agent in many Asian countries [34]. Previous phytochemical investigations of plants in the genus *Holarrhena* have led to the isolation of steroidal alkaloids [35, 36] and triterpenoids [37] with a wide range of biological activities such as cytotoxic [35], anti-diabetic [38] and antibacterial [39] activities.

*Gymnema griffithii* Craib and *Holarrhena curtisii* King & Gamble are widely distributed in the dry dipterocarp forests in the northern and southwestern parts of Thailand. However, since no phytochemicals of *Gymnema griffithii* fruits and *Holarrhena curtisii* pods have been reported, this research aimed to investigate the phytochemicals of both plants. Therefore, the main objectives of this research are

1. To isolate and purify phytochemicals from fruits of *G. griffithii* and pods of *H. curtisii*.
2. To determine chemical structures of the isolated compounds by spectroscopic techniques.
3. To evaluate anticancer and anti- $\alpha$ -glucosidase activities of the isolated compounds.