CHAPTER 1

INTRODUCTION

1.1 Background

Acne vulgaris, a chronic inflammatory disorder in adolescents consists of the pilosebaceous follicles, characterized by comedones, papules, pustules, cysts, nodules and often scars, chiefly on face, neck and upper trunk (Lalla *et al*., 2001). It may cause disfiguration and permanent scarring and it may also have an adverse effect on psychological development, resulting in profound emotional scarring, which may lead to social phobias, withdrawal from society, and clinical depression. The four main pathogenic factors in the development of acne are increased sebum production, disorders of the microflora, cornification of the pilosebaceous duct, and inflammation (Ozkan *et al*., 2000).

Normal skin commensals including *Propionibacterium acnes*, *Propionibacterium granulosum*, *Staphylococcus epidermidis* and *Malassezia furfur*, proliferate rapidly during puberty and are often involved in the development of acnes (Hamnerius, 1996). The predominant organism in the follicular flora is the anaerobic organism, *Propionibacterium acnes*.

P. acnes is an immobile, gram positive, lipophilic anaerobe that colonizes in the follicular duct. Evidence demonstrates the role of *P. acnes* in the production of acne. Although a relationship exists between increased levels of *P. acnes* and acne development in teenage years, a correlation with acne severity has not been demonstrated. Local inflammation caused by this organism results from antibody production (i.e., IgG, IgM). The combination of complement activation and secretion of chemotactic factors lead to an array of immunological responses (e.g., mast cell degranulation, neutrophil chemotaxis) and the release of lipases, proteases, hyaluronidases, reactive oxygen species (ROS), and lysosomal enzymes. This process damages the epithelial layer of the follicle and causes its contents to be spilled onto the skin surface, resulting in inflammatory acne. Further, lipase from *P. acnes* breaks down glyceride to free fatty acids (FFAs) and glycerol. FFAs directly compromise the integrity of the follicular environment

resulting in the release of IL-1-∝, which possesses proinflammatory properties as mentioned previously.

The general therapy in the treatment of acne vulgaris includes oral and topical therapy employing comedolytics (benzoyl peroxide, tretinoin, azaleic acid) and antibiotics (tetracycline, erythromycin, etc.) for both oral and topical use (Song *et al*., 2004). Focusing on topical therapy, benzoyl peroxide is considered a potent antimicrobial agent against bacteria and yeast as well as a mild keratolytic. Its mechanism of action may involve the release of free oxygen radicals that harm bacterial proteins. Tretinoin is a retinoic acid (vitamin A acid) that increases the turnover rate and decreases the aggregation of follicular cells. Topical retinoids effectively target the formation of microcomedones, thereby sustaining remission and preventing the formation of new lesions. Azelaic acid possesses antibacterial activity against *P. acnes* by inhibiting thiorodoxin reductase, thus preventing the synthesis of bacterial DNA. It also targets microcomedone formation by affecting the turnover rate of follicular epithelial cells. Azelaic acid is suggested for mild to moderate inflammatory acne due to its effects on chemotaxis suppression and attenuation of inflammatory mediator production. Additionally, it reduces a number of *P. acnes*. Clindamycin and erythromycin preparations reduce comedonal and inflammatory acne. These agents are often used as monotherapy for mild papular and pustular acne. They may also serve as good alternatives to oral antibiotics by minimizing systemic effects.

These drugs have several side effects such as skin irritation, dry skin, peeling, burning, erythrema sunlight sensitivity, abnormal skin pigmentation, edema, blistering, scabs (Brand *et al*., 2003). In addition, antibiotics resistance has been increasing in prevalence within the dermatologic setting (Swanson, 2003).

Plants used in folk medicine have been accepted as one of the main sources of drug discovery and development. In Thailand, there is a rich treasury of ethnobotanical knowledge and over past decades several research has been carried out on this subject. During our studies, we have noticed the following herbal remedies being used in the treatment of skin diseases and related inflammatory. Thus, Thai medicinal plants have been extensively studied as the alternative treatments for acne vulgaris.

In the present study, 18 medicinal plants, including (*Centella asiatica*, *Zingiber officinalis*, *Ocimum americanum*, *Ocimum sanctum*, *Boesenbergia pandurata*, *Piper betle*, *Senna*

alata, *Alpinia galanga*, *Punica granatum*, *Morus alba*, *Azadirachta indica*, *Cinnamomum verum*, *Plumbago zeylanica*, *Dioscorea membranacea*, *Syzygium aromaticum*, *Andrographis paniculata*, *Cymbopogon citratus*, *Rhinacanthus nasutus*, which have been traditionally used as antimicrobial and anti-inflammatory agents (นันทวัน บุณยะประภัศร และ อรนุช โชคชัยเจริญพร, 2539; มาโนชน์ วามานนท์ และ เพ็ญนภา ทรัพย์เจริญ, 2537; Biswas *et al*., 2002; Farnsworth and Bunyapraphatsara, 1992; Navarro *et al*., 1996; Wannissorn, *et al*. 2005) were investigated for antibacterial activities against *P. acnes.*

1.2 Literature review

1.2.1 Acne vulgaris

1.2.1.1 Definition

Acne vulgaris is a self-limited disease, seen primarily in the adolescent age range, involving the sebaceous follicles. There are usually a variety of lesions (Figure 1.1) consisting of comedos, papules, pustules, nodules, cysts, and, as sequelae to active lesions, pitted or hypertrophic scar (Fitzpatrick *et al*., 1979).

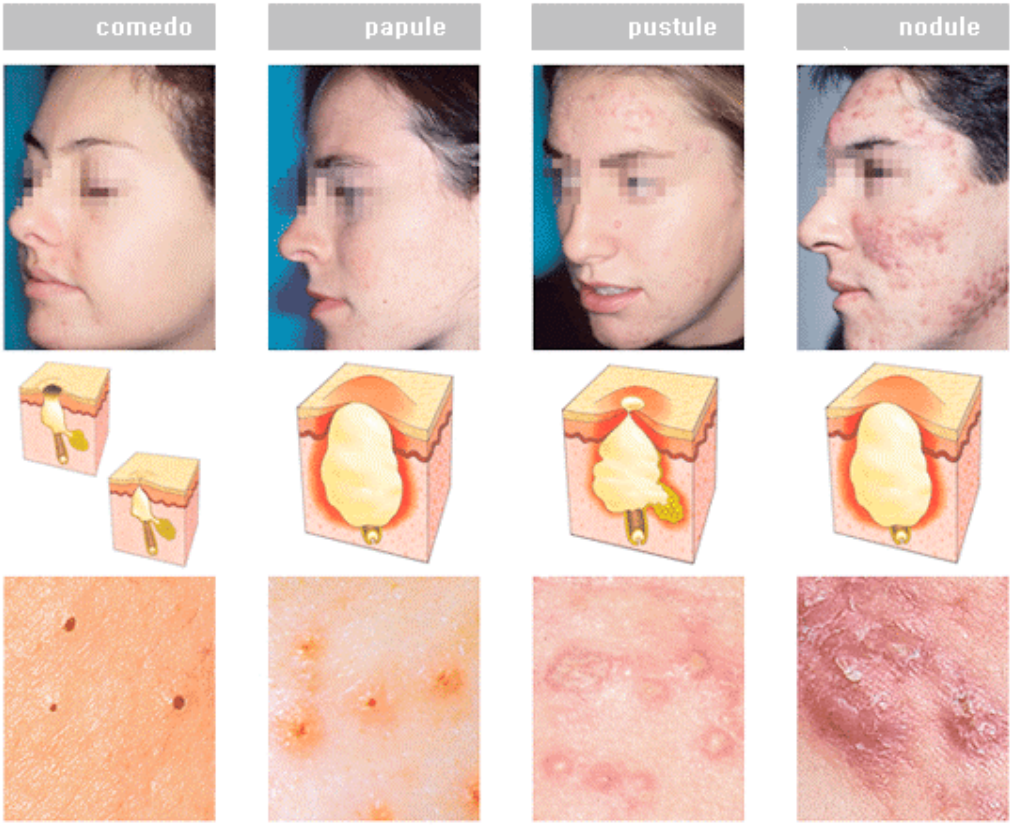

Figure 1.1 Lesions of acne vulgaris (www.selebean.com)

1.2.1.2 Epidemiology

This disease is sufficiently common that has often been termed physiology. It is occasionally present at birth. However, it is not until puberty begins that it becomes a common problem. The disease may be an early manifestation of the puberal spectrum, although in the very young patient the predominant lesions are comedos, and inflammatory lesions are rare. In girls, it may precede menarche by more than a year. The greatest number of cases is seen during the middle-to-late teen-age period, then the incidence of the disease decreases. However, particularly in women, acne may persist through the third decade or even later. Acne appears to affect males more severely during adolescence, whereas similar prevalence is observed in females during the second decade of life. Dark skinned populations may be at higher risk for developing abnormal skin color changes and scarring as a result of acne. Because acne affects visible parts of the body (e.g., face, neck, upper trunk), this disorder may negatively impact self-esteem (Fitzpatrick *et al*., 1979).

1.2.1.3 Classification and symptoms

Acne may be classified as comedonal, papular, pustular, cystic, and nodular. Comedonal acne is noninflammatory and divided into two types: whiteheads and blackheads. Whiteheads (closed comedo) present as fresh or white colored, raised bumps whereas blackheads (open comedo) present as open pores containing dark colored skin roughage consisting of melanin, sebum, and follicular cells. Papules appear as red, solid, elevated lesions often less than 5 mm in diameter. Pustules are circumscribed skin elevations containing purulent material. Cysts and nodules are solid, elevated lesions involving deeper dermal and subcutaneous tissue. Cysts are less than 5 mm in diameter whereas nodules exceed 5 mm.

According to the combined acne severity classification, acne is stratified into three severity levels (Table 1.1): mild, moderate, and severe based on lesion type and quantity of lesions (Song *et al*., 2004).

Mild acne displays less than 30 lesions comprised of comedos or inflammatory papules and pustules. Moderate acne displays 30 to 125 comedos, papules, or pustules. Severe acne exhibits more than 125 comedos, papules, pustules, cysts, or nodules. Severe acne is more prone to scarring after the condition abates.

Table 1.1 The combined acne severity classification

Acne Severity	Lesion Numbers	Lesion Type
Mild	<30	Comedos or inflammatory papules and pustules
Moderate	30-125	Comedos, papules, or pustules
Severe	>125	Comedos, papules, pustules, cysts, or nodules

Table 1.2 illustrates a useful approach to grade the severity of facial. The grading system allows for the classification of acne by first separating a body site of involvement (e.g., forehead, nose, chest), then identifying the primary lesion type (i.e., comedo, papule, pustule, cyst, nodule) in that area, and lastly counting the number of lesions and grading them accordingly (Song *et al*., 2004). The chest and back are evaluated separately from the face

because of the potential variance on overall severity and treatment outcomes. This system is scaled to grades 0, I, II, III, and IV.

Table 1.2 Different parameters of the grading system

Grade	Lesion Numbers	Lesion Type	Site
0	None	Open comedo	Forehead
1	1-10	Closed comedo	Nose
2	11-20	Papule	Cheek
3	>20	Pustule	Chin
4	Presence of severe inflammatory acne	Nodule/ Cyst	Chest, Back

Symptoms of acne may present differently according to acne types. Patients with comedos are asymptomatic. Papules and pustules may cause itching at the site of involvement. Cysts and nodules are often painful.

1.2.1.4 Pathogenesis of acne vulgaris

The pathogenesis of acne involves multiple physiological factors. These include follicular hyperproliferation, increased sebum production due to higher androgen levels, and colonization of *P. acnes*. Novel concepts have emerged to help better understand its pathogenesis, these include variations in target cell sensitivity, biological markers, neuroendocrine, genetic, and environmental factors (Song *et al*., 2004).

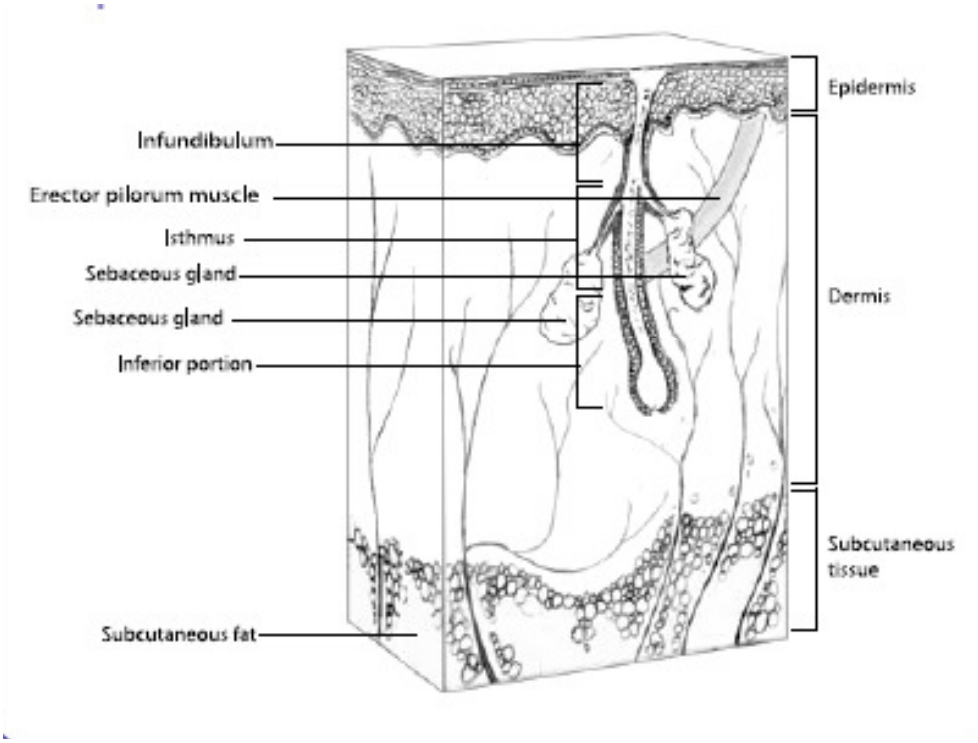

Figure 1.2 The pilosebaceous unit (Song *et al.,* 2004)

Acne develops in the follicular pilosebaceous unit (Figure 1.2). These units are largest on the face, neck, and upper trunk where acne is most distributed. The hair follicle where the pilosebaceous unit is embedded consists of three main parts including infundibulum, isthmus, and bulb. The infundibulum starts from the epidermal surface down to the sebaceous unit. The isthmus is where the arrector pili muscle and sebaceous gland are found and it lies between the infundibulum and bulb. The sebaceous gland produces sebum that empties into the follicle. Typically, the follicular bulb is situated in the subcutaneous tissue. The cells that make up the epidermis and the cells that line the infundibulum are the same.

The first step in the formation of an acne lesion is the production of a microcomedone. Clinically, a microcomedone is unobservable to the naked eye. An important pathophysiological process in comedogenesis is follicular hyperproliferation. Keratinocytes in the comedo proliferate at a higher rate compared to those in a normal follicle and the cohesiveness of these keratinocytes is enhanced (Figuer 1.3). These abnormally differentiated keratinocytes aggregate in the follicle along with sebum, lipids, and bacteria, occluding the follicle and ultimately forming an open or closed comedo.

Lipids, androgens, and local cytokines are believed to contribute to acne production. Introduction of specific lipids into the sebaceous follicle may be associated with hyperproliferation. High levels of free fatty acids (i.e., squalene, squalene oxide) demonstrated an augmentation in epithelial keratinocyte adhesion (Leyden, 1995). Likewise, a decrease in certain fatty acids (i.e., linoleic acid) led to increased basal keratinocyte proliferation and unusual keratinocyte differentiation. Various cytokines may also play a contributory role in acne production. *In vivo* cultures demonstrate interleukin-1-∝ (IL-1-∝) may induce hyperkeratinization via its proinflammatory properties and stimulation of abnormal desquamation (Ingham *et al*., 1992). This cytokine also results in chemoattraction of polymorphonuclear leukocytes (PMNLs) and possibly the production of pustules. Suggestively, other cytokines are thought to be involved and include tumor necrosis factor-∝, interferon-γ, epidermal growth factor, and transforming growth factor-∝.

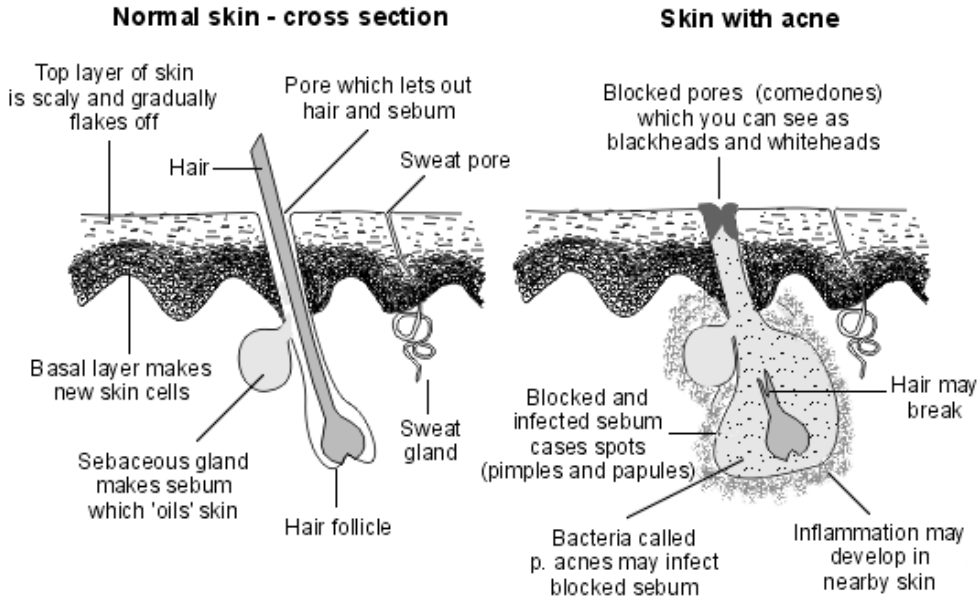

Figure 1.3 Comparison between normal skin and skin with acne (Song *et al*., 2004)

Androgens contribute to microcomedone formation through increased sebum production (Song *et al*., 2004). Sebum is composed of glycerides, wax esters, and cholesterol. Androgens are considered to be the "major sebotropic" hormones. A marked rise in androgen levels ("adrenarche"), occurring as early as 7 to 8 years of age to puberty, stimulates the growth and differentiation of sebocytes in the sebaceous glands and the production of sebum. Androgens

bind *via* a coupling mechanism to androgen receptors on sebocytes, leading to gene transcription and initiating the differentiation of sebocytes.

Evidence demonstrates the role of *P. acnes* in the production of acne (Song *et al*., 2004). Although a relationship exists between increased levels of *P. acnes* and acne development in teenage years, a correlation with acne severity has not been demonstrated. Local inflammation caused by this organism results from antibody production (i.e., IgG, IgM). The combination of complement activation and secretion of chemotactic factors lead to an array of immunological responses (e.g., mast cell degranulation, neutrophil chemotaxis) and the release of lipases, proteases, hyaluronidases, reactive oxygen species (ROS), and lysosomal enzymes. This process damages the epithelial layer of the follicle and causes its contents to be spilled onto the skin surface, resulting in inflammatory acne. Further, lipase from *P. acnes* breaks down glyceride to free fatty acids (FFAs) and glycerol. FFAs directly compromise the integrity of the follicular environment resulting in the release of IL-1-α, which possesses proinflammatory properties as mentioned previously. New evidence suggests glycerol also contributes to the negative effects of *P. acnes*.

Recent concepts on the pathogenesis of acne suggest sebaceous glands on certain areas of the body demonstrate a greater response to androgens.

Neuroendocrine factors may also play a role in the pathogenesis of acne (Song *et al*., 2004). The skin contains a mesh of peripheral sensory nerves comprised of various fibers including C fibers that may play a role in skin inflammation that ultimately leads to acne. A neuropeptide known as substance P may also lead to acne by facilitating hyperkeratinization, enlarging sebaceous glands, and increasing sebum production.

The skin encounters various physical stresses compromising its function as a barrier. Corticotropinreleasing hormone (CRH) is an endocrine hormone released during periods of stress suggesting that CRH and its receptors (i.e., CRH-R1, CRH-R2) may serve as a mechanism in acne development. Genetic factors may predispose certain individuals to developing acne. A retrospective study involving 1,557 sets of twins demonstrated a significant association with the development of acne (p<0.0001). In contrast, individual factors such as lipid profile and blood glucose levels did not correlate with the development of acne. Additionally, aberrant genetic coding may interfere with normal androgen receptor production and/or function,

thus preventing sebum production and acne development. Environmental factors such as smoking and sun exposure may possibly influence acne production. Ultraviolet A and B rays may induce sebum production and decrease IL-1-α and interleukin-10 (IL-10). This finding contradicts the aforementioned theory that IL-1-α induces acne thru its proinflammatory properties. While these findings are not firmly conclusive, it appears that acne at least in part involves a dysfunctional immune system represented by a struggle to balance IL-1-α levels in the body (Lee *et al*., 2003).

1.2.1.5 **Treatment** (Fitzpatrick *et al*., 1979; Song *et al*., 2004)

Various treatment options exist according to drug class, mechanism of action, dosage form, route of administration, and cost. Selection of the most appropriate therapy should be based on a comprehensive evaluation of the patient and the pharmacological profile of the agents. The available treatment options for acne are as follows.

A. Physical therapy: There are many treatments including acne surgery, laser and phototherapy, cryotherapy, and using intralesional corticosteriods.

B. Systemic therapy: The two major systemic modalities used in acne are antibiotics and estrogenic hormones. Both represent major steps forward in the therapy of this disease. This therapy uses for moderate to severe cases.

C. Local therapy: The general therapy including topical agents tretinoin, adapalene, tazarotene, azelaic acid, salicylic acid, benzoyl peroxide, and antibacterials (clindamycin, erythromycin).

Tretinoin is a retinoic acid (vitamin A acid) that increases the turnover rate and decreases the aggregation of follicular cells. These topical retinoids effectively target the formation of microcomedones, thereby sustaining remission and preventing the formation of new lesions. Furthermore, these agents mimic antibiotic action by altering immune response and decreasing inflammatory lesions. Tretinoin may significantly reduce both noninflammatory and inflammatory lesions by 81% and 71%, respectively ($p<0.05$) (Song *et al*., 2004). Because tretinoin and retinoid analogs work well against microcomedones and inflammatory lesions, current practice standards are now suggesting topical retinoids as first-line agents in acne treatment. Maintenance therapy with retinoids is now recommended in mild to moderate acne to

prevent the relapse of microcomedone formation often observed when initial treatment is terminated.

Common adverse effects include sunlight sensitivity, abnormal skin pigmentation, irritation, erythema, edema, blistering, and scabs. Initial application of tretinoin may cause flaring of the skin that resolves on its own after 2 to 3 months. Allergic contact dermatitis may also occur, but the incidence is rare. To minimize the incidence of skin irritation, a lower concentration, frequency, and amount of medication (i.e., a pea-sized amount) should be initiated and then gradually increased. Patients should also be advised to apply tretinoin on a dry skin surface using dry fingers 30 minutes after washing.

Adapalene is a third generation topical retinoid analog that selectively binds to retinoic acid receptors (RARs) in the epidermis. This controls hyperproliferation of follicular epithelial cells and halts the production of microcomedones. Adapalene shares similar properties to that of tretinoin and works well against mild to moderate comedonal and inflammatory acne. Adapalene is available as a 0.1% topical gel, cream, and solution. A meta-analysis of five clinical studies compared 900 subjects who received adapalene 0.1% or tretinoin 0.025% gel. This meta-analysis concluded that adapalene is similar or superior in efficacy compared to tretinoin. However, the conclusion of this study is limited because it only compared the lowest strength of tretinoin.

Common adverse effects associated with adapalene use include erythema, scaling, dryness, pruritis, and burning sensation of the skin. An initial flare (i.e., pruritis, burning sensation, acne) may also occur in some patients. This agent should be applied at bedtime on a dry, washed surface.

Tazarotene is a third generation synthetic topical retinoid prodrug originally approved for the treatment of psoriasis. Its active form, tazarotenic acid, binds specifically to RARs as does adapalene. Tazarotene is available as a topical cream or gel in 0.05% and 0.1% strengths. While only the 0.1% strength is indicated for the treatment of acne, the lower tazarotene strength (0.05%) may also be effective. Thus, both strengths may in fact be beneficial in acne therapy. Tazarotene is an effective alternative to tretinoin and adapalene. Studies suggest tazarotene's superior efficacy to tretinoin and equal efficacy to adapalene. When compared to adapalene, tazarotene may be useful in patients with a history of noncompliance as well as

possibly offer a lower cost benefit based on every other day tazarotene therapy *versus* once daily adapalene therapy.

Common adverse effects such as desquamation, burning or stinging sensations, dry skin, erythema, and pruritis are found. Patients should apply a thin layer of this drug once daily in the evening after washing the face. The skin surface should be dry when applying this drug. Tazarotene is approved only for mild to moderate facial acne.

Azelaic acid possesses antibacterial activity against *P. acnes* by inhibiting thiorodoxin reductase, thus preventing the synthesis of bacterial DNA. This drug also targets microcomedone formation by affecting the turnover rate of follicular epithelial cells. Azelaic acid also has activity against inflammatory acne. Azelaic acid is indicated for mild to moderate inflammatory acne. Azelaic acid is available as a topical 15% gel and 20% cream. This drug is well tolerated because it does not cause the same degree of irritation to the skin as do the other agents.

Azelaic acid may also cause allergic contact dermatitis. This medication should be applied thinly to a dry, washed surface and massaged wholly to the affected area twice daily.

Salicylic Acid/Sulfur/Resorcinol: These topical agents provide keratolytic and to a lesser degree, antibacterial properties that aid in the treatment of acne. The combination of these agents with benzoyl peroxide (BPO) is believed to have synergistic activity against acne. For this purpose, a lotion containing BPO and sulfur is available as a prescription. Similarly, combined salicylic acid (SA) and BPO is more effective than either agent alone in the reduction of total acne lesions.

Common adverse effects include brown scaling with resorcinol, unpleasant odor with sulfur, and skin irritation and stinging with SA.

Benzoyl Peroxide is considered a potent antimicrobial agent against bacteria and yeast as well as a mild keratolytic. Its mechanism of action may involve the release of free oxygen radicals that harm bacterial proteins. BPO has been shown to lower *P. acnes* count better than topical antibiotics (e.g., clindamycin). The onset of clinical improvement improved from several days to a few weeks and *P. acnes* count improved by 90% to 98% (Gollnick *et al*, 2003). In a study using BPO 6% gel and clindamycin phosphate 1% lotion applied twice daily for 2 weeks, BPO lowered *P. acnes* count significantly greater and quicker compared to clindamycin (*p*

<0.01) (Gans and Kligman, 2002). Unlike topical clindamycin and erythromycin, bacterial resistance does not develop to BPO. Although the superiority of topical antibiotics (e.g., erythromycin, clindamycin) over BPO has not been demonstrated, the combination of the two has demonstrated better tolerance and efficacy in reducing *P. acnes* levels compared to topical antibiotics alone (Gollnick *et al*, 2003). An important caveat to using these combination agents is the degree of clinical effects do not consistently relate to changes in *P. acnes* count. However, combination therapy is not associated with an increased risk of resistant bacteria compared to the antibiotic alone. BPO is recommended for mild to moderately severe acne and is intended only for topical use. Because the Food and Drug Administration (FDA) does not classify BPO generally recognized as safe (GRAS), caution should be taken to prevent overuse of this product. BPO is available in concentrations ranging from 1% to 10% and vehicles including creams, gels, lotions, washes, and cleansers. Gels are more potent, stable, and provide a predictable drug release compared to creams and lotions. Cleansers enable administration during showering, thus expanding the coverage area and minimizing noncompliance. Some of the combination products need to be reconstituted with sterile water or alcohol, while some are premixed.

Common adverse effects associated with BPO use include erythema, peeling, and dryness, particularly in alcohol-based preparations. Up to 3% of patients may experience contact dermatitis. Initiating BPO at a low dose and titrating the dose higher may help minimize this occurrence. BPO should be applied twice daily to dry, washed skin, but patients should be forewarned that BPO could bleach clothes. Further, it should be applied to the entire face, in addition to the affected area(s). This helps prevent the development of future comedos.

Antibacterials (clindamycin, erythromycin): Topical antibacterial agents are indicated for inflammatory acne due to its effects on chemotaxis suppression and attenuation of inflammatory mediator production. Additionally, they reduce the number of *P. acnes*. Clindamycin and erythromycin preparations reduce comedonal and inflammatory acne. These agents are often used as monotherapy for mild papular and pustular acne. They may also serve as good alternatives to oral antibiotics by minimizing systemic effects. Topical antibiotics in combination with topical retinoids are more effective than antibiotics alone in treating acne lesions. As mentioned earlier, topical retinoids facilitate the action of antibiotics. Normally,

topical antibiotics should not be continued more than 6 to 8 weeks if no improvement is observed, unless improvement occurs earlier at which time they should be discontinued.

Common adverse effects associated with topical antimicrobials are mild and include erythema, pruritis, peeling, dryness, and burning sensation. Topical clindamycin has been rarely reported to cause *Pseudomembraneous colitis* (*P. colitis*) compared to oral dosage forms. Antibiotic resistance is also a problem with topical antibiotic use, but this has not shown to cause significant acne inflammation as a consequence of growing resistant *P. acnes* numbers.

1.2.2 Medicinal plants used as antibacterial agents

Eighteen Thai medicinal plants were selected for investigation of antibacterial activity against *P. acnes*. Selection of plants was based on their traditionally uses as antimicrobial, anti-inflammatory agents in primary healthcare and/or previously reports on antimicrobial and/or anti-inflammatory activities. The data of 18 Thai medicinal plants were as follows.

1.2.2.1 *Centella asiatica*

Scientific name: *Centella asiatica* Linn.

Synonym: *Hydrocotyle asiatica*

Common name: Asiatic pennyworth, Gotu kola, Bua bok, Pa-na-e-khaa-doh (Karen-Mae Hong Son), Phak waen (Peninsulin), Phak nok (Northern)

Family name: Umbelliferae

Botanical description: The plant is a perennial herb (Figure 1.4). The stems are long, creeping and rooting at the nodes. Leaves are simple, 2-10 fascicled at the node, orbicular reinform, 1-7 cm long, 1.5-9 cm broad, entire, crenate or lobulate. Petioles are 4-10 cm long. Flowers are 3-4-flowered umbel. There are 2-5 umbels arising in axillary. Peduncles are 0.5-5 cm long, erected at first then curved; pedicels are almost none. Each flower has 2-3 bracts; 5 sepals; 5 petals which are 1-1.5 cm long, purple, 5 stamens alternate with petals. Fruits are flattened, 2-3 mm long, 3-4 mm broad (Farnsworth and Bunyapraphatsara, 1992).

Figure 1.4 *Centella asiatica* Linn.

Part used: Fresh leaves

Traditional uses: For health promotion, wound healing, to enhance wound repair, stomach ulcers, treatment of skin diseases, wounds, burns (Farnsworth and Bunyapraphatsara, 1992)

Chemical constituents: Sugars, glycoside, tannin, potassium sulfate, magnesium carbonate, asiaticoside, asiatic acid, madecassic acid (Shukla *et al*., 1999)

Biological activity: It has been reported that asiaticoside isolated from *C. asiatica* exhibited wound healing. Topical applications of 0.2% solution of asiaticoside produced 56% increase in hydroxyproline, 57% increase in tensile strength, increased collagen content and better epithelisation. Solution of asiaticoside (0.4 %) over punch wounds increased hydroxyproline content, tensile strength, collagen content and epithelisation thereby facilitating the healing *in vivo* (Shukla *et al*., 1999). In addition cream and injection preparation of Pennyworth are used to treat wound healing or wound after operation (มาโนชน์ วามานนท์ และ เพ็ญนภา ทรัพย์เจริญ, 2537).

1.2.2.2 *Zingiber officinale*

Scientific name: *Zingiber officinale* Roscoe

Synonym: *Amomum angustifolium* Salisb., *Amomum zingiber* L.

Common name: Ginger, Khing, Khing klaeng, Khing daeng (Chanthaburi), Khing phueak (Chianmai), Sa-e (Karen-Mae Hong Son)

Family name: Zingiberaceae

Botanical Description: It is a herb, having horizontal, white or pale yellow, fleshy and aromatic rhizome; and stem leafy (Figure 1.5). Leaves are lanceoate, 12-20 by 1.5-2 cm; tapering gradually to the apex; narrowing to base and clasping the stem by their long sheaths. Inflorescencs are borne separately on a bladeless leaf-sheath; consisting of flowers zygomorphic, with bracts and bracteoles subtending the flowers, bracts closely appressed against each other; calyx shortly 3 lobed; corolla tubular, divided into 3 subequal lobes; fertile stamen one only; very rarely flowers. Fruit is a dehiscent capsule (Farnsworth and Bunyapraphatsara, 1992).

Figure 1.5 *Zingiber officinale* Roscoe

(www.medplant.mahidol.ac.th)

Part used: Rhizome

Traditional uses: Enhancing appetite, for longevity, flatulence, stomach discomfort, carminative, anti-emetic, prevent peptic ulcer, anti-bacterial and anti-inflammatory properties (Farnsworth and Bunyapraphatsara, 1992)

Chemical constituents: Amino acid, zingiberene, gingerol, camphor, calcium, zingiberol, citral, zingirol, zingiberine, bisabolene, ∝-curcumene, linalool, cineole, gingerol and gingerone (Wang and Ng, 2005)

Biological activity: It has been reported that ginger rhizomes exerted antifungal activity toward various fungi including *Botrytis cinerea*, *Fusarium oxysporum*, *Mycosphaerella arachidicola*, and *Physalospora piricola* (Wang and Ng, 2005).

It has been reported that the extract of ginger significantly inhibited gr A hemolytic Streptococci, *Staphylococcus aureus*, *Streptococcus faecalis* with the effects being more pronounced against the first 2 organisms (Farnsworth and Bunyapraphatsara, 1992).

1.2.2.3 *Ocimum americanum*

Scientific name: *Ocimum americanum* Linn.

Synonym: *Ocimum basilicum* Linn. Var. *citratum*

Common name: Hoary basil, Hairy basil, American basil, Lemon basil, Spice basil, Lime basil, Perennial basil, Thai basil, Thai lemon basil, Wild basil, Mang lak, Komkokhaao (Northern)

Family name: Labiatae

Botanical description: The plant is an erect herb, 30-50 cm high, much branched; consisting of stem and branches striate, more or less pubescent, with strong odor (Figure 1.6). Leaves are simple, opposite, 2.5-5 by 1-2.5 cm; having blade lanceolate to elliptic; apex and base acute; margin entire or narrowly ovate tooth; both surfaces glabrous and glandular dotted; petiole slender, 1-2.5 cm long. Inflorescences are in terminal raceme-like, simple or branched, 7-15 cm long; consisting of bract 2-3(-5) mm long, tip acute, hairy; pedicels very short or sessile; flowers white or purple; calyx campanulate, 2-2.5 mm long (to 4-4.5 mm in fruit), 2-lipped, the upper lip large with decurrent margin, the lower with 4 narrow pointed teeth, hairy inside, outside scattered with white hair; corolla campanulate, 2-lipped, the upper truncate, subequally 4 lobed, the low entire; stamens 4, in 2 pairs, exserted; style 2 lobes. Fruit is composed of 4 dry 1-seeded nutlets. Nutlet is ellipsoid, 1.2 mm long, black, dotted (Farnsworth and Bunyapraphatsara, 1992).

Figure 1.6 *Ocimum americanum* Linn.

Part used: Leaves

Traditional uses: Leaves are useful in skin infections like eczema, carminative, anti-inflammation, skin diseases, antifungal (Wannissorn, *et al*. 2005).

Chemical constituents: Borneol, L-β-cadinene, 1-8 cineol, β-caryohyllene, eugenol, limonene, linalool, methyl chavicol, myrcene
(มาโนชน์ วามานนท์ และ เพ็ญนภา ทรัพย์เจริญ, 2537)

Biological activity: It has been reported that an alcohol extract of Hairy basil showed bactericidal effects on both gram positive and gram negative bacteria (Farnsworth and Bunyapraphatsara, 1992).

In addition, it had antimicrobial activity against zoonotic enteropathogens including *Salmonella spp*., *Escherichai coli* O157, *Campylobacter jejunii* and *Clostridium perferingens* (Wannissorn *et al*., 2005).

1.2.2.4 *Ocimum sanctum*

Scientific name: *Ocimum sanctum* Linn.

Synonym: *Ocimum tenuiflorum* Linn.

Common name: Basil, Sacred basil, Holy basil,Tulsi, Kaphrao, Komko, Komko dong (Chiang Mai), Ka phrao khaao, Ka phrao daeng (Central), Ho-kwo-suu, Ho-tuu-pluu (Karen-Mae Hong Son), Im-khim-lam (Shan-Mae Hong Son)

Family name: Labiatae

Botanical description: *Ocimum sanctum* is an erect herb, 30-60 cm high, having much branches and soft hairs all over (Figure 1.7). Leaves are simple, opposite; elliptic or elliptic-oblong; 2-4.5 by 1-2.5 cm; consisting of apex and base acute or obtuse; margin remotely serrate; short hairs along the vein; petiole 1-3 cm long. Flowers are small, borne on the axis, in terminal raceme-like or panicle, 8-14 cm long. Each flower consists of bract ovate, tip acute, 2-3 mm long, margin hairy; pedicels 3-4.5 mm long, pubescent; calyx 2.5 mm long (to 3-3.5 mm in fruit), 2-lipped, upper lip suborbicular, reflexed, the lower longer, 4 teethed; corolla 2-lipped, 3.5-4 mm long; stamens 4, in 2 pairs, filament slender, exserted, the upper pair with a small appendage at base; style 2-lobed. Fruit contains 4 dry 1-seeded nutlets. Nutlets are ellipsoid, 1.2 mm long, glabrous (Farnsworth and Bunyapraphatsara, 1992).

Figure 1.7 *Ocimum sanctum* Linn.

Part used: Leaves

Traditional uses: For the improvement of blood circulation, treatment of skin diseases, urticaria, chronic cough, carminative, antiflatulence (Farnsworth and Bunyapraphatsara. 1992).

Chemical constituents: Camphor, cineol, eugenol, limonene, pinene, sabinene, terpineol, ocimol, linalool

Biological activity: Fixed oil of *O. sanctum* was found to possess anti-inflammatory activity against carrageenan and different other mediator-induced paw edema in rats. It also inhibited arachidonic acid and leukotriene-induced paw edema. The anti-inflammatory activity of *O. sanctum* supported the dual inhibition of arachidonate metabolism as indicated by its activity in inflammation models that are insensitive to selective cyclooxygenase inhibitors (Singh *et al*., 1996). Water and hot water extracts of *O. sanctum* (0.5 ml/disc) showed no antibacterial activity against *Bacillus subtilis* both H-17 (rect+) and M-45 (rec -) (Farnsworth and Bunyapraphatsara, 1992).

1.2.2.5 *Boesenbergia pandurata*

Scientific name: *Boesenbergia pandurata* Roxb.

Synonym: *Gastrochilus panduratus* Ridl., *Boesenbergia rotunda* Linn., *Kaempferia pandurata* Roxb.

Common name: Finger root, Kra chaai (general), Ka aen, Ra aen, Chee-puu, See-phuu (Shan-Maehongson), Waan phra aa thit (Bangkok)

Family name: Zingiberaceae

Botanical description: The plants are rhizomeatous herbs; having roots cylindrical, fascicled, 6-10 cm long; tip acute, out side light brown, inside yellow, scented (Figure 1.8). Leafy shoot is very short, consisting of 3-4-leaved; petioles 12-25 cm long, tincted red; blade elliptic or oblong, 10-30 cm long, 5-10 cm wide; apex acute; base cuneate or obtuse; margin entire. Inflorescences are terminal, subsessile, enclosed by the leaf sheaths; bearing 2-ranked bracts each subtending a single flower. Bracts are linear-lanceolate up to 5 cm long. Bracteoles are as long as the bracts but narrower. The uppermost flower opens first. Calyx is about 2 cm, bifid. Corolla is pink, tube exceeding the bracts; lobes about 1.5 cm, oblong. Labellum is bag-shaped about 2.5 cm long, 2 cm wide. Lateral staminodes are slightly shorter than corolla lobes and mottled purple. Fruits are ellipsoid (Farnsworth and Bunyapraphatsara, 1992).

Figure 1.8 *Boesenbergia pandurata* Roxb.

(www.aidsthai.org)

Part used: Rhizomes

Traditional uses: Treatment of stomatopathy, for health promotion, for dysentery, ringworm, chloasma, abscesses, antiflatulence and carminative (มาโนชน์ วามานนท์ และ เพ็ญนภา ทรัพย์เจริญ, 2537; Farnsworth and Bunyapraphatsara, 1992)

Chemical constituents: 1,5-Cineol, dl-pinostrobin, camphor, flavonoid, chromene (มาโนชน์ วามานนท์ และ เพ็ญนภา ทรัพย์เจริญ, 2537), boesenbergin A, boesenbergin B, panduratin A, cardomin, cardomonin, pinostrobin, pinocembrin, alpinetin, isopanduratin and 5-hydroxy-7-methoxyflavanone (Hwang *et al*., 2004)

Biological activity: It has been reported that *B. pandurata* had antibacterial activity against *Bacillus subtilis* (มาโนชน์ วามานนท์ และ เพ็ญนภา ทรัพย์เจริญ, 2537).

Isopanduratin A isolated from *B. pandurata* had antibacterial activity against *Streptococcus mutans.* The minimum inhibitory concentration (MIC) of isopanduratin A was 4 mg/l. The bactericidal test showed that isopanduratin A completely inactivated *S. mutans* at 20 mg/l in 1 min. Significant inhibitory activity of isopanduratin A was also observed against *S. sobrinus*, *S. sanguinis* and *S. salivarius* with MIC of 4 mg/l. Thus isopanduratin A could be employed as a potential antibacterial agent for preventing dental caries (Hwang *et al*., 2004).

1.2.2.6 *Piper betle*

Scientific name: *Piper betle* Linn.

Synonym: *Chavica betle* Miq., *Chavica auriculata* Miq.

Common name: Betal vine, Phlu, See-keh (Malay-Narathiwat)

Family name: Piperaceae

Botanical description: The plant is stout creeper, climbing by adventitious roots at the nodes, quite glabrous (Figure 1.9). Leaves are simple, alternate, broadly ovate or rounded, 5-18 by 2-10 cm, having apex acute or acuminate, unequally rounded at the base or broadly heart-shaped, coriaceous, having prominent vein beneath. Flowers are very minute, in cylindrical male or female spikes, pendulous, male spikes are 2-12 cm long, having pedulous, 1.5-3 cm long, female spikes are long-peduncled, without calyx and corolla, having one small bract with each flower; ovary with one cell and one ovule. Fruit is a berry, small, round, pulpy; containing one globose seed (Farnsworth and Bunyapraphatsara, 1992).

Figure 1.9 *Piper betle* Linn.

Part used: Leaves

Traditional uses: Allergy, inflammation, beating by insect, kill insect (insecticide), help driving gas out, help curing urticaria and treatment of skin diseases (มาโนชน์ วามานนท์ และ เพ็ญนภา ทรัพย์เจริญ, 2537)

Chemical constituents: Chavicol, chavibitol, cineol, eugenol, carvacrol, caryophyllene, β-sitosterol (Ramji *et al*., 2002)

Biological activity: It has been reported that allylpyrocatechol (APC) from *P. betle* leaves showed promising activity against obligate oral anaerobes responsible for halitosis. The biological studies with APC indicated that the potential to reduce methylmercaptan and hydrogen sulfide was mainly due to the anti-microbial activity as established using dynamic in vitro models (Ramji *et al*., 2002).

The ether leaf extract of the leaves *P. betle* had good antimicrobial activity against *Trichophyton mentagrophytes*, *T. rubrum* and *Epidermophyton floccosum*, *Staphylococcus aureus* and *p*-hemolytic *Streptococcus* Group A (ลัดดาวัลย์ บุญรัตนกรกิจ และ ถนอมจิต สุภาวิตา, 2528).

1.2.2.7 *Senna alata*

Scientific name: *Senna alata* Linn.

Synonym: *Cassia bracteata*, *Cassia herpetica*, *Herpetica alata*, *Cassia alata*

Common name: Ringworm bush, Candle bush, Acapulo, Calalabra bush, Chumhet thet (Central, Peninsular), Kheekhaak, Lapmuen luang, Maak Kaling thet (Northern), Chumhet yai (Central), Ta-see-pho (Karen-Mae Hong Son)

Family name: Leguminosae

Botanical description: The plant is an erect shrub, about 1-2-(5) m high (Figure 1.10). Leaves are paripinnate, 30-60 cm long; consisting of 8-20 pairs of leaflets, each leaflet is oblong or elliptic oblong, rounded at both ends, 5-15 by 3-4 cm, glabrous; the petiolules are robust, 2-3 cm long. Flowers are densely in axillary racemes, about 20-50 cm long, 3-4 cm broad. The bracts are caduceus, 2-3 by 1-2 cm. The pedicels are very short about 2-4 m long. There are 5, unequal, oblong, 10-20 by 6-7mm, green sepals. The petals are bright yellow, ovate-orbicular to spathulate, short-clawed, 2 by 1-1.5 cm. There are 9-10 stamens; 2 large, 4 small and 3-4 stamens are reduced. The anthers are opening by apical pores. There is only one pistil and glabrous ovary. Fruit is a thick, flattened, wing, glabrous pod, 10-15 by 1.5-2 cm; the wings are 5 mm broad. Seeds are about 50, flattened, more or less quadrangular, 7-10 by 5-8 mm, black (Farnsworth and Bunyapraphatsara, 1992).

Figure 1.10 *Senna alata* Linn.

(www.medplant.mahidol.ac.th)

Part used: Fresh or dry leaves

Traditional uses: It can be used to cure eczema, treatment of skin diseases, ringworm, Tinea versicolor and laxative (มาโนชน์ วามานนท์ และ เพ็ญนภา ทรัพย์เจริญ, 2537).

Chemical constituents: Aloe-emodin, chrysophanol, emodin, sennoside, rhein, kaempferol (นันทวัน บุณยะประภัศร และ อรนุช โชคชัยเจริญพร, 2539)

Biological activity: It has been reported that ethanolic extract of *S. alata* leaves exhibited high activity against various species of dermatophytic fungi but low activity against non-dermatophytic fungi. However, bacterial and yeast species showed resistance against *in vitro* treatment with the extract. The minimum inhibitory concentration (MIC) values of the extract against *Trichophyton mentagorphytes* vat. *interdigitale, Trichophyton mentagrophytes* var. *mentagorophyte, Trichophyton rubrum* and *Microsporum gypseum* were 125 mg/ml, whereas against *Microsporum canis* was 62.5 mg/ml (Ibrahim and Osman, 1995).

Crude ethanol and water extracts of the bark had antimicrobial activity against fungi, *Candida albicans*. In addition, crude extract of the leaves had antimicrobial activity against bacteria, *Staphylococcus aureus* (Somchit *et al*., 2003).

The volatile oil from the leaves showed antibacterial activity. A 95% alcohol extract of the leaves exhibited bactericidal activity against *Bacillus subtilis*, *Serratia marcescens*, *Staphylococcus aureus*, *Escherichia coli*, and *Klebsiella pneumoniae*. A 50% alcohol extract of

the aerial part of *S. alata* possessed the bactericidal activity against *B. subtilis*, *S. aureus*, *Salmonella typhosa* and *E. coli* (25.0 μg/ml) and also against *Agrobacterium tumefaciens* (Farnsworth and Bunyapraphatsara, 1992).

1.2.2.8 *Alpinia galanga*

Scientific name: *Alpinia galanga* Linn.

Synonym: *Languas galanga* Linn.

Common name: Greater Galangal, Katuk karohinee (Central), Khaa, Khaa luang (Northern), She-ae-khoei, Sa-e-choei (Karen-Mae Hong Son)

Family name: Zingiberaceae

Botanical description: The plant is a perennial herb with underground stem, 2-2.5 m high, having aerial stem leafy rhizome with conspicuously nodes and internodes, slightly aromatic (Figure 1.11). Leaves are simple, rising from the under ground stem; 20-50 by 7-11 cm; glabrous; consisting of blade lanceolate or elliptic-oblong; apex and base acute; margin entire; petiole 5-7 mm long, slightly hairy, and leaf-sheath. Inflorescence is terminal raceme, 15-30 cm long, having peduncle glabrous, rachis minutely hairy, bearing many small flowers; pedicel 8-9 mm long; bract ovate, 2.5 cm long; calyx greenish white, about 8 mm long, tubular, with 3-toothed, hairy; corolla short tubular, 2.5-3 cm long, apex divided into 3 lobes, the upper lobe broader, the lower lobes oblong, spreading when anthesis; lip distinctly clawed, 1.5-2 cm long; stamen 1, curved, 2.5 cm long, filament flattened, anther 6-7 mm long; ovary suborbicular, 4 mm long, 3 locule, 1-2 ovule in each locule. Fruit is globose or ellipsoid, 1 cm in diameter, orange-red, black when fully matured; containing 2-3 seeds (Farnsworth and Bunyapraphatsara, 1992).

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Figure 1.11 *Alpinia galanga* Linn.

Part used: Rhizomes

Traditional uses: The old tuber is used to prick and apply on the area of eczema or mix with alcohol for applying on the urticaria area, treating indigestion, nausea and flatulence, Tinea versicolor, Tinea capitis, abscesses, ring worm, stomach upset (Farnsworth and Bunyapraphatsara, 1992).

Chemical constituents: Methyl cinnamate, cineol, eugenol, α-pinene, 1′-acetoxychavicol acetate, terpinen-4-ol, acetoxychavicol acetate (Oonmetta-aree *et al*., 2005), 1,8-cineole, kaempferol, quercetin (Farnsworth and Bunyapraphatsara, 1992)

Biological activity: It has been reported that *A. galanga* extract had inhibitory effect against *Staphylococcus aureus* 209P*s*. The minimum inhibitory concentration (MIC) of the galangal extract was 0.325 mg/ml and the minimum bactericidal concentration (MBC) at 1.3 mg/ml. The major compound of the extract was D,L-1′-acetoxychavicol acetate, which was identified by GC-MS and NMR (Oonmetta-aree *et al*., 2005).

The ethanolic and chloroform extracts of *A. galanga* rhizome showed antifungal activity against *Microsporum gypseum, Trichophyton rubrum* (Archararit *et al*., 1984). Some reports showed that *A. galanga* was safety, no effect of acute and chronic toxicity (Mokkhasmit *et al*., 1971) and no effect of mutatogenic activity (Rompelberg *et al.,* 1995).

1.2.2.9 *Punica granatum*

Scientific name: *Punica granatum* Linn.

Synonym: *Punica nana* Linn.

Common name: Pomegranate, Tubtim, Siae lin (Chinese), Phi laa (Nong khai), Philaa khaao (Nan), Ma koh (Northern), Maak-chang (Shan-Mae Hong Son).

Family name: Punicaceae

Botanical description: The plant is an erect shrub up to 3 m high, much branched from the base, having branchlets slender, often ending in a spine (Figure 1.12). Leaves are simple; oblong-lanceolate, 1-9 by 0.5-2.5 cm; consisting of obtuse or emarginated apex; base

acute, shiny, glabrous. Flowers are showy, orange red, about 3 cm in diam, 1-5 borned at branch tips, the others solitary in highest leaf-axils, sessile or subsessile; consisting of calyx 2-3 cm long, tubular, lobes erect or recurved, thick, coriaceous; petals the same numbers as the calyx lobes, rounded or very obtuse, from edge of hypanthium, caduceus; stamen numerous within upper half of hypanthium, filament free; inferior ovary, ovules numerous, style1, stigma capitate. Fruit is globose berry, crowded by persistent calyx-lobes, having pericarp leathery filled with numerous seeds, which are surrounded by pink and red, transparent, juicy, acid, pleasant-tasting pulp (Farnsworth and Bunyapraphatsara, 1992).

Figure 1.12 *Punica granatum* Linn.

Part used: Fruit rind

Traditional uses: Anthelmintic, astringent, for wound heeling, pus-foamimg, antidysentery, cough, antidiarrheal (Navarro *et al*., 1996)

Chemical constituents: Gallotannic acid, tannin (Navarro *et al*., 1996), pelletierine pulp (Farnsworth and Bunyapraphatsara, 1992).

Biological activity: It has been reported that methanolic extract of *P. granatum* possessed strong *in vitro* antibacterial activities against *Escherichia coli* and *Staphylococcus aureus* (Melendez and Capriles, 2005). In addition, it has been reported that *P. granatum* possessed strong *in vitro* antimicrobial activity against *S. aureus, E. coli, Pseudomonas aeruginosa* and *Candida albicans* with MIC values of 0.62, 10.0, 10.0 and 10.0 mg/ml respectively (Navarro *et al*., 1996). The peel extract of pomegranate had astringent activity because of tannin and gallotannin acid. Thus it could treat diarrhea.

1.2.2.10 *Morus alba*

Scientific name: *Morus alba* Linn.

Synonym: None

Common name: Mulbery, Mhon

Family name: Moraceae

Botanical description: Mulberry is a deciduous tree, 30-50 feet tall with almost equal spread, dense with a rounded top. The leaves are, simple, green and polymorphic (many shapes). Flowers are inconspicuous greenish-white in the early spring. The fruits go from white to pink to dark red or purple, are small fleshy drupes and very tasty (Figure 1.13).

Figure 1.13 *Morus alba* Linn.

(www.motherherbs.com)

Part used: Leaves, bark, roots

Traditional uses: Reduce blood cholesterol, reduce blood sugar, anti hypertension. It is helpfull in cough, dyspepsia, facial dropsy, oedema and injury (www.motherherbs.com).

Chemical constituents: Flavonoid (mulberrofuran G, morusin and camphor)

(นันทวัน บุณยะประภัศร และ อรนุช โชคชัยเจริญพร, 2539; Sohn *et al*., 2004) gamma amino butyric acid, phytosterol, sitosterol, fiber, deoxynojirimycin, calcium, vitamin A, vitamin B1, vitamin B2, vitamin C, sodium, potassium

Biological activity: It has been reported that some prenylated flavonoids from *M. alba* had antimicrobial activities against *Escherichia coli*, *Salmonella typhimurium*, *Staphylococcus epidermidis* and *S. aureus*. Mulberrofuran G and albanol B showed strong antibacterial activity with 5-30 μg/ml of MICs (Sohn *et al*., 2004). *M. alba* leaf methanolic extract and its fractions (chloroform, butanol, and aqueous fractions) were found to inhibit NO production in LPS-activated RAW264.7 macrophages without an appreciable cytotoxic effect at concentration from 4 to 100 μg/ml. In addition, *M. alba* leaf extract and its fractions significantly decreased the production of TNF-α (Choi and Hwang, 2005).

1.2.2.11 *Azadirachta indica*

Scientific name: *Azadirachta indica* A. Juss.

Synnonym: *Antelaea azadirachta* (L.) Adelb., *Azedarach fraxinifolia* Moench, *Melia azadirachta* L., *M. fraxinifolia* Adelb., *M. indica* (A. Juss.) Brandis, *M. pinnata*

Common name: Neem, Neem-tree, Indian lilac, White cedar (Eng.), Margosa tree (Port.), Azad-darakht-ihindi (Persian), Tamaka, Bowtamaka, Tama, Sadao india, Sadao thai (Thai).

Family name: Meliaceae

Botanical description: Medium sized tree, up to 15 m tall, rarely 25 m, with short, straight bole and long spreading branches, forming a dense, large, oval or rounded crown. Evergreen or, under extreme heat and drought, deciduous. Old bark turning dark grey, thick and furrowed. Leaves imparipinately compound with 7-17 pairs of leaflets, which are ovate or lanceolate, falcate with uneven base and dentate margins, 6-8 cm long, 1-3 cm wide. Inflorescence a 10-30 cm long panicle with many, small white to cream coloured flowers (Figure 1.14). Neem is sometimes confused with the chinaberry, *Melia azedarach* L., but they are easily distinguished by the leaves. *Azadirachta* spp. have simple pinnate leaves, while those of *Melia* spp. are 2-to 3-pinnate (Schmidt and Joker, 2000).

Figure 1.14 *Azadirachta indica* (www.homedd.com)

Part used: Leaves

Traditional uses: Dental diseases, skin diseases, leprosy, skin ulcers, iching and burning sensation (Biswas *et al*., 2002)

Chemical constituents: Isoprenoids (diterpenoids and triterpenoids), protomeliacins, limonoids, azadirone, gedunin, nimbin, salanin, nimboline and azadirachtin (Biswas *et al*., 2002, Poddar and Mahato, 1988)

Biological activity: It has been reported that *A. indica* leaf extract had antibacterial activity against *Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, Neisseria gonorrhea, Proteus vulgaris, Pseudomonas aeruginosa, Corynebacterium diptheriae, Neisseria* spp*., Salmonella* spp. (Talwar *et al*., 1997). In addition, the leaf extract of *A. indica* had anthelmintic activity and antidysentery. The lotion from leaf extract of *A. indica* was used for treatment of acute or chronic symptoms of skin diseases, 3-4 and 2 weeks, respectively (Biswas *et al*., 2002).

1.2.2.12 *Cinnamomum verum*

Scientific name: *Cinnamomum verum* Presl.

Synonym: *Cinnamomum zeylanicum* Blume.

Common name: Cinnamon, Ob choey

Family name: Lauraceae

Botanical description: Trees; young branches dark brown, terete, glabrous. Leaves opposite or subopposite, coriaceous, ovate to broadly ovate, 10-15 cm long, 4-8 cm wide, tripliveined, glabrous, apex blunt or slightly acute, petioles stout, ca. 1 cm long. Flowers gray pubescent, in axillary, sparsely strigose inflorescences as long as or longer than leaves; tepals 6, equal, erect; fertile stamens 9. Fruit an ellipsoid berry, ca. 1 cm long, subtended by a cupule with persistent tepals attached to the rim. (www. hear.org/pier/species/cinnamomum_verum.htm)

Figure 1.15 *Cinnamomum verum* Presl.

(www. toptropicals.com)

Part used: Bark (Figure 1.15)

Traditional uses: Antidysentery, antiseptic, antifungal agents, stimulant, astringent and carminative, as an antidote for diarrhoea and stomach upsets
(นันทวัน บุณยะประภัศร และ อรนุช โชคชัยเจริญพร, 2539)

Chemical constituents: Eugenol, benzaldehyde, linalool and α-perpineol
(นันทวัน บุณยะประภัศร และ อรนุช โชคชัยเจริญพร, 2539)

Biological activity: It has been reported that *C. verum* possessed an anti-nociceptive effect against both acetic acid-induced writhing and hot plate-induced thermal stimulation (Atta and Alkofahi, 1998). The essential oil from *C. verum* exhibited antibacterial activities against *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Enterococcus* spp., *Escherichia coli*, *Serratia marcescens*, *Enterobacter cloacae*, *Klebsiella pneumoniae* strains isolated from pediatric patients severly infected (Hersch-Martinez *et al*., 2005).

1.2.2.13 *Plumbago zeylanica*

Scientific name: *Plumbago zeylanica* Linn.

Synonym: *Plumbago viscosa* Blanco.

Common name: White leadwort, Jettamoonplerng-khaw

Family name: Plumbaginaceae

Botanical description: This is a spreading or somewhat climbing, half-woody plant, 1 to 2 m in length, and smooth except for the glandular calyces (Figure 1.16). The leaves are oblong-ovate to ovate, 4 to 10 cm long, and pointed at the tip; the base of the stalk is dilated and clasps the stem. The spikes are 5 to 25 cm in length. The calyx is green, about 1 centimeter long, and covered with long-stalked, glandular hairs. The corolla is white or very pale blue, about 1.5 cm in diameter; it has a slender tube, about 2 cm long, and spreading limb (Farnsworth and Bunyapraphatsara, 1992).

Figure 1.16 *Plumbago zeylanica* Linn.

Part used: Root

Traditional uses: Effective in intestinal disorders, cures wounds, fever, skin disorders, rheumatism and white spots of skin and dental diseases (นันทวัน บุณยะประภัศร และ อรนุช โชคชัยเจริญพร, 2539)

Chemical constituents: Plumbagin (Paiva *et al*., 2003)

Biological activity: It has been reported that plumbagin isolated from roots of white leadwort had antimicrobial activity against *Staphylococcus aureus* and *Candida albicans* with minimum inhibitory concentrations of 1.56 μg/ml and 0.78 μg/ml, respectively (Paiva *et al*., 2003).

1.2.2.14 *Dioscorea membranacea*

Scientific name: Dioscorea membranacea Pierre

Common name: Hua-khaw-yen

Family name: Dioscoreaceae

Botanical description: The rhizome is a wide running, perhaps even to 2 m. It is dark brown with white flesh. The stem is slightly ridged and unarmed. Leaves are deeply trifid above a cordate base with the short acuminate 9 nerved, two primary nerves reaching the forerunner tip along with the midrib and the second pair reaching the tips of the letheral lobes (Figure 1.17). The petioles are 1/2-2/3 of the length of the blade. Male flowers have small subsessile cymes with up to 4 flowers, sepals 1 mm long, and long-ovate. Stamens, alike the filaments insert just below the sepals 0.3 mm long. The anther is small and introse. Female flowers are on downwardly directed spike-like racemes. Outer sepals are obovate, inner ones are lanceolate, and the inner are a little shorter than the outer. Style is short. Capsules are apart, about 1 -2 cm (Burkill, 1951).

Figure 1.17 *Dioscorea membranacea* Pierre

Part used: Rhizome

Traditional uses: Treatments of dermopathy, lymphopathy, inflammation, cancers, veneral diseases, and leprosy (Tewtrakul and Itharat, 2006)

Chemical constituents: Isoflavone, 7,6′-dihydroxy 3′-methoxy isoflavone, taxifolin and astilbin (Yijun *et al*., 1998), naphthofuranoxepins, dioscorealides A and B, and 1,4-phenanthraquinone, dioscoreanone (Itharat *et al*., 2003).

Biological activity: It has been reported that the ethanolic extract of *D. membranacea* roots showed cytotoxic activity against lung cancer cell lines (IC_{50}= 4.6 μg/ml), prostate cancer cell lines (IC_{50}= 17.55 μg/ml) and normal cell lines (IC_{50}= 66.05 μg/ml) (Saetung *et al*., 2005).

In addition, the ethanolic extract had antimicrobial activities against *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli* and *E. floccosum* with MIC values of <1.25, <1.25, 2.5 and < 1.25 mg/ml, respectively (Itharat, 2002). The ethanolic extract of *D. membranacea* exhibited potent inhibitory activity against β-hexosaminidase release as a marker of degranulation in RBL-2H3 cells, with an IC_{50} value of 37.5 μg/ml. Dioscorealide B possessed the highest antiallergic activity with an IC_{50} value of 5.7 μM, followed by dioscoreanone

(IC_{50} = 7.7 μM), dioscorealide A (IC_{50} = 27.9 μM), and diosgenin (IC_{50} = 29.9 μM) (Tewtrakul and Itharat, 2006).

1.2.2.15 *Syzygium aromaticum*

Scientific name: *Syzygium aromaticum* (Linn.) Merr & Perry.

Synonym: *Eugenia caryophyllus* (Sprengel) Bullock & Harrison

Common name Clove, Kan pluu, Chan-jee

Family name: Myrtaceae

Botanical description: The plant is an evergreen tree 5-10 m high; having dark grey or light brown; all parts glabrous. Leaves are simple, opposite, elliptic or oblongobovate, 7-12 cm long, 3-5 cm wide, shiny above, paler beneath, pellucid-dotted; consisting of tip acuminate, margin entire, base cuneate, dark green. Petioles are 2-3 cm long with swollen reddish base. Flowers are bisexual, 3-20 in paniculate cymes, having angled peduncles and short pedicels, about 5 mm long. Each flower consists of 4 freshly triangular sepals; petals 4, implicate, rounded, tinced red, falling as flower opens; stamens numerous, small, filaments slender, anthers pale-yellow; ovary inferior, 2-3 celled with several ovules; style about 3 mm; stigma 2-lobed. Fruit is a freshy drupe, obovoid-ellipsoid or oblong obovoid, about 2-3 by 1.2 cm, containing 1, rarely 2 seeds. Seeds are oblong, about 1.5 cm long, groovedon one surface (Farnsworth and Bunyapraphatsara, 1992).

Figure 1.18 *Syzygium aromaticum* (Linn.) Merr&Perry.

Part used: Flowers (Figure 1.18)

Traditional uses: For masking alcoholic smell on the breath, stomachache, fainting, toothache, gastrointestinal disturbances, antiseptic, antiflatulence, treatment of beri beri (มาโนชน์ วามานนท์ และ เพ็ญนภา ทรัพย์เจริญ, 2537)

Chemical constituents: Eugenol, β-caryophyllene, acetyl eugenol, methyl amyl ketone, chavicol, eugenol acetate (นันทวัน บุณยะประภัศร และ อรนุช โชคชัยเจริญพร, 2539)

Biological activity: It has been reported that the volatile oil of clove exhibited antibacterial activity against *Bacillus subtilis, Enterobacter aerogenes, Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus*, *Streptococcus faecalis* (Umehara *et al*., 1992; Dean *et al*., 1995), *S. paratyphi* and *S. dysenteriae* (Ahmad and Beg, 2000). In addition both clove oil and eugenol exhibited inhibitory action against *Trichophyton*, *Achorion*, and *Epidermophyton*. They were found to be effective at dilutions of 1:8000 to 1:16000 and the microbes failed to become resistant to the oil. The oil showed no irrigation action (Farnsworth and Bunyapraphatsara, 1992).

1.2.2.16 *Andrographis paniculata*

Scientific name: *Andrographis paniculata* (Burm.f.) Nees

Synonym: *Justicia paniculata* Burm. f.

Common name: Fa thalaai (Bangkok), Fa thalaai joan, Yaa kannguu (Songkhla), Khee-pang-hee (Chinese)

Family name: Acanthaceae

Botanical description: The plants are annual herbs about 30-100 cm high, having stem erect, 4-angled, much branches (Figure 1.19). Leaves are simple, opposite, sessile or short petioled, elliptic or lanceolate, 2.5-8 cm long, 1-3 cm wide, glabrous on both surfaces. Flowers are in racemes, 2.5-10 cm long, consisting of flowers distant; frequently 1-sided; bract small, linear; pedicel 0-6 mm; calyx 1, green, about 3 mm long, connate at the base, divided into 5 linear segments, hairy; corolla white, tubular, divided into 2 lips, upper lip 3-lobed, rose-purple spotted, hairy; lower lip small, 2-lobed; stamens 2, filaments hairy, upwards, anther dark-purple; ovary 1, style slender, tip minutely bifid. Fruit is a linear-oblong capsule about 1.5 cm long, 3-5

mm wide, loculicidal, nearly glabrous. Each capsule contains 6-12 seeds which are subquadrate, bony, yellow or deep brown, slightly translucent (Farnsworth and Bunyapraphatsara, 1992).

Figure 1.19 *Andrographis paniculata* (Burm.f.) Nees

Part used: Leaves

Traditional uses: Curing flu and sore-throat, treatment of abscesses, antidysentery, wound healing, anti-inflammation and antidiarrhoeal (มาโนชน์ วามานนท์ และ เพ็ญนภา ทรัพย์เจริญ, 2537; Farnsworth and Bunyapraphatsara, 1992)

Chemical constituents: Andrographolide, diterpene lactone, andrographiside, paniculide, diterpenoids, farnesol (นันทวัน บุณยะประภัศร และ อรนุช โชคชัยเจริญพร, 2539; Farnsworth and Bunyapraphatsara. 1992)

Biological activity: It has been reported that the aqueous extract, andrographolides and arabinogalactan proteins from *A. paniculata* showed antimicrobial activity against *Candida albicans*, *Escherichia coli, Pseudomonas aeruginosa* and *Bacillus subtilis* (Singha *et al*., 2003).

It has been demonstrated that 95% ethanol extract of *A. paniculata* showed antibacterial activity against *Staphylococcus aureus* while the hot water extract showed no effect. However, both extracts were active against *E. coli* (Farnsworth and Bunyapraphatsara, 1992).

1.2.2.17 *Cymbopogon citratus*

Scientific name: *Cymbopogon citratus* Stapf.

Synonym: *Andropogon citratus*

Common name: Lemon grass, Lapine, Takhrai, Khaa-hom (Shan-Mae Hong Son), Khrai (Peninsular), Cha khrai (Northern), Soet-kroei, Loe-kroei (Khmer-Surin), Ho-wo ta-po (Karen-Mae Hong Son), Hua-sing-khai (Khmer-Prachin-buri)

Family name: Gramineae

Botanical description: *C. citratus* is a perennial aromatic herb with tufted culms, erect, up to 1 m high, terete and hard (Figure 1.20). It is scarcely flowered. Leaves are aromatic when crushed due to essential oils; consisting of terete and glabrous leaf sheaths; linear blade, narrow base, acute apex, up to 100 cm long and 2 cm wide; chartaceous ligule, about 2 mm long, truncate, minutely ciliate. Inflorescence is a large false panicle; racemes paired, subtended by spathes. Spikelets are paired; consisting of the upper pedicellate; the lower sessile, about 4 mm long, lanceolate, as long as the spikelet, acute, having margins inrolled, 2-keeled, hispid along keels, 5-veined; upper glume is lanceolate, chartaceous, about 4 mm long, 1-keeled, having margin inrolled and fimbriate, inconspicuously 3-vained; lower lemma is membranous, lanceolate, margins broadly inrolled and fimbrate, cuspidate, 1-veined; upper lemma is lanceolate, having membranous, about 3 mm long, having margins fimbrate, 1-veined, aristate (Farnsworth and Bunyapraphatsara, 1992).

Figure 1.20 *Cymbopogon citratus* Stapf.

Part used: Stalks, whole plant

Traditional uses: Anti-flatulance, treatment of disorders of urination, Tinia versicolor, strangury, as an appetite stimulant (มาโนชน์ วามานนท์ และ เพ็ญนภา ทรัพย์เจริญ, 2537).

Chemical constituents: Citral, myrcene, citronellal, geraniol, menthol, citronellol, eugenol, borneol (นันทวัน บุณยะประภัศร และ อรนุช โชคชัยเจริญพร, 2539).

Biological activity: It has been reported that *C. citratus* exhibited antimicrobial activities against *Salmonella* spp., *Escherichai coli* O157, *Campylobacter jejunii* and *Clostridium perferingens* (Wannissorn *et al*., 2005). Pure lemongrass oil from *C. citrates* posessed antibacterial activity against *P. acnes* with MIC and MBC values of 0.6 μl/ml (Lertsatitthanakorn *et al*., 2006).

1.2.2.18 *Rhinacanthus nasutus*

Scientific name: *Rhinacanthus nasutus* (Linn.) Kurz.

Synonym: *Justicia nasuta* L.

Common name: Thong phan chang, Yaa man kai (Central)

Family name: Acanthaceae

Botanical description: The plant is a small shrub, up to 1.5 m high; the stem is obtusely quadrangular, when young it is covered with fine, up curved hairs (Figure 1.21). Leaves are simple opposite; elipptic or lanceolate; 4-6 by 2-3 cm; chartaceous; entire; light green; shortly pubescent having acute base and apex. Flowers are white, in short axillary clusters; densely appressed pubescent. The calyx is divided into 5 deeply acute parted, light green, 5-6 mm long. The corolla-tube is about 2 cm, having brownish purple spots at the throat of the tube, bilabiate, upper lip erect, bifid, lower lip 3-lobed; stamens 2, inserted in the throat; ovary 2-loculed. Capsule is loculicidally 2-valved pulp (Farnsworth and Bunyapraphatsara, 1992).

Figure 1.21 *Rhinacanthus nasutus* (Linn.) Kurz.

Part used: Fresh leaves

Traditional uses: To cure eczema, pruritis, abscess pain, skin diseases, anti-inflammatory, Tinea versicolor, ringworm and rash (นันทวัน บุณยะประภัศร และ อรนุช โชคชัยเจริญพร, 2539; Farnsworth and Bunyapraphatsara, 1992)

Chemical constituents: 4-acetonyl-3, 5-dimethoxy-p-quinol, rhinacanthin-A, rhinacanthin-D, rhinacanthin-Q, rhinacanthone, ρ-hydroxybenzaldehyde, methyl vanillate, syrengaldehyde, lupeol, wogonin, oroxylin A, (+)-praeruptorin, allantoin, β-amyrin, stigmasterol,

sitosterol, stigmasterol-4-en-3-one, 2-methylanthraquinone, 2, 4-dimethoxybenzoquinone, 2-methoxy-4-propionylphenol, syringic acid, vanillic acid (Sattar *et al*., 2004)

Biological activity: It has been reported that aqueous ethanolic extract of *R. nasutus* exhibited a potent dose dependent anti-fungal activity against *Candida albicans* and *Trichophyton*. In addition, anti-bacterial activity of the plant is also observed against gram-positive bacteria (*Bacillus subtilis, B. cereus, B. globigii*). However, it was ineffective against gram-negative bacteria (*Proteus morgani, P. mirabilis, Samonella typhi, Pseudomonas aeruginosa, Escherichia coli* (Sattar *et al*., 2004).

1.2.3 *Alpinia galanga*

1.2.3.1 Chemical constituents of *A. galanga*

Rhizomes: (1′S)-1′-acetoxychavicol acetate, (1′S)-1′-acetoxyeugenol acetate, 1′-acetoxychavicol acetate, 1′-acetoxyeugenol acetate, D-camphor, chavicol, chavicol acetate, 1,8-cineole, trans-coniferyl diacetate, tran- *p* -coumaryl diacetate, di-(*p*-hydroxyl-cis-styryl) methane, essential oil, eugenol, eugenol acetate, trans-β-farnesene, galangin, 7-hydroxy-3, 5-dimethoxy flavone, 4-hydroxybenzaldehyde, 1′-hydroxy-chavicol acetate, *p*-hydroxycinnamaldehyde, isorhamnetin, kaempferol, kaempferol-4′-methyl ether, kaempferol-7-methyl ether, methylcinnamate, methyleugenol, pinenes, quercetin, quercetin-3-methyl ether, resins, sesquiterpenoids (Farnsworth and Bunyapraphatsara, 1992)

Fruits: 1'-acetoxychavicol acetate, 1′-acetoxyeugenol acetate (Farnsworth and Bunyapraphatsara, 1992)

Seeds: galanal A, galanal B, (E)-8,17-epoxylabd-12-ene-15, 16-dial (Farnsworth and Bunyapraphatsara, 1992)

Not specified part used: D,L-1′-acetoxychavicol acetate, dl-1′-acetoxyeugenol acetate, anethol, benzaldehyde, benzyl benzoate, benzyl salicylate, camphor, caryophyllene, 1,8-cineole, cinnamic aldehyde, *p*-cymene, dilupiol, elemicin, essential oil, eugenol, isosafrole, limonene, lialool, methylchavicol, methyleugenol, nerolidol, phellandrene, ∝-pinene, β-pinene, safrole (Farnsworth and Bunyapraphatsara, 1992; Yang and Eilerman, 1999)

1.2.3.2 Pharmacological activities of *A. galanga*

Antimicrobial activity

It has been reported that galangal extract exhibited inhibitory effect against *Staphylococcus aureus* 209P*s* with MIC value of 0.325 mg/ml and MBC value of 1.3 mg/ml. The major compound of the extract was D,L-1′-acetoxychavicol acetate (Oonmetta-aree *et al*., 2005).

Antifungal activity

It has been reported that chloroform extract of *A. galanga* possessed antifungal activity against *Cryptococcus neoformans* and *Microsporum gypseum*, but exhibited weak activity against *Cantida albican*s (Phongpaichit *et al*., 2005).

The ethanolic extract of *A. galanga* rhizome had inhibitory activity against a variety of human pathogen fungi, including *Cryptococcus neoformans*, *Wangiellia dermatitidis*, *Alternaria alternate*, *Aspergillus fumigatus*, *Fusarium oxysporum*, *Microsporum gypseum*, *Pseudallescheria*, *Rhizopus* species and *Tricophyton mentagrophytes* (Ficker *et al*., 2003).

Antitumor activity

It has been reported that 1′-acetoxychavicol acetate (ACA) isolated from *A. galanga* had antitumor activity. It suppressed chemically induced carcinogenesis in Ehrlich ascites tumor cells. The anticarcinogenic effects of ACA might be partly due to perturbation of the polyamine metabolic pathway and triggering of caspase-3-like activity, which result in apoptosis (Moffatt *et al*., 2000).

Cytotoxic activity

It has been reported that *A. galanga* exhibited cytotoxic activity. 1′-Acetoxychavicol acetate, the major compound had cytotoxic activity against COR L23 lung cancer cell line and MCF7 breast cancer cell line with IC_{50}values of 7.8 μM and 23.9 μM, respectively (Lee and Houghton., 2005).

Enzyme inhibition activity

It has been reported that xanthine oxidase inhibitors were isolated and identified as trans-*p*-coumaryl diacetate, trans-coniferyl diacetate, (1′S)-acetoxychavicol acetate, (1′S)-acetoxyeugenol acetate and 4-hydroxybenzaldehyde from *A. galanga*. The inhibitory action of the first two compounds was mediated through a non-competitive reaction with the substrate xanthine. It was also reported that *A. galanga* rhizomes elicited slight amylase-inhibitory activity (Farnsworth and Bunyapraphatsara, 1992).

Smooth muscle stimulating activity

An hydroalcoholic (1:1) extract of rhizomes was reported to have smooth muscle stimulating effect on the isolated guinea pig ileum (Farnsworth and Bunyapraphatsara, 1992).

Hypoglycaemic activity

It has been reported that *A. galanga* powdered rhizome and its methanol and aqueous extracts significantly lowered blood glucose in normal rabbits but *A. galanga* and its methanol and aqueous extracts did not produce significant reduction of blood glucose in alloxan diabetic rabbits (Akhtar *et al*., 2002).

Antiallergic activity

It has been reported that 80% aqueous acetone extract of the rhizomes of *A. galangal* inhibited release of beta-hexosaminidase, a marker of antigen-IgE-mediated degranulation in RBL-2H3 cells. 1′S-1′-acetoxychavicol acetate and 1′S-1′-acetoxyeugenol acetate isolated from *A. galanga* exhibited potent inhibitory activity with IC_{50}values of 15 and 19 μM, respectively, and inhibited ear passive cutaneous anaphylaxis reactions in mice and the antigen-IgE-mediated TNF-α and IL-4 production (Matsuda *et al*., 2003a).

Anti-inflammation

It has been reported that 80% aqueous acetone extract of *A. galanga* rhizomes showed nitric oxide (NO) production inhibitory activities in mouse peritoneal macrophages.

Galanganal (IC_{50}=68 μM), galanganols B (88 μM) and C (33 μM), 1′S-1′-acetoxychavicol acetate (2.3 μM), 1′S-1′-acetoxyeugenol acetate (11 μM), trans-*p*-hydroxycinnamaldehyde (ca. 20 μM), trans-*p*-coumaryl alcohol (72 μM), and trans-*p*-coumaryl diacetate (19 μM) isolated from the aqueous acetone extract were found to show inhibitory activity (Toshio *et al*., 2005).

Immunostimulating activity

It has been reported that hot water polysaccharide extracts of *A. galanga* had immunostimulating activity. It showed a stimulate effect on the reticulo-endothelial system (RES) and increased the number of peritoneal exudate cells (PEC), and spleen cells of mice. The optimum dose was 25 mg/kg. On the other hand, polysaccharide extract of *A. galanga* enhanced the proliferation of the murine spleen cells *in vitro* (Bendjeddou *et al*., 2003).

Antioxidative activity

It has been reported that ethanolic extract of *A. galanga* had antioxidant activity. It exhibited strong superoxide anion scavenging activity, Fe^{2+} chelating activity. The antioxidant activity of the extract correlated well with reducing power. Furthermore, ethanolic extract *A. galanga* acted as radical scavenger and also as lipoxygenase inhibitor (Juntachote and Berghofer, 2005).

Gastroprotective effect

It has been reported that 1′S-1′-acetoxychavicol acetate and 1′S-1′-acetoxyeugenol acetate isolated from *A. galanga* rhizomes inhibited the ethanol-induced gastric mucosal lesions (ED_{50}0.61 and ca. 0.90 mg/kg). In addition, 1′S-1′-acetoxychavicol acetate inhibited the lesions induced by 0.6 M HCl (ED_{50}0.73 mg/kg) and aspirin (ED_{50}0.69 mg/kg). In addition 1′-acetoxyl group of 1′S-1′-acetoxychavicol acetate and 1′S-1′-acetoxyeugenol acetate was found to be essential for their strong activity (Matsuda *et al*., 2003b).

1.3 Objectives

The aims of the present study were as follows:

1. To investigate the antibacterial activity of the selected plants against *P. acnes*

2. To select the plant extract that exhibited the strongest antibacterial activity against *P. acnes*

3. To isolate the active compound from the selected plant using a bioassay-guided isolation

4. To establish HPLC system for quantitative determination of the active compound

5. To study on preliminary formulation study on formulation of anti-acne cream using the extract of the selected plant as an active ingredient