CHAPTER I

INTRODUCTION

Malaria is caused by the protozoan parasite, *Plasmodium*, a member of the phylum Apicomplexan. There are four species that infect humans: *P. vivax*, *P. falciparum*, *P. malariae* and *P. ovale*, of which *P. falciparum* and *P. vivax* are the most important. It is still a serious endemic disease in more than 100 countries in Africa, Asia, Oceania, Latin and South America. Approximately 300 million people are affected with the parasitic disease and reports of 1-2 million deaths per year are attributed to malaria. Travelers from nonendemic areas are at risk of exposure and thousands of cases are reported in the US and in Europe annually (Murray and Perkins, 1996: 141).

Malaria is also one of the major public health problems in Thailand. During the past 5 years, the malaria mortality rate in Thailand has decreased from 1.8 per 100,000 persons in 1992 to 1.4 per 100,000 persons in 1995 (Malaria Division, 1996). However, this number may be less than the actual rate since many cases may have occurred without being reported.

Although the death rate has decreased, the remaining major problem is the drug resistance of the parasites, particularly *Plasmodium falciparum*, to clinically used antimalarial drugs including chloroquine, mefloquine, quinine, amodiaquine and sulfadoxine-pyrimetamine (Phillipson *et al.*, 1995). In order to cope with the problem more effectively, we need to search for new antimalarial agents for 2 purposes, namely, to replace the current drugs or to use them in combination therewith.

Searching antimalarial agents from medicinal plants has been one of the most promising strategies for drug discovery on this area. So far, higher plants have provided two major clinically useful drugs which are:

1. Quinine, an alkaloid which was isolated from the stem bark of *Cinchona* as early as 1820. The sources of cinchona bark are *Cinchona succirubra* (Red bark), *C. ledgeriana* (Ledger's bark) and *C. calisaya* (Yellow bark).

2. Artemisinin, an unusual sesquiterpene containing an endoperoxide moiety, was isolated by Chinese scientists in the early 1970 from the Chinese medicinal herb, *Artemisia annua* in the family Asteraceae (Phillipson *et al.*, 1995).

A recent report (Rupprecht, Hui and McLaughlin, 1990) described an antimalarial compound from *Goniothalamus giganteus*. Thus, there might be some possibility of finding other antimalarial chemicals from the plants in this genus.

The plant which was investigated in this study is *Goniothalamus tenuifolius* King. It belongs to the tribe Mitrephoreae of the family Annonaceae. Many members of this family are main sources of bioactive compounds. Sinclair (1955: 435) has described the characteristics of this plant as follows.

Shrub or small tree 2-7 m high. *Young twigs* slender, pubescent, later glabrous and striate. *Leaves* membranous, varying considerably in shape and size, lanceolate or oblong lanceolate, acuminate, base acute, rarely rounded, the margins sometimes slightly undulate, glabrous or pubescent on the midrib and fveins beneath; main nerve - 11 pairs, fine, curving and interarching 5 mm from margin; reticulations faint and lax; length 8-18.5 cm; breadth 2-6 cm; petiole 5-8 mm long, glabrous or pubescent. *Flowers* solitary, axillary, pendulous. *Pedicels* 5 mm-2 cm long, glabrous or pubescent with 2-3 minute bracts at base. *Sepals* ovate, acute or acuminate, membranous, several-nerved and reticulated, persistent, varying much in size, 7 mm-2.7 cm long and 6 mm-2.2 cm broad. Petals yellowish to pinkish, thinly coriaceous, pubescent, outer broadly lanceloate, acuminate, much contracted at the base, varying much in length with age, 2-3 cm long, inner ovate, acuminate, 1 cm long or less. *Stamens* 2 mm long, numerous with flat-topped of convex connectives. *Ovaries* about 3 mm long, narrow; style filiform, stigma funnel-shaped, split down the inner side. *Ripe carpels* ovoid,

slightly apiculate, pubescent or glabrescent, 1-1.2 cm long; stalks 4-5 mm long. *Seeds* 1 rarely 2.

Up to this date, there has been no report on the phytochemistry and antimalarial activity of this plant. In a preliminary antimalarial activity evaluation, a chloroform extract of *G. tenuifolius* showed significant antimalarial activity (EC_{50} = 5 μg/ml). It is therefore interesting to investigate this plant both chemically and biologically.

The main objectives in this investigation are as follows.

1. to isolate and purify compounds possessing antimalarial activity from the stem bark of *G. tenuifolius*.

2. to determine the chemical structure of each isolated compound.

3. to evaluate the antimalarial potential of each isolated compound.