CHAPTER 1

INTRODUCTION

Although hair loss or alopecia may not be a serious life-threatening problem, it seriously impacts people's quality of life, mental health and personality. Since hair and psyche are reflecting each other, when alopecia occurred, especially in women, they lacked confidence and may lead to many psychological problems (Neste and Shaker, 2001).

There are many types of alopecias; the most common is androgenic alopecia (androgenetic alopecia or AGA) (Sinclair, 2004). AGA is a genetic-involved and androgen-dependent disorder, caused by excessive activity of 5α-reductase enzyme (5αR) in the hair follicle. This enzyme has two isoforms, 5α-reductase type1 (5αR1) and 5α-reductase type 2 (5αR2). Both of them play a role in metabolism of androgen testosterone into dihydrotestosterone (DHT), which is a more potent androgen. An excessive production of DHT produces many androgen-related disorders such as hirsutism, alopecia, benign prostatic hyperplasia and acne.

AGA affects both men and women, while the severity of hair loss in women is lower. AGA can be found at every stage of people's life, it affects up to half of men by the age of 50 years and increases in the later of life (Sawaya, 1998; Trüeb, 2002).

Nowadays, there are two classes of synthetic medicines that are approved to treat AGA by the USFDA. Firstly, minoxidil at the concentration range between 2 to 5 % has been used in its topical form for the treatment of AGA. Minoxidil is a vasodilator that has been used to treat cardiovascular disorders, but when using this medicine the side effect of hirsutism was observed. However, when it is topically used, local irritation, itching, dryness and erythema was observed. Additionally, serious systemic side effects such as dizziness, tachycardia, increases in left ventricular end-diastolic volume, cardiac output and left ventricular mass was observed with the use of 2% minoxidil solution. Moreover, the most regretful drawback to minoxidil therapy is that the newly grown hairs would fall again within one to three months after discontinuation of the medicine (Abramowicz, 1998).

Another approved medication is 5α-reductase inhibitors, such as finasteride (5αR2 selective inhibitor) and dutasteride (dual 5αR1 and 5αR2 inhibitor), are used to treat such disorders (Robinson et al., 2003). Unfortunately, these medicines have many side effects that affected the quality of life, for examples, abnormal sexual function, gynecomastia, testicular pain and impairment of the muscle (Lacy et al., 2008).

Being known that Thailand is located in the Southeast Asia, where biodiversity of plants are observed. Thousands varieties of plants have been identified, which some of them may be useful for the treatment of androgen-related disorders. Among these plants, several kinds of them have been used for treating hair loss by using simple traditional methods such as decoction, maceration with liquor and directly applied to scalp or use as a shampoo. These simple methods may not efficient for delivered active substance into the hair follicle and acts as hair growth

promoter and enzyme inhibitor. In addition, mechanisms involving in their activity have not yet been proved.

As mentioned above, Thai plants with an anti-5αR activity may have potential in the treatment of androgen-related disorders including AGA. Not only to avoid side effects from those mentioned medicines, the use and promotion of local plant in the treatment for AGA would make them known world-wide. In addition, the development of herbal plants into pharmaceutical or cosmeceutical products may have a benefit in reduction of imported chemicals which may lead to reduction in trade deficits.

Currently, there are many reports indicated that many plants have potential to inhibit 5αR. For example, an American dwarf palm (*Serenoa repens*, *Sabal serrutala*, saw palmetto) which is rich in free fatty acid such as oleic, lauric, myristic, and linoleic acids can inhibit both 5αR1 and 5αR2 (Niederprûm et al., 1994). Various types of mushrooms, for example Ling zhi, *Pleurotus ostreatus* (oyster mushroom) and *Lentinula edodes* (shiitake) are also able to inhibit the enzyme (Fujita et al., 2005).

Some other plants which can be found in Thailand with reported 5αR inhibitory activity are *Piper nigrum* (black pepper) leaf (Hirata et al., 2007), *Alpinia officinarum* (lesser galangal) rhizome (Kim et al., 2003), *Lygodium japonicum* (Japanese climbing fern) spore (Matsuda et al., 2002).

Interestingly, many reports indicated that plants or substances with an anti-5αR activity were also able to promote hair growth. For example, *Myrica rubra* (red bayberry) bark (Matsuda et al., 2001), *Thujae occidentalis* (white cedar) semen (Park et al., 2003), *Piper nigrum* (Black pepper) leaf (Hirata et al., 2007), *Boehmeria nipononivea* (Shimizu et al., 2000a), and epigallocatechin-3-gallate (EGCG) found in

green tea (Kwon et al., 2007) are able to promote hair growth as well as inhibit 5αR enzyme.

For the succession of transfollicular drugs delivery system, nanoparticles may be used. Previous research indicated that substances with particle size less than 1 μm are able to absorb into the hair follicle (Schaefer and Lademann, 2001). The usage of nanostructured lipid carriers (NLC), which is the nanoparticle with size less than 1 μm are responsible for incorporated and protected active substances in plant extract, may be useful for enhancing the absorption of plant extract into the hair follicle and increasing stability of the extract by protection against environmental degradation.

In this study, 26 Thai plants were selected based on their traditional usages involving in hair caring or their phytochemical constituents that suspected or proved to be able to inhibit the 5αR. In addition, these plants have not yet been studied either for 5α-reductase inhibitory activity or hair growth promoting activity before. This research will focus on using plant extract which can inhibit the 5α-reductase enzyme and promote hair growth to formulate into a NLC hair lotion for hair loss prevention and hair growth promotion.

Objectives of the Study

1. To determine 5α-reductase inhibitory activity of the 26 selected Thai plants extracts by using rat microsomal enzyme
2. To determine hair growth promoting activity of some Thai plants extracts in mice
3. To develop hair lotion containing plant extract-loaded NLC for 5α-reductase inhibition and hair growth promotion

4. To evaluate the physical properties, stability, irritation and efficacy of the hair lotion containing plant extract-loaded NLC