CHAPTER I

INTRODUCTION

In recent years, many skin-whitening products have become available and gained a biggest share in Thailand. Of more than 4.5 billion baht (approx. US$100,670,000) spent on facial care, approximately 60% (2.7 billion baht) goes into whitening products. Sales increased 20% over last year [1]. In accordance with the dramatic increase in the demand for skin-whitening products, many researchers actively search for new, highly efficient, and non-irritating substances. Much has been learned about the functions of melanocytes, enzymes, their genetic regulation, and other regulatory factors in melanin biosynthesis to develop a new skin whitening material.

As mentioned above, much of melanin and melanocyte functions have been thoroughly studied. Melanin is the main factor determining the skin color. Its major function is to provide protection against UV irradiation. Two types of melanin occur in mammals: eumelanin and phaeomelanin. The color of tissues containing eumelanin is commonly dark brown to black, whereas those containing phaeomelanin are yellow to reddish brown. Melanogenesis occurs in melanocytes, which are found in the epidermal basal layer. Tyrosinase, one of the limiting enzymes, plays a key role in melanin biosynthesis by converting tyrosine to DOPA and then melanin. Thus, many people have tried to seek substances that can either block the synthesis of tyrosinase or inhibit its activity so that melanogenesis is prevented. Moreover, they tried to combine several compounds with different mechanisms to achieve the most efficient and least toxic skin lightening effect. Some examples of mechanisms of skin whitening actions are shown below [2].

The action mechanism of depigmentation materials

1. Cut off UV: sunscreen agents
2. Scavenge free radicals: tocopherol
3. Inhibit tyrosinase synthesis: glucosamine, galactosamine, monosamine, tunicamycin, lactic acid, others

4. Inhibit tyrosinase activity:	hydroquinone, vitamin C derivatives, kojic acid, arbutin, glutathione, mulberry extract, and licorice extract
5. Interrupt intermediates in melanin biosynthesis	kojic acid
6. Cytotoxic effect on melanocytes	hydroquinone
7. Reduce melanin formation	tocopherol, vitamin C derivatives
8. Stimulate melanin elimination through the keratinocytes	placental protein, azelaic acid
9. Accelerate keratinocyte turnover	lactic acid

Nowadays, more and more people tend to consume natural products in every area of life and try to depend less on the synthetic and artificial substances. Of course, many researchers have been looking for depigmenting materials in extracts from plants. Because of this, licorice, mulberry, and paper mulberry extracts are highly popular. In Thailand, Mahaad, has been discovered as one of the natural products expressing tyrosinase inhibitory activity. Sritularak et.al. found that the extract from Mahaad-Haad heartwood (Puag-Haad) had the ability to inhibit tyrosinase activity *in vivo* and expressed powerful tyrosinase inhibition which was greater than many well-known tyrosinase inhibitors like kojic acid and arbutin [3]. Because of the many advantages such as its availability, low cost, and high whitening activity [3], Puag-Haad was selected and combined with other whitening agents in this study in order to obtained highest benefit and least toxicity.

Therefore, the purposes of this study are as follows:

1. To study the skin whitening activity *in vivo* of Puag-Haad (0.25% dried stem extract of *Artocarpus lakoocha*) in comparison with other compounds (niacinamide, tranexamic acid, and lactic acid) and their combinations in guinea pigs and human volunteers.
2. To evaluate skin irritation potential of the above substances upon long-term application.