CHATER 2

LITERATURE SURVEY

2.1 Literature Survey

2.1.1 The way of life of Lanna people:

2.1.1.1 The way of life of Lanna people

The life of Lanna people has revealed the Lanna traditional medicine and medicinal herbs as follows (Taoprasert and Taoprasert, 2005). Lanna, situated in the upper-northern region of Thailand, has more than 800 years history of its own intangible cultural heritage for traditional medical practices and medicinal herbs. Wisdom, knowledge and beliefs of the people intertwined to form the basis of concept and practices for its people to stay healthy. Bodies of accumulated knowledge usually derived from actual experiences and tested through a long trial-and-error process. These were passed on from generation to generation, mainly within families in various forms or through certain community institutes such as temples and monks. The traditional health related practices have become part of the community's way of life and integrated in the community health care system. The knowledge was formed on a piece-by-piece basis whereby little effort was put into systematizing them in theoretical framework. Unfortunately, rapid changes due to modernization and development had left many of the traditional practices behind and broken the chain of passing-on-processes. Though some traditional health practices remain and local herbs and medicinal plants have begun to find its way into wider commercial purpose,

the intangible cultural heritage for traditional medical practices and medicinal herbs are gradually disappearing from the Lanna cultural context.

In Lanna context, there are various reasons for continuing the herbal usage: to conserve, to revive, to improve, to apply and to inherit the intangible cultural heritage of the Lanna people. These beneficial views form a strong basis of beliefs and practices of indigenous ways in preventing and healing diseases.

2.1.1.2 Medicinal plants with anti-inflammatory activity of Lanna

On the matter of health, Lanna people believed that the good healths are important. Therefore, they have kept their health in balance on both the physical and mental aspects. However, traditional healers in the Lanna region also used the local wisdom and knowledge to prepare thousands of medicinal plant recipes from herbs and plants for those who experienced ill health and needed to correct them. The current health care system has also used medicinal plant recipes in the form of fresh and dried plants in accordance with health promotion and prevention measures (Taoprasert and Taoprasert, 1993).

Lanna anti-inflammatory medicinal plant recipes for can be found in the Lanna Medicinal Plants Database produced by the Natural Products Research and Development Center (NPRDC), Faculty of Pharmacy, Chiang Mai University, Thailand. A total of 11,130 recipes from the "MANOSROI II" database was collected from 7 provinces of the upper northern part of Thailand, which were Chiang Mai, Chiang Rai, Lamphun, Lampang, Payao, Phrae and Nan. Among these, 17 recipes indicated the anti-inflammatory activity (Manosroi *et al*., 2008). Inflammation, according to Lanna, is exhibited by a range of signs and symptoms that are caused from the internal and external factors. External factors include insect

sting/bite, snake bite, toothache and skin injury. For the internal factors, according to the Lanna belief, were due to the imbalance of diet taken, personal characteristic in relation to the emotion, the pathological condition and others (Taoprasert, 2003). The Lanna recipes for snake bite, for instance, have been used for the oral and topical application in the treatment described as follows (Taoprasert, 2003):

A. An example of the traditional medicinal recipe for snake-bite for oral administration:

Leaves of *Barleria lupulina* Lindl. and *Clinacanthus nutans* (Burm.f.) Lindau. are used. Fifty grams of leafs from each plant are ground and then mixed with 40 % alcohol. Patient has to drink the preparation at every 20 minutes interval until getting a better sign.

B. An example of the traditional medicinal recipe for snake-bite for topical administration:

The root of *Croton tiglium* is scraped and applied on the snakebite wound of a patient. Another recipe uses the root of *Calotropis gigantea* (Linn.) R.Br.ex Ait., *Moringa oleifera* Lam. and *Butea monosperma* (Lam.) Taub. They are scraped, mixed together and then applied on the snake-bite wound.

2.1.2 Inflammation Process

Inflammation is a response of the organism to the pathogen which is a complex process involving several characteristic features. The mechanism of inflammation occurs when biogenic amines from mast cell release histamine. Vasodilatation increases blood flow causing the redness and increasing heat. Increased permeability of the blood vessels results in an exudation (leakage) of plasma proteins and fluid into the tissue (edema), manifesting as swelling. The

histamine is maintained by kinins, notably bradykinin, released from the substrate kininogen by kinin then forming enzymes activated during early phase of inflammation that increase the sensitivity to pain. There is a wave of polymorphonuclear leukocyte (PMN) migrating from blood vessels to the inflamed tissue. Subsequently, monocytes which are in the process of margination, adherence, diapedesis, and chemotactic movement to the site of inflammation, are activated to become macrophages. These two cell types, polymorphonuclear leukocyte and monocyte, in combination with the vascular changes, are able to resolve the acute inflammatory response and cause the tissue to return to normal. However, the inflammation process is considered a helpful, protective mechanism (Williamson, 1987).

Inflammatory responses occur in three distinct phases, each apparently mediated by different mechanisms: (1) an acute transient phase, characterized by local vasodilation and increased capillary permeability; (2) a delayed, subacute phase, most prominently characterized by infiltration of leukocytes and phagocyte; and (3) a chronic proliferative phase, in which tissue degeneration and fibrosis occur (Roberts and Morrow, 2001). There are two types of inflammation, acute and chronic which can be described as follows (Kumar *et al.*, 2005):

2.1.2.1 Acute Inflammation: the three major components involved here are: (1) alterations in vascular caliber that lead to an increase in blood flow; (2) structural changes in the microvasculature that permit plasma proteins and leukocytes to leave the circulation; and (3) emigration of the leukocytes from the microcirculation, their to accumulate in the focus injury and activation to eliminate the offending agents.

The redness (*rubor*), warmth (*calor*), and swelling (*tumor*) of acute inflammation are caused by the increased blood flow and edema. Toxic metabolites and proteases extracellularly released during the inflammation process also cause tissue damage. During the damage, one of the local symptoms is pain (*dolor*). The key events in acute inflammation are vascular and leukocyte changes.

A. Vascular changes: It is an important process and initial occurrence of acute inflammation that can be described into two following characteristics:

A1. Changes in vascular flow and caliber which are main responsible for a concentration of red cells in small vessels and increases viscosity of the blood (stasis).

A2. Increased vascular permeability which causes edema. This occurs in three distinct phases: immediate transient response lasting for 30 minutes or less; delayed response starting at about 2 hours and lasting for about 8 hours; and prolonged response which is most noticeable after direct endothelial injury.

B. Cellular event: leukocyte extravasation and phagocytosis

2.1.2.2 Chronic Inflammation: Chronic inflammation is the result of a balance between continuing tissue damage on the one hand, eradication of the damaging stimulus, following by healing and scar formation on the other. Chronic inflammation is characterized by the followings:

A. Infiltration with mononuclear cells including macrophages, lymphocytes, and plasma cells.

B. Tissue destruction induced by the persistent offending agent or by the inflammatory cells.

C. Attempts at healing by connective tissue replacement of the damaged tissue, accomplished by proliferation of small blood vessels (angiogenesis) and, in particular, fibrosis. Tissue destruction is one of the hallmarks of chronic inflammation.

The inflammation is differentiated as acute and chronic inflammation phase, which is different in the onset, duration and profound signs and symptoms characteristic as shown in Table 2.1.

Table 2.1 The comparison of acute and chronic inflammation (Kumar *et al*., 2005)

Factors	**Inflammation**	
	Acute	**Chronic**
Response	Immediate reaction of tissue to injury	Persisting reactions of tissue to injury
Onset	Rapid	Slow response
Immunity	Innate	Cell mediated
Predominant cell type	Neutrophil	Lymphocytes, plasma cells, macrophages
Duration	Hours-weeks	Weeks/months/years
Vascular response	Prominent	Less important

2.1.3 Anti-inflammatory Drugs and Its Mechanisms of Action: Anti-inflammatory drugs (NSAIDs) inhibit both cycloxygenase-1 (COX-1, constitutive) and cycloxygenase-2 (COX-2); induced in settings of inflammation activities, and

thereby synthesis of prostaglandins and thromboxane. COX-1 contributes to the physiological function of organs. Inhibition inevitably produces unwanted effects, such as mucosal injury, renal damage, hemodynamic changes, and disturbances of uterine function. COX-2 is induced by inflammatory processes and produces prostaglandins that sensitize nociceptors, evoke fever, and promote inflammation by causing vasodilatation and an increase in vascular permeability. However, in some organs, COX-2 is also expressed constitutively (kidney, vascular endothelium, uterus, and CNS) (Lullmann *et al*., 2005). The arachidonic acid pathway constitutes one of the main mechanisms for the production of pain and inflammation, as well as controlling homeostatic function (Figure 2.1). The pathway produces four classes of products which are as follows (Kadowitz *et al*., 2004):

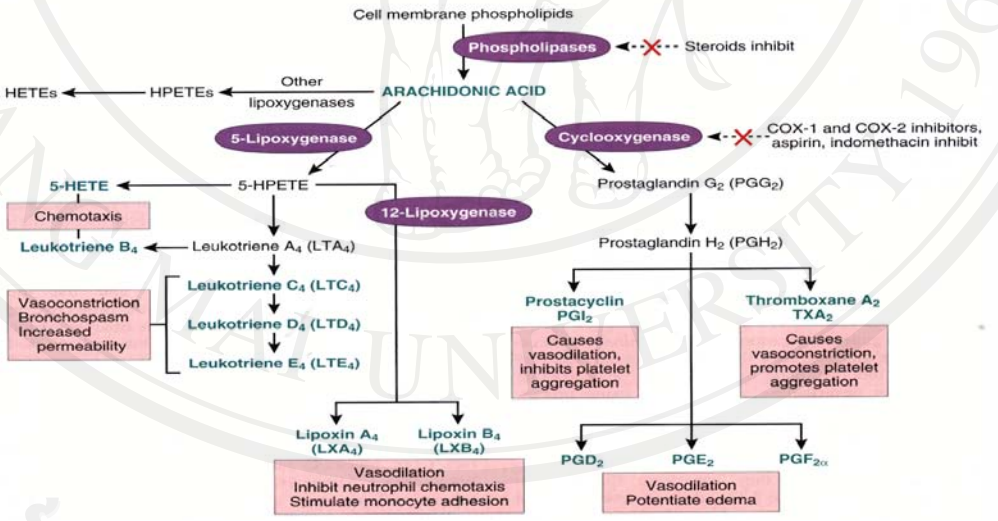

Figure 2.1 The arachidonic acid pathway-the actions (Kumar *et al*., 2005)

2.1.3.1 The prostaglandins modulate immune function via the lymphocyte. They are mediators of the vascular phases of inflammation and are potent vasodilators. They increase vascular permeability. Prostaglandins are involved in the regulation of physiological and pathophysiological process. Cycloxygenases are the

rate-limiting step of the formation of prostaglandins, after the substrate arachidonic acid is released from phospholipid cell membrane, prostaglandins such as PGE_2, PGF_2 alpha and PGD_2 are rapidly formed.

2.1.3.2 The prostacycline is a vasodilator which reduces platelet aggregation (PGI_2).

2.1.3.3 Thromboxane TxA_2 is a powerful vasoconstrictor which increases platelet aggregation.

2.1.3.4 The leukotrienes catalyze the addition of molecular oxygen to specific double bonds in polyunsaturated fatty acids. The most important lipoxygenases are the 5-1ipoxygenases. Products of the 5-lipoxygenase pathway are important mediators of inflammation. They cause vasoconstriction, but increase microvascular permeability. They are important mediators of bronchial asthma. They cause leukocyte adherence to the vascular endothelium and activate the leucocytes to secrete their enzymes. They contract smooth muscle, such as in the bronchi and blood vessels. Anti-inflammatory medication reduces the inflammatory process. There are three categories of anti-inflammatory medications which are analgesic (to relieve pain) antipyretic (to reduce fever) and anticoagulants (to inhibit blood clotting). Corticosteroids, such as prednisone are frequently used as anti-inflammation agent. This group of drugs can control inflammation by suppressing or preventing many of the components of the inflammatory process at the injured site (Kamienski and Keogh, 2006).

Many NSAIDs are considered to have equivalent efficacy and different side effects (Geis *et al*., 1991; Fries *et* al., 1991). The study in the guinea pig macrophage model of Engelhardt showed the ratio of the COX-2 to COX-1. This mechanism

assessed the balance of inhibition of the inducible COX-2. As a result, the ratios and side effects of the older conventional non-steroidal anti-inflammatory show that the lower the ratio, the lower the COX-1 inhibition, and the lower the overall side effect profile. Meloxicam had a ratio in the order of 0.33, diclofenac of 2.2 and piroxicam of 33 as shown in Table 2.2 (Engelhardt *et al.*, 1995).

Table 2.2 IC_{50} values and COX-2/COX-1 ratios of different NSAIDs in guinea pig peritoneal macrophage model (Engelhardt *et al.*, 1995)

NSAIDs	COX-2 IC_{50} mM	COX-1 IC_{50} mM	Ratio of COX-2/COX-1
Meloxicam	0.0019	0.0058	0.33
Diclofenac	0.0019	0.0009	2.20
Piroxicam	0.1750	0.0053	33.00
Tenoxicam	0.3220	0.2010	15.00
Indomethacin	0.0064	0.0002	30.00
Tenidap	47.8000	0.3930	122.00

However, the study of celecoxib, as a cycloxygenase 2 (COX-2) inhibitor type of analgesic and anti-inflammation, has demonstrated the equivalent analgesic efficacy, with a lower incidence of gastrointestinal mucosal injury than other NSAIDs, but minimal benefit for clinical outcomes such as gastric perforations, ulcers, or bleeds. The use of celecoxib for chronic musculoskeletal conditions demonstrated faster diffusion than for acute pain (Kozyrskyj *et al.*, 2007).

2.1.4 Medicinal plants with anti-inflammatory activities: There are several studies of traditional medicines that used plants both in recipes and single plant for their anti-inflammatory activity.

2.1.4.1 Researches of some medicinal plant recipes which have anti-inflammatory activity

A. The study of anti-inflammatory activity of Joint Care B, a polyherbal formulation has been evaluated in acute and chronic models of inflammation. Joint Care B contained *Alpinia galanga, Commiphora wightii, Boswellia serrata, Foeniculum vulgare, Glycyrrhiza glabra, Vitex negundo* and *Anethum graveolens*. The study used carrageenan induced rat paw edema and croton oil-induced granuloma pouch as a model for anti-inflammatory activity test. The results indicated that Joint Care B at a dose of 700 mg/kg b.w. significantly inhibited paw oedema at 1.5 hrs ($p<0.05$), 3 and 5 hrs ($p<0.01$) respectively. The study also showed no sign of side effect like non-steroidal drugs. For granuloma-induced by croton oil at a dose of 350 and 700 mg/kg, it significantly inhibited with $p<0.01$ and $p<0.001$ respectively (Venkataranganna, 2000).

B. The study of anti-inflammatory and analgesic activity in the polyherbal formulation, Maharasnadhi Quathar (MRQ), has aimed to determine the anti-inflammatory and analgesic potential of MRQ (*Alpinia calcarata, Ricinus communis, Kempteria galangal, Adhatoda vasica, Terminalia chebula, Cyperus rotundus, Tinospora cordifolia, Finiculum vulgare, Withania sominfera, Cassia fistula, Nigella sativa, Coriandrum sativum, Solanum xanthocarpum*). The MRQ is used in traditional medicine for a variety of purposes. The study has used animal and human rheumatoid arthritis patient as study population. The results showed that

MRQ can significantly and dose-dependently inhibit carrageenan-induced rat paw oedema. MRQ also exerted a dose-dependent in the following manners: (a) protective effect on heat-induced erythrocyte, and (b) inhibition of 5-lipoxygenase activity. In rheumatoid arthritis patients, after 3 months of MRQ treatment, there was a marked improvement in the pain and inflammation experienced by the patients as well as in the mobility of the affected joints (Thabrew *et al*., 2002).

C. Anti-inflammatory activity of *Quercus infectoria*, *Glycyrrhiza uralensis*, *Kaempferia galangal and Coptis chinensis*, the main components of Thai herbal remedies for aphthous ulcer has been investigated *in vitro* and *in vivo* anti-inflammatory activity. It was found that a traditional herbal recipe had significantly higher anti-inflammatory activity than each of the isolated plants by inhibiting the IL-6 and PGE_2 production with the IC_{50} value of 0.04±0.01 and 0.08±0.01 μg/ml, respectively. Moreover, the anti-inflammatory effect is significantly higher than prednisolone and the COX-2 inhibitor (Aroonrerk and Kamkaen, 2009).

D. The study on anti-inflammatory activity of Chinese medicinal vine plants has aimed to evaluate the activity against a panel of key enzymes relating to inflammation. The vine plants were extracted from the stem of *Spatholobus suberectus* Dunn, the stem of *Trachelospermum jasminoides* Lem., the root from *Tripterygium wilfordii* Hook. f., the stem of *Sinomenium acutum* Rehder and Wilson, the stem of *Piper kadsura* (Choisy) Ohwi, the stem of *Polygonum multiflorum* Thunb., the root and stem from *Tinospora sagittata* Gagnep., the root of *Tinospora sinensis* (Lour.) Merrill, and the stem of *Clematis chinensis* Osbeck. The results have shown the inhibitory activities against at least one of the enzymes in various percentages depending on the concentrations. The most potent COX-1, COX-2 and 5-

LOX inhibition was observed in the extract of *T. wilfordii* with the IC_{50} values of 27, 125 and 22 ìg/ml, respectively. The traditional Chinese medicine has used this recipe for the treatment of inflammatory conditions (Li *et al*., 2003).

E. The study of anti-inflammatory activity of two Ayurvedic formulations containing Guggul which was consisted of Chandraprabha Vati (CPY) and Mahayogarafa Guggulu (MYG). The study has aimed to evaluate these two formulations by using rat hind paw edema method. Ibuprofen was used as a standard compound. The plants contained in the formulations including 37 and 32 kinds of the CPY and MYG respectively. The formulations showed dose dependent anti-inflammatory activity with the maximum edema inhibition of 45% (CPY) and 49% (MYG) in rat paw edema at a dose of 500 mg/kg. The samples showed significant better activity as compared to the commercial sample ($p<0.05$) (Bagul *et al*., 2005).

F. The study on the effect of formulation on the experimental model of inflammatory bowel disease has aimed to evaluate the anti-inflammatory activity. This formulation contained four kinds of plants including: *Aegle marmelos, Coriandrum sativum., Cyperus rotundus. and Vetiveria zinzanioids.* The two different experimental animal models of inflammatory bowel disease have used acetic acid to induce colitis in mice and indomethacin to induce enterocolitis in rats. Prednisolone was used as the standard drug. The formulation showed significant inhibitory activity against inflammatory bowel disease when compared to the standard drug (Jagtap *et al*., 2004).

G. The screening of Indian plants for biological activity of the extract of *Azadirachta indica*, the fresh stem bark which was applied externally at the dose of 1.0% was active versus croton oil-induced inflammation of the rat ear. The extract,

when administered intragastrically to rats at the dose of 1.0 gm/kg, was active versus carrageenan-induced pedal edema (Dhawan *et al*., 1980).

H. The study on the pharmacological effects of *Azadirachta indica* leaves has used ethanol (95%) extract of the dried leaf of *Azadirachta indica* administered intragastrically to rats at the dose of 1.0 gm/kg showed potent anti-inflammtory activity versus carrageenan-induced pedal edema (Tandan *et al*., 1990).

I. The anti-inflammatory activity of *Azadirachta indica* study has used ethanol (70%) extract of the fresh bark and leaf administered by gastric intubation to rats with the dose of 400 mg/kg showed potent anti-inflammatory activity versus carrageenan-induced pedal edema (Okpanyi and Ezeukwu, 1981).

2.1.4.2 The chemical compound with anti-inflammatory effect of the single plant. The medicinal effects of certain plants have been well recognized as follows:

A. *Aegle marmelos* (L.) Corrêa ex Roxb. (Bael fruit): Bael is used in traditional medicines for anti-inflammatory activity, antiasthmatic, antiulcerous and ophthalmic. The leave contains alkaloid, anthraquinone and triterpenes (lupeole). The pharmalogical study of the leaves showed the anti-inflammatory activity (Veerappan *et al.*, 2005). The chemical structure of lupeole was shown in Figure 2.2.

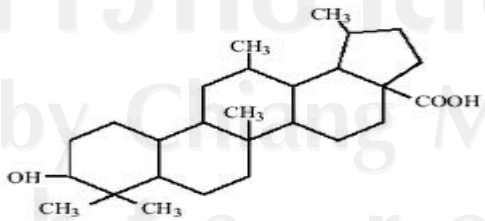

Figure 2.2 Chemical structure of lupeole

B. *Curcuma longa* (Turmeric): This Indian spice comes from the roots of *Curcuma longa* and contains diferuloyl methane (curcumin), demethoxycurcumin, and bisdemethoxycurcumin, all of which are known as curcuminoids. Curcumin (the lipid-soluble component in turmeric) has been shown to exert an anti-inflammatory activity in several clinical studies, due in part to the inhibition of COX-2 enzyme and iNOS. Curcumin has also been shown to have an effect on the release of inflammatory mediators e.g. (eicosanoids), which may further explain its role as an anti-inflammatory agent. However, the water-soluble portion of turmeric that contains turmerin does not have an anti-inflammatory effect, although it has been shown to have antidepressant effects that may be due to inhibition of monoamine oxidase in the brain. According to Commission E in Germany (the German authority on evaluating herbal preparations), the recommended dose is 1.5 to 3 g of cut root daily; preparations of *Curcuma longa* are infusion powders, tinctures (1:5), and fluid extracts. Moreover the use of curcumin is indicated in bile duct obstruction because it enhances the secretion of bile (Achi., 2003). The chemical structure of curcumin as shown in Figure 2.3.

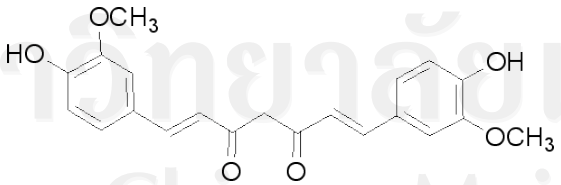

Figure 2.3 Chemical structure of curcumin

C. *Zingiber officinale* Roscoe. (Ginger): Ginger is commonly used as food and medicines in the traditional medicines. The main ingredients in ginger that have an analgesic and anti-inflammatory effects, is (6)-gingerol, which is the pungent constituent of ginger. Intraperitoneal administration of (6)-gingerol (25mg/kg-50mg/kg) produced an inhibition of acetic acid-induced writhing response and formalin-induced licking time in the late phase. The (6)-gingerol (25mg/kg-50mg/kg) also produced an inhibition of paw edema induced by carrageenin. These results suggested that (6)-gingerol possessed analgesic and anti-inflammatory (Young et al., 2004). The chemical structure of **(**6)-gingerol was shown in Figure 2.4.

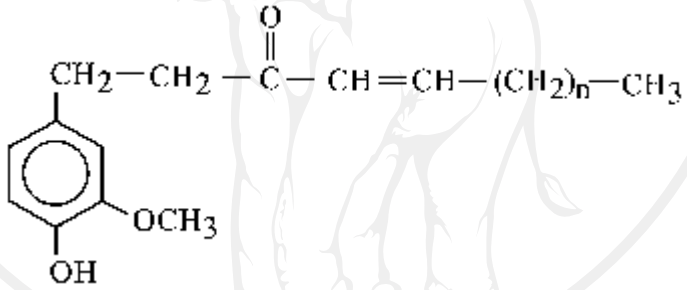

Figure 2.4 Chemical structure of **(**6)-gingerol

D. *Glycyrrhiza glabra* (Licorice): The roots of *Glycyrrhiza glabra* contain glycyrrhizin, a compound with anti-inflammatory activity. The aglycone, β-glycyrrhetinic acid, may cause this action of glycyrrhizin. Glycyrrhizic acid, another major constituent in licorice, also has anti-inflammatory activity. Glycyrrhizin, in addition to having anti-inflammatory actions, may also act as a chemoprotective agent against tumors. The dose of licorice is 5 to 15 g daily of cut or powdered roots that should contain 200 to 600 mg of glycyrrhizin. Licorice use is contraindicated in patients with high blood pressure, cardiac diseases, or liver cirrhosis (Achi., 2003). The chemical structure of glycyrrhizin was shown in Figure 2.5.

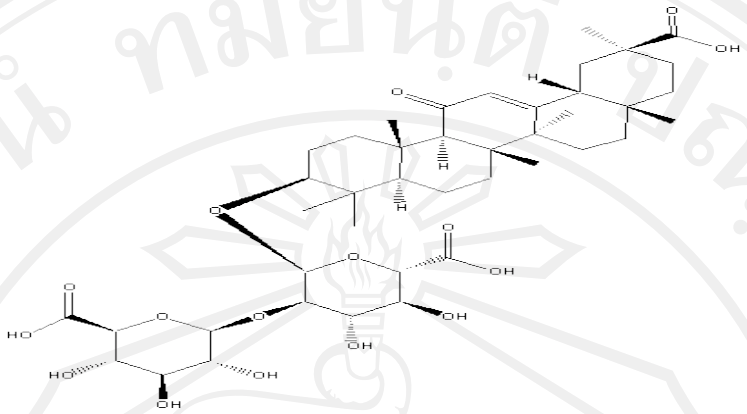

Figure 2.5 Chemical structure of glycyrrhizin

E. *Salix alba* (White Willow): The role of salicylates in inflammation and pain management is well documented in medicine. The bark of this plant contains salicin. Following oral administration of salicin, it was found in serum mainly in the form of salicylic acid. After an oral dose (240 mg) was given to healthy volunteers, the Tmax was less than two hours and Cmax was 1.2 mg/L, respectively. Salicylic acid is eliminated in urine as salicyluric acid. A daily dose equivalent to 60 to 120 mg of salicin is recommended by the German Commission. Willow can trigger an allergic response in individuals sensitive to willow or to aspirin (Achi., 2003). The chemical structure of salicin was shown in Figure 2.6.

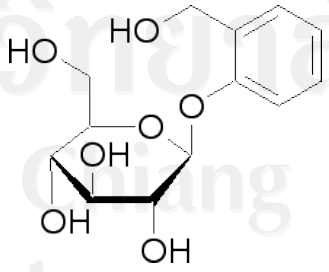

Figure 2.6 Chemical structure of salicin

Furthermore, the other plants in the family Meliaceae, such as *Aglaia odorata* Lour (Hayashi *et al*., 1982) are used for inflammation, cough and traumatic injury. Chinese traditional medicine has used *Lagenaria siceraria* (Mol.) Standl for the treatment of aching teeth and gums, boils and vermifuge (Duke and Ayensu, 1985). The anti-inflammatory compounds in plants which are shown in Table 2.3 (Harborne *et al.*, 1999):

Table 2.3 The chemical compounds with anti-inflammatory activity in plants (Harborne *et al.*, 1999)

Group of compounds	**Chemical compound**	**Botanical name**
Phenolics		
minor flavonoids	Kolaflavonone	*Garcinia kola.* (Clusiaceae)
flavones and flavonols	Baicalein	*Scutellaria galericulata*. (Lamiaceae)
	Chrysin	*Populus spp.* (Salicaceae), *Pinus spp.* (Pinaceae), *Escallonia spp.* (Saxifragaceae)
	Gossypin	*Gossypium indicum., Hibiscus*
	Luteolin	*Antirrhinum majus.* (Scrophulariaceae)
	Myricitrin	*Myrica rubra.* (Myricaceae)
	Santin	*Tanacetum parthenium* (Compositae)

Table 2.3 The chemical compounds with anti-inflammatory activity in plants (Harborne *et al.*, 1999)

Group of compounds	**Chemical compound**	**Botanical name**
Isoflavonoids and Neoflavonoids	Magnoshinin	*Magnolia salicifolia.* (Magnoliaceae)
Phenols and Phenolic	Gallic acid	*Allanblackia floribunda and*
Acids		*Garcinia densivenia.* (Clusiaceae)
	Protocatechuic acid	*Erica australis.* (Ericaceae), *Rosa canina.* (Rosaceae), *Picea koraiensis.* (Pinaceae)
Phenylpropanoids	Caffeic acid	*Coffea arabica*., *Cinchona cuprea*. (Rubiaceae)
	Curcumin	*Curcuma longa*., *Curcuma aromatic*., *Curcuma xanthorrhiza.* (Zingieraceae)
	(6)-Shogaol	*Zingiber officinale*
	Sinapine	*Lepidium sativum*., *Draba nemorosa.* (Brassicaceae)
Xanthones	6-Deoxyjacareubin	*Calophyllum zeylanicum.*, *Kielmeyera speciosa*. (Clusiaceae)
	Euxanthone	*Calophyllum, Bonnettia, Garcinia*

Table 2.3 The chemical compounds with anti-inflammatory activity in plants (Harborne *et al*., 1999) (continued)

Group of compounds	**Chemical compound**	**Botanical name**
		and Haploclathra spp. (Clusiaceae)
	Mangostin	*Garcinia mangostana.* (Clusiaceae)
Alkaloids		
Isoquinoline	Fetidine	*Thalictrum foetidum.* (Ranunculaceae)
	Fumaricine	*Fumaria offucinalis*. (Fumariaceae)
	Hernandezine	*Stephania hernandiifolia*. (Menispermaceae), *Thalictrum simplex*. (Ranunculaceae)
	Sanguinarine	*Papaver somniferum*, *Dicentra spectabillis*. (Papaveraceae)
Monoterpenoid and Alkaloids	Gentianine	*Gentiana kiriowi*. (Gentianaceae)
Steroidal Alkaloids	Cyclobuxine D	*Buxus sempervirens*. (Buxaceae)
	Imperialine	*Petilium eduardii*., *Thinopetalum bucharicum*. (Liliaceae)

2.1.5 Preparation of plants extract and phytochemical test

Phytochemistry is conducted with an aim to analyse the chemicals from various parts of plants or trees such as leaves, flowers, seeds, barks, roots and shrubs. The extraction is a process thereby the desired constituents of a plant are removed by using a solvent. The plant extraction is screened for the presence of constituents such as alkaloids, glycosides, flavonoids, anthraquinone and tannins. There are many methods for the preparations of plant extracts, namely, infusion, decoction, maceration, hot extraction and percolation (Heinrich *et al*., 2004). For the fresh plants, dried and powdered plant materials, infusion or decoction is normally used. Decoction is usually the method of choice when working with tougher and more fibrous plants, barks and roots. The plant material is boiled for a longer period of time to soften the harder woody materials and release its active constituents (Taylor, 2004).

Phytochemical screening is performed to detect various phytoconstituents in the plants. Different kind of chemical tests can be performed for establishing profile of a given extract for its chemical composition. Alkaloids, flavonoids, saponins, tannins, anthraquinone and terpenoids are also examined. A preliminary phytochemical screening of all extracts is carried out by using the standard method of Trease and Evans (1989).

2.1.6 Plants under study and the evidences of pharmacological activities in relation to anti-inflammatory activities and others

The Lanna medicinal plant recipes used plants for many purposes such as health promotion and prevention and cure. The plants are used both as single plant or in recipes. The plants those found in many Lanna recipes of anti-inflammatory activities composed of several active chemical constituents for the treatment. All of the plants in the study were confirmed with the forest herbarium (The Forest Herbarium, 2001). The detailed description and different usages in Lanna traditional medicine were as follows:

1) *Aegle marmelos* (L.) Corrêa ex Roxb. Rutaceae (Figure 2.7)

Local name: Bael Fruit Tree (Thai name - Ma toom)

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailand.

Description: A medium to large sized deciduous, glabrous and armed tree with axillary and 2.5 cm long spines. Leaves are alternate, 3-5 foliate, leaflets with ovate to lanceolate, crenate, acuminate, membranous and petiole. Flower presents in short axillary panicles, large and scented, calyx, pubescent and four lobed, 4 petals, white and gland dotted, stamens-many, ovary, ovoid, cells 10-20, ovules-many. Fruit is globose, grey or yellowish, rind woody, seeds many, oblong, compressed, embedded in reddish yellow coloured sweet pulp (Chauhan, 1999).

Uses in traditional medicine: Root, bark, leaves and fruits are hypoglycaemic, astringent and febrifuge. Root, stem and bark are antidiarrhoeal and antivenin. Leaf is antiinflammatory, expectorant, anticatarrhal, antiasthamatic, antiulcerous and ophthalmic. Flower is emetic. Unripe fruit is stomachic and demulcent. Ripe fruit is antigonorrhoeal, cardiotonic, restorative, laxative, antitubercular, antidysenteric and antiscorbutic. Seed is anthelmintic and antimicrobial (Warrier *et al*., 1993).

Chemical constituents: Bark - alkaloid, Fruit - tannin, astringents, Leaf - aromatic substances, alkaloid, anthraquinone and triterpenes (lupeol) (Burkill, 1985; Williamson, 2002). Pharmalogical activity of the leaves gave the anti-inflammatory activity (Veerappan *et al.*, 2005).

Figure 2.7 *Aegle marmelos* (L.) Correa ex Roxb. (Sinchai, 2006)

2) *Anethum graveolens* L. Apiaceae (Figure 2.8)

Local name: Dill (Thai name - Tien Ta Tukkatan)

Collecting location: Obtained from local market in dried seeds.

Description: It is a vascular plant without significant woody tissue above or at the ground. Forbs and herbs may be annual, biennial, or perennial but always lack significant thickening by secondary woody growth and have perennating buds borne at or below the ground surface (Applequist, 2006). The glabrous aromatic herb has a 10-15 cm long fusiform taproot. The main stem is glaucous cylindrical, dichotomously branched with five to eight branches bearing decompounds trippinnate leaves. The fluorescence is a compound umbel, the terminal on the main axis has a 20 cm long peduncle, leaving 28-40 umbellules. The terminal umbels possess 30-40 flowers. The fruits are separated into two mericarps, each ovoid, compressed, singed,

about 2-3 mm wide with three longitudinal ridges on each side and four dorsal vittae (Bajai, 1995).

Uses in traditional medicine: In Thailand, it is used for flatulence, digestion, carminative (Wutthithummavej, 1998).

Chemical constituents: The two flavonoids have been isolated from Dill seed, quercetin 3-O-beta-D-glucuronide and isoharmentin 3-Obeta-D-glucuronide, have antioxidant activity and antigastic irritation activity (Hosseinzadeh *et al*., 2002). The methanol extract of Dill fruit has found monoterpenoid, six new monoterpenoid glycosides a new aromatic compound glucoside and a new alkyl glucoside (Ishikawa *et al.*, 2002). The fruits of dill contain kaempferol 3-glucuronide (Teuber *et al*., 1978), isorhamnetin 3-sulfate and quercetin 3-sulfate (Fukuoka *et al.*, 1980).

Figure 2.8 *Anethum graveolens* L. (Sinchai, 2006)

3) *Azadirachta indica* A. Juss. var. siamensis Valeton. Meliaceae (Figure 2.9)

Local name: Neem Tree (Thai name - Sa-dao)

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailand.

Description: Tree is 16 m high, crown globose, densely deciduous; bark, red-brown or grey, longitudinal fissured or scaly cracking gum yellow. Leaves are compound, paripinnate alternate, leaflets, opposite, blade lanceolate ovate, apex acuminate, base

oblique, margin serrate, both of surfaces shiny, dark green. Flower is white, inflorescences, 30 cm long, lax, axillary, terminal, scented. Fruit is subglobose 1-2 mm long. Seed 1-3. Growing in any soil, moderate moisture, propagation by seed (Chayamarit and Phupattanapong, 1992).

Uses in traditional medicine: In Thailand, extract of the dried flower is taken orally as a bitter tonic, hot water extract of the dried fruit is taken orally as an anthelmintic, laxative, bitter tonic and for ferve, in case of dried unripe fruit,it is taken orally as a bitter tonic and for fever, then its dried gum is used as abitter tonic. Indo-China, the hot water extract of the bark, leaf is taken orally for malaria. (Ross, 2001).

Chemical constituents: Nimbinin, azadirachtin, quercitin, β-sitosterol, palmitic acid, oleic acid, kaempferol, catechin, coumarin (Bunyapraphatsara and Chokchaicharoenporn, 1998); dried leaves contains flavanoid quercetin, nimbosterol (β-sitosterol), kaempferol and myricetin, seed and oil contains desacetylnimbin, azadirachtin; trunk bark contains nimbin, nimbinin, nimbidin, nimbostero, essential oil and tannins (Thakur *et al*., 1989).

Figure 2.9 *Azadirachta indica* A. Juss.var. siamensis Valeton (Sinchai, 2006)

4) *Baliospermum solanifolium* (Burm) Suresh. Euphorbiaceae (Figure 2.10)

Local name: Plao-Tong Tak

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailand.

Description: Shrub is up to 2 m high; leaves, petiole 2-13 cm long, blade usually ovate to oblong, chartaceous, base usually rounded, rarely cuneate, margin serrate or crenate, apex obtuse or acute, glabrous or strigose on both surfaces; inflorescences, glabrous to pubescent; staminate flowers sepals orbicular to ovate; pistillate flowers, pedicels 0.2-1 cm long; sepals 5, ovate or triangular, pubescent outside; ovary subglobose, pubescent; fruits, pendulous, subglobose, calyx persistent; seeds ovoid, brown (Chayamarit and Welzen, 2005).

Uses in traditional medicine: The root is used for purgative, aneamia and spleen abscess (Wuthithummavej, 1998).

Chemical constituents: no evidence

Figure 2.10 *Baliospermum solanifolium* (Burm) Suresh. (Sinchai, 2006)

5) *Caesalpinia digyna* Rottle. Leguminosae - Caesalpinioideae (Figure 2.11)

Local name: Teripod Plant **(**Thai name - Nham-Jai)

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailand.

Description: A prickly climber or scandent shrub, 2-5 m tall. Pinnae in 8-13 pairs, leaflets in 6-12 pairs, oblong-elliptic, 5-13 mm x 2.5-5 mm, subsessile. Flowers in long racemes, fairly large, with petals 8-10 mm long, yellow. Pods oblong-elliptic, 3-6 cm x 1.5-2 cm, constricted between the seeds (1-)2-3(-4)-seeded (Rezia-khatun and Rahman, 2006).

Uses in traditional medicine: It is used for insect sting/bite, snake bite, astringent (Manosroi and Manosroi, 1984).

Chemical constituents: The roots contain bergenin, which has the antioxidant, anti-inflammatory and antiulcer activity (Rastogi and Rawat, 2008). Tannins show in the bark and the seed (Sharma, 1993).

Figure 2.11 *Caesalpinia digyna* Rottle. (Sinchai, 2006)

6) *Caryota bacsonensis* Magalon. Arecaceae (Figure 2.12)

Local name: Jaggery Palm (Thai name - Toa Rang)

Collecting location: The scrub, Mae Tang District, Chiang Mai Province, Thailand.

Description: Tree is straight around 3 m tall, slender trunk and a typical tall crown with relatively short, tillers then big sucker; compound leaves, bipinnate, pinn flabellate, emarginated terminal, incised and inorder, leaf base oblique cuneiform. flower, large inflorescence at the side of trunk, white small spikelets; fruit, round shape, red turning brown when ripe (Bunyapraphatsara and Chokchaicharoenporn, 1998).

Uses in traditional medicine: Lanna identified its use in treatment of edma and cancer (Manosroi *et al.*, 2005). Thai traditional medicine uses the root and the corm part to cure abscess of the liver, lung, and heart (Bunyapraphatsara and Chokchaicharoenporn, 1998).

Chemical constituents: The fruit contains luaric acid, myristic acid, palmitic acid oleic acid and lindeic acid (Bunyapraphatsara and Chokchaicharoenporn, 1998; Rabarisoa *et al*., 1993).

Figure 2.12 *Caryota bacsonensis* Magalon. (Sinchai, 2005)

7) *Cassia alata* L. Leguminosae-Caesalpinioideae (Figure 2.13)

Local name: Ring Worm Cassia (Thai name - Chum-Het-Ted)

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailand.

Description: It is erected shrubby, legume with dark green compound leaves on stout branches. Leaves are orange rachis, 16-28 leaflets each leaf, axis, golden yellow flowers, produces 4-winged pods containing 50-60 flattened, triangular seeds. Flowers are enclosed by yellow-orange bracts that are later shed (Bunyapraphatsara and Chokchaicharoenporn, 1998).

Uses in traditional medicine: Different parts of plants are used: the leaves for the treatment of ringworm, diuretics and laxative, the tree for an anthelmintic for earthworm (Pongbunrod, 1984, In: Nantachit, 2009).

Chemical constituents: Bark contains a group of alkaloids such as sennosides anthraquinoids, aloe-emodin, chrysophanol, chrysophanic acid, rhein (cassic acid) and adenine, moreover the flavonoids like kaempferol 3-O-gentiobi was found as well. In order to the pharmacological activity, the compounds from the bark part posses the activities of antifungal, analgesic, antiinflammatory and hypoglycaemic (Mazumder *et al.*, 2008); and antioxidant (Phansawan and Poungbanpho, 2007). Furthermore, an alcoholic extract of the leaves was found the kaempferol 3-O-sophoroside for anti-inflammatory action (Palanichamy and Nagarajan, 1990).

Figure 2.13 *Cassia alata* L.Roxb. (Sinchai, 2006)

8) *Cassia occidentalis* L. Leguminosae-Caesalpinioideae (Figure 2.14)

Local name: Coffee Senna (Thai name - Khe-Lek-Phuage)

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailand.

Description: The shrub is erect; branched, smooth, half woody herb or shrubby plant, 0.8 to 1.5 m height; the leaves, pinnate and about 20 cm long, rachis, a large gland at the base; leaflets, rank-smelling, occur in 5 pairs, oblong-lanceolate, pointed at the base, and taper gradually to a fine pointed tip. Flowers are yellow and 2 cm long, and borne on axillary and terminal racemes; pods, 10 cm long, 9 mm wide and thickened, and contain about 40 seed**.** (Bunyapraphatsara and Chokchaicharoenporn, 1998).

Uses in traditional medicine: The leaves are for headache, yellow fever, and conjunctivitis; the root for treatment of the anti-inflammatory activity and antimalarial hepatoprotective; arial part for purgative and laxative (Mazumder *et al.*, 2008).

Chemical constituents: The main compounds were from the leaves which gave, anthraquinones, A bianthraquinone, flavonoid glycosides matteucinol 7-rhamnoside chysophanol and emodin; roots which gave chrysophanol, emodin, pinselin, questin, germichrysone, methylgermitorosone singueanol-I pinselin and 1,7-dihydroxy-3-methylxanthone, 1,8-dihydroxyanthraquinone, 2 new bis (tetrahydro) anthracene derivativeoccidentalol-1 and occidentalol-II were isolated from the roots C-glycosidic flavonoids, cassiaoccidentalins A, B and C anthraquinones. These compounds from the roots part gave the anti-inflammatory activity (Mazumder *et al.*, 2008).

Figure 2.14 *Cassia occidentalis* L. (Sinchai, 2006)

9) *Coccinia grandis* L. Voigt. Cucurbitaceae (Figure 2.15)

Local name: Ivy Gourd (Thai name - Tum leung)

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailand.

Description: It is perennial herbaceous vine, stems mostly glabrous, produced annually from a tuberous rootstock, tendrils simple, axillary; leaves, alternate, simple, blade broadly ovate, acute and mucronate at the apex, cordate with a broad sinus at the base, surfaces glabrous or scaly, margins denticulate; Inflorescence, solitary; axillary flowers, calyx, recurved lobes 2-5mm long on the hypanthium, peduncle 1-5cm long, corolla campanulate; fruit, smooth, bright red, ovoid to ellipsoid berry 2.5-6 cm long (Phupattanapong and Wongprasert, 1987).

Uses in traditional medicine: The roots for antifever, antivomitting, wound healing, the stem for anti-inflammatory activity; the leaves for anti-itching, reduce sputum; the flowers for antiiching (Phupattanapong and Wongprasert, 1987). Indigenous people in India use various parts of the plant to get relief from asthma and cough (Varier and

Sala, 1994). Some healer in India uses this plant for hepatoprotective acitivity (Mukherjee, 2009; Sunilson *et al.*, 2009).

Chemical constituents: The leaves of the plant possess antidiabeitc, anti-inflammatory, antipyretic, analgesic, antispasmodic, antimicrobial, anthelmintic, cathartic and expectorant activities (Asolkar *et al*., 1992; Nadkami and Nadkami, 1992). Its leaves contain triterpenoids, alkaloids and tannins (Rastogi and Mehrotra, 1990). Further report found the compounds which were pectin, cucurbitacin B, cytosine, 5-methyl, daucosterol β-sitosterol, taraxerone (Bonyapraphatsara and Chokechaicharoenporn, 1999). The fruits contain thiamine, riboflavin, niacin, ascorbic acid (Rubatzky and Yamaguchi, 1997).

Figure 2.15 *Coccinia grandis* L. Voigt. (Sinchai, 2006)

10) *Croton longissimus* Airy shaw. Euphorbiaceae (Figure 2.16)

Local name: Plao-Noi

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailand.

Description: The shrub is unknown size, shoot apex distinctly pubescent but very soon glabrescent; flowering with mature leaves; leaves, alternate, epetiole 0.7-1.5 cm long, with distinct but not dense hairs, blade narrowly elliptic to obovate, chartaceous,

base acute to obtuse, margin serrate, apex acute to subacuminate, slightly brighter below, glabrous above, subglabrous to slightly pubescent below; basal glands sessile, veinlets visible; inflorescences, greenish, solitary or surrounded by several buds; pistillate flowers, densely pubescent; fruits 6 by 5.5 mm, sulcate, surface sparsely pubescent, smooth and seeds no caruncle seen (Chayamarit and Welzen, 2005).

Uses in traditional medicine: The roots are for skin disease, anti-cancer; the barks for digestion, anti-diarrhea; sap wood for contraceptive, digestion, heart wood for release blood and pus; the leaves for anti-diarrhea; the flowers for anthelmintic; the fruits for postpartum, well blood circulation (Bunyapraphatsara and Chokechaicha-roenporn, 1998).

Chemical constituents: no evidence

Figure 2.16 *Croton longissimus* Airy shaw. (Sinchai, 2006)

11) *Croton Oblongifolius* Roxb. Euphorbiaceae (Figure 2.17)

Local name: Plao-Yai

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailand.

Description: Small perennial tree. The young leaves are brown. The leaves are simple, alternate, oblong, obovate-elliptic oblong or lanceolate. The inflorescences

appear at terminal twig with greenish yellow petals. The fruits are round, the dry has 3 lobe, breakable (Chayamarit and Welzen, 2005).

Uses in traditional medicine: The leaves are for tonic, the flowers against flat worms, the fruits for dysmenorrhoea, the seeds as purgative (Sommit *et al.*, 2003), the bark used to treat dyspepsia and the roots used to treat dysentery (Ngamrojnavanich *et al.*, 2003). The bark is also used to treat chronic enlargement of the liver and remittent fever. It is applied externally to the hepatic region in chronic hepatitis (Ahmed *et al*., 2002).

Chemical constituents: Compounds from the stem bark have shown cytotoxcity against human tumour cell-line, the diterpenoids (Roengsumran *et al*., 1999), the cembranoid diterpenes crotocembranoic acid and neocrotocembranal (Roengsumran *et al*., 1999), the labdane nidorellol, the furoclerodane croblongifolin and the clerodane crovatin (Roengsumran *et al.*, 2002), the halimanes crotohalimaneic acid, crotohalimoneic acid and 12-benzoyloxycrotohalimaneic acid (Roengsumran, 2004).

Figure 2.17 *Croton oblongifolius* Roxb. (Sinchai, 2006)

12) *Croton tiglium* L. Euphorbiaceae (Figure 2.18)

Local name: Rushfoil (Thai name-Hat Sakhuen)

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailand.

Description: Shrub or very small tree is erect; leaves, alternate, usually rounded at the base, pointed at the tip and toothed at the margins; flowers, very small and borne on terminal inflorescence; fruits, capsules, ellipsoid, or obscurely 3-angled, and contains a single seed; seed, ovoid or oblong, the testa dark-brown or blackish, thin and brittle and of faint odor (Chayamarit and Welzen, 2005).

Uses in traditional medicine: Used in Chinese medicine, seed and oil is purgative, rubefacient and anti-dote for snakebite. The seeds and oil are acrid, bitter, thermogenic, emollient, drastic purgative, digestive, carminative, anthelmintic, antiinflammatory, vermifuge, deterent, diaphoretic, expectorant, vesicant, irritant and rubefacient (Duke and Ayensu, 1985). In India uses for the anti-inflammatory activity, digestive and carminative (Joy *et al.*, 1998).

Chemical constituents: Properties and activity oil contains phorbol myristate acetate (Husain *et al*, 1992). Seeds contain 20% protein and 30-50% lipids. Iso-guanine-D-ribose (crotoniside) and saccharose were isolated from the seeds. The per hydrogenated parent hydrocarbon of phorbol is a perhydrocyclopropabenzulene called tigliane and phorbol is 1, 1aa, 1bb, 4, 4a, 7aa, 7b, 8, 9, 9a-decahydro-4ab, 7a, 9b, 9aa-tetrahydroxy-3-(hydroxymethyl)-1, 1, 6, 8a tetramethyl-5-H-cyclopropa [3,4] benz [1.2-e]azulen-5- one. Phorbol, a tetracylic diterpene with a 5, 7, 6 and 3- membered ring has 6 oxygen functions. Twentyfive phorbol-12, 13-diesters have been detected (Hecker *et al*., 1974). A toxin croton 1, mol.Wt 72,000 has been isolated from the seeds (Lin *et al*., 1978). The seed is a source of phorbol derivatives containing tigliane phorbol esters which have the main irritant component, 12-*O*-

tetradecanoylphorbol-13-acetate, as a tumor promoter used in experimental mice cancer research (Salatino *et al.*, 2007).

Figure 2.18 *Croton tiglium* L. (Sinchai, 2006)

13) *Cyperus rotundus* L. Cyperaceae (Fig. 2.19)

Local name: Nut Grass (Thai name - Ya haew mhu)

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailand.

Description: Pestiferous perennial weed is dark green glabrous culms, arising from a system of underground tubers, erect, triangular with rounded angle; leaves, radical, sheathing, shorter than the culms; roots, rhizome, tuberous, sweet smelling, rounded black and hard like a knot (Bunyapraphatsara and Chokchaicharoenporn, 1998).

Uses in traditional medicine: In Chinese medicine, it is used for liver disease, amenorrhoea, sedative (Heinrich *et al*., 2004); root, tubers are analgesic for anti spasmodic, antiutssive, astringent, carminative, stomachic, (Duke and Ayensu,1985); rhizomes uses for treatment of stomach and bowel disorder and inflammatory disease (Seo *et al*., 2001); antibacterial (Sripanidkulchai *et al*., 2002). In Ayuravedic uses for diarrhea, heart tonic and skin disease (Samy *et al*., 2008).

Chemical constituents: Sesquiterpene alkaloids from the rhizomes: rotundines A-C (Jeong *et al*., 2000) are found. Also contained are triterpenes, oleanolic acid (Ha *et al*., 2002); steroid glycoside, sitosteryl-β-D-galactopyranoside, furochromones, khellin, visnagin, ammiol, coumarin, salicylic acid, caffeic acid, protocatechuic acid, *p*-coumaric acid, tricin and isorhamnetin (Sayed *et al*., 2007). In case of pharmacological action, it used for wound healing in the form of ointment (Puratchikody *et al.*, 2006).

Figure 2.19 *Cyperus rotundus* L. (Sinchai, 2006)

14) *Datura metel* L.var.fastuosa (Bernh.) Danert. Solanaceae (Figure 2.20)

Local name: Thorn Apple (Thai name - Makoea Ba Dokdum)

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailand.

Description: It is an erect succulent branched undershrub divaricate often purplish branches and ovate pubescent leaves which are oblique at the base of lamina. Flowers are large, solitary, short pedicelled, purplish outside and white inside. Fruits are sub-globose capsules covered all over with numerous, fleshy prickles, irregularly breaking when mature. Seeds are numerous, smooth, yellowish brown (Joy *et al.*, 1998).

Uses in traditional medicine: Indiginous use as hallucination (Heinrich *et al*., 2004),

Chemical constituents: The alkaloids hyoscyamine and hyoscine (scopolamine) and meteloidine are found in all parts of the plant (Joy *et al*., 1998). There is scopolamine (hyoscine) (Heinrich *et al*., 2004). In addition, the ethyl alcohol extract of the flowers were found the new compounds, yangjinhualine A and five known megastigmane sesquiterpenes which gave pharmacological effects of the flowers with strong anti-inflammatory of skin and anaphylaxis actions (Kuang *et al*., 2008).

Figure 2.20 *Datura metel* Linn. var. fastuosa (Bernh.) Danert (Sinchai, 2006)

15) *Dioecrescis erythroclada* (Kurz.) Tirveng. Rubiacieae (Figure 2.21)

Local name: Tirveng (Thai name - Makang-Dang)

Collecting location: Obtained from a local herb market.

Description: It usually grows in the deciduous dipterocarp forest. In this monotypic tree genus paired, straight thorns are normally found on most lateral branches of young individuals. On older trees, thorns are typically seen on clustered lateral branches (presumably having arisen due to serial bud/shoot formation) which come from the basal parts of the main trunk. Often, several tiers of such thornbearing branch clusters can be observed. The life-span of these branches is limited, so that very old individuals may lack thorns altogether. The presence of these thorn-bearing

branches along the lower part of the trunks could be interpreted as a protection against browsing animals. Thorn-bearing branches normally have a “regular” appearance as all thorns are of roughly the same length, paired and arranged in a decussate fashion (Puff and Chamchumroon, 2003).

Uses in traditional medicine: It is used to relief stomach-ache, abdominal pain and stop bleeding (Wuthithummavej, 1998).

Chemical constituents: There are apodanthoside, mussaenoside, gardenoside, benzyl alcohol O-b-D-apiofuranosyl-(1 fi 6)-b-D-glucopyranoside, phenethyl alcohol O-b-D-apiofuranosyl-(1 fi 6)-b-D-glucopyranoside, and oct-1-en-3-ol a-L-arabinopyranosyl-(1 fi 6)-b-D-glucopyranoside from the leave and brach extract of *Dioecrescis erythroclada* (Kaewkrud, 2007).

Figure 2.21 *Dioecrescis erythroclada* (Kurz.) Tirveng. (Sinchai, 2006)

16) *Dregea volubilis* (L.F) Hook. f. Asclepiadaceae (Figure 2.22)

Local name: Kratung-Ma-Ba

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailand.

Description: The shrub is tall stout, stems green, smooth then turn branches ash-coloured, glabrous when old; leaves, opposite and distinchous, simple, the bases rounded or cordate; inflorescences, in axillary umbelliform cymes, many-flowered, subglobose, pendant; flowers, pedicellate, bisexual, actinomorphic, pentamerous, hypogynous; fruit, a follicetum, ellipsoid, rugosely striated; seeds broadly ovoid, smooth, with a tufted micropylar coma of long silky hairs (Lemmens, 2003).

Uses in traditional medicine: In Ayurvedic medicine, it is used to cure tumours, piles, leukoderma asthma and urinary discharges, also useful in treatment of duspepsia, inflammations, biliousness and disease of the eye. The root and tender stalk are considered to be emetic and expectorant; the leaves are used for external application to boils and abscess (Chopra, 2006). In Lanna consider to cure for heart disease, disurea, tumours, sexual transmitted disease (Manosroi and Manosroi, 1984).

Chemical constituents: Three new polyhydroxy pregnanes named dregealol, volubilogenone and volubilol were isolated from the flowers of *Dregea volubilis* (Panda *et al*., 2003). The flowers gave compound, polyoxypregnane glycosides, volubiloside A, B and C (Sahu *et al.*, 2002). For pharmacological activity, it was found the antioxidant property (Sirival, 2008). The saponins from the dried leaves extract of *Dregea volubilis* gave anti-inflammatory and analgesic activities (Nandi *et al*., 2009). Petroleum ether extract of the fruits of *Dregea volubilis* has been shown the anti-inflammatory activity by the taraxerol (Biswas *et al.*, 2009).

Figure 2.22 *Dregea volubilis* (L.F) Hook. f. (Sinchai, 2006)

17) *Fagraea fragrans* Roxb. Loganiaceae (Figure 2.23)

Local name: Tembusa (Thai name - Kan-Kraw or Niam Ruesi)

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailand.

Description: Tree is large with 20 m tall and 70 cm wide, fissured, corky bark, dark brownish gray bark; leaves, opposite, stipulate, narrow elliptic, apex and base acute, 10 cm long and 5 cm wide, margin entire, surface smooth; inflorescence; at the terminal; fruit, globose, turning dark orange when ripe, 1 cm in diameter, with 5-7 seeds (Bunyapraphatsara and Chokechaicharoenporn, 1998).

Uses in traditional medicine: In Thailand, it is used for promoting long life, treatment of burning pain, malaria (Wuthithummavej, 1998).

Chemical constituents: There is an alkaloid, gentianine and swertiamarin (Bunyapraphatsara and Chokechaicharoenporn, 1998). The fagraldehyde, secoiridoids, gentiopicroside, sweroside, and swertiamarin were isolated from the bark and leaves (Jonville *et al*., 2008).

Figure 2.23 *Fagraea fragrans* Roxb. (Sinchai, 2006)

18) *Foeniculum vulgare* Mill. var. vulgare (Miller) Thell. Apiaceae (Figure 2.24)

Local name: Fennel Fruit, Fennel Seed, Sweet Fennel (Thai name - Tien-khao-phloug)

Collecting location: Obtained from local market (dried seed)

Description: Fennel is a tall 50 cm long to 2 m, umbrella with 6-40 peduncle and long 6-10 mm and width 3-4 mm, young green after dark brown or slightly green to brown slightly yellow-brown completely; fruit oval, ribbed long 6-10 mm, width 3- 4 mm, ribbed. Ripe fruit has a distinctive aromatic smell, taste when trying as relatively kamfer (WHO, 2007).

Uses in traditional medicine: For boils, bronchitis, bruises, burns, calculus, candidiasis, headache, herpes, hysteria, inflammation, jaundice, leprosy, myalgia, polyps, rheumatism, tumors and whitlow (Duke and Ayensu, 1985), increase the libido and aid digestion, as a remedy for flatulence, to treat indigestion and menstrual irregularities, and to increase breast milk (WHO, 2007).

Chemical constituents: It has reported the substance from the seed of *Foeniculum vulgare* like gallic acid (phenolic) (Raaman, 2006) and volatile oils (anethole,

dianethole, photoanethole, fenchone, estragole, limonene, camphene, alpha pinene), fixed oils (oleic acid, linoleic acid, petroselinic acid), tocopherol, vitamins, minerals, umbelliferone, terpinene, terpinolene (WHO, 2007), flavonoids glycoside and flavonoid aglycone (Parejo, 2004; Sebastian, 2006; Nickavar and Abolhasani, 2009). The fruit methanolic extract exhibited inhibitory effects against acute and subacute inflammatory diseases (Choi and Hwang, 2004). The pharmacological active agents are polymers of anethol, such as dianethol and photoanethol which found from the fruits of Fennel. Anethol has been shown to have antioxidant and anti-inflammatory activities (Aggarwal and Shishodia, 2004).

Figure 2.24 *Foeniculum vulgare* Mill. var. vulgare (Miller) Thell. (Sinchai, 2006)

19) *Gardenia turgida* Roxb. Terveng. Rubiaceae (Figure 2.25)

Local name: Ka-Bian

Collecting location: Obtained from a local market (dried fruit)

Description: A small decidous tree, with smooth bark, branch armed with thorn; leaves large opposite or whorled, ovate or obovate, sub-sessile rounded at apex, entire globrous toward the end of the branches, stipule caducous; Flower, large white,

unisexual male fascicled, female solitary fragrant arising from young leafless shoots; Calyx of male flower turbinate, pubescent, cylindric, smooth, with 5 small teeth; Fruit grey, obovoid or globose, 2-3 inch long ; endocarp woody, placentas 2-6. The branches and leaves as well as gum and resin somewhat acidic pungent in taste (Trivedi, 2006).

Uses in traditional medicine: In India has used almost the parts of tree for cure people ill. The crushed roots are applied on knee for the remedy of guinea worm infection. The warmed paste of seeds applied locally for the treatment of mumps. The infusion plant is often used to cure abdominal disorders, ingenstion and colic pains. For the decoction of barks and leaves often used as remedy for the treatment of Malaria (Trivedi, 2006).

Chemical constituents: The roots contain oleanolic acid (Fai and Tao, 2009). There are alpha amyrin, gardenin A/B/E, oleanolic acid and β-sitosterol (Bunyapraphatsara and Chokchaicharoenporn, 1998).

Figure 2.25 *Gardenia turgida* Roxb. Terveng. (Sinchai, 2006)

20) *Jatropha gossypifolia* L. Euphorbiaceae (Figure 2.26)

Local name: Belly Yache Bush (Thai name - Sa-Bu-Dang)

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailand.

Description: Shrubs can be up to 3 m tall, indumenta long glandular hairs allover, easily visible, sticky; stipules filiform, gland-tipped; leaves, petiole 3-14 cm long, blade 3-5 palmatifid with the lobe ovate and the lateral one slightly smaller; inflorescences up to 14 cm long, bract elliptic up to 1.3 mm long, apex acuminate; staminate flowers c. 8 mm in diameter; sepals elliptic, c. 2.5 by 1 mm, apex acute; petals broadly obovate to spade-like, apex rounded, glabrous, reddish purple, disc gands free; stamens 8, th 5 outer filaments united in the lower half, the 3 inner ones united for two thirds; pistillate flowers, sepals and petals twice as large as in the staminate flowers; fruits trilobed, smooth, springly girsute to subglabrous, dehiscing both sepitcidally and partly loculicidally; seeds compressed-ovoid. caruncle; key to the species, plants sticky with long glandular hairs, well visible with the naked eyed (Welzen and Chayamarit, 2007).

Uses in traditional medicine: The plant parts are used with various medicinal purposes; the leaves for treatment of malaria; various extracts for cure cancer; leaf tea for laxative, fever, hepatitis, diarrhea, constipation, ulcers, colic, diabetes and verneral disease; externally, it is apply to sore and rashes; seed oil as treatment of leprosy; the sap is applied to burns, ulcer and sore in the mouth; the roots are for caring of kidney, liver and bladder problems together with snakebite (Nellis, 1997).

Chemical constituents: There are some toxic properties ; the seeds contain the toxic protein curcin and purgative oil containing the irritating diterpene 12-deoxy-16

hydroxyphobal, the roots and barks contributed bitter alkaloid jartrophine; the leaves contain histamine and tannin (Heinrich *et al*., 2004); the stem contains jatrodien (Das, 1996). The methanolic and petroleum ether extract of the dried aerial parts possessed anti-inflammatory acitivity (Panda *et al.*, 2009). It was found three known flavonoids, vitexin, isovitexin and apigenin isolated from leaves which also possessed anti-inflammatory activity (Subramanian *et al.*, 1971).

Figure 2.26 *Jatropha gossypifolia* L. (Sinchai, 2006)

21) *Lagenaria siceraria* (Molina) Standl. Cucurbitaceae (Figure 2.27)

Local name: Bottle Guard (Thai name - Num-Tao)

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailand.

Description: It is a large softly pubescent climbing or trailing herb which is said to be indigenous in India, the Molucas and in Abyssinia. It has stout 5-angled stems with bifid tendrils. Leaves are ovate or orbiculate, cordate, dentate, 5-angular or 5-lobed, hairy on both surfaces. Flowers are large, white, solitary, unisexual or bisexual, the males long and 130 females short peduncled. Ovary is oblong, softly pubescent with short style and many ovules. Fruits are large, usually bottle or dumb-bell-shaped, indehiscent and polymorphous. Seeds are many, white, horizontal,

compressed, with a marginal groove and smooth. There are sweet fruited and bitter-fruited varieties (Kirtikar and Basu, 1998).

Uses in traditional medicine: The seeds yield clear limpid oil which is cooling and is applied to relieve headache. The pulp of the cultivated forms is employed as and adjunct to purgatives and considered cool, diuretic and antibilious, useful in cough, and as an antidote to certain poisons. Externally it is applied as a poultice. The leaves are purgative and recommended to be taken in the form of decoction for jaundice (Nadkarni, 1998). The roots, leaves, flowers, fruits and seeds are emetic, purgative and anti-inflammatory activity, the leaves are bitter, refrigerant, emetic, purgative, expectorant, dropsy and febrifuge (Warrier *et al*., 1995).

Chemical constituents: It is found fucosterol and compesterol, flavonoid (Shirwaikar and Sreenivasan, 1996). The fruit juice extract in rats has confirmed the analgesic and anti-inflammatory activity and gave flavonoids, cucurbitacin, saponins, proteins, and carbohydrates (Ghule *et al*., 2006).

Figure 2.27 *Lagenaria siceraria* (Molina) Standl. (Sinchai, 2006)

22) *Lepidium sativum* L. Brassicaceae (Figure 2.28)

Local name: Garden Cress Seed, Common Cress (Thai name - Tien-Dang)

Collecting location: Obtained from a local market (dried seed)

Description: Vascular plant without significant woody tissue above or at the ground. Forbs and herbs may be annual, biennial, or perennial but always lack significant thickening by secondary woody growth and have perennating buds borne at or below the ground surface. In plants, graminoids are excluded but ferns, horsetails, lycopods, and whisk-ferns are included (Warrier *et al*., 1993-1995).

Uses in traditional medicine: The seeds, are used for the treatment of bacterial and fungal infections; for the soaked seeds which are the mucilaginous, valued as a remedy for diarrhea and dysentery and externally as liniment of bronchitis and cough, and as a poison antidote (Iwu and M.M., 1993). In Morocco used for antidiabetes (Tahraoui *et al*., 2007).

Chemical constituents: The imidazole alkaloid (Maier *et al*., 1998), palmitic, stearic, lignoceric (Karnick, 1994) has been reported in the *Lepidium sativum* L. The pharmacological study showed the anti-inflammatory activity of the ethanolic extract of Cress seeds then the preliminary phytochemical screening found the alkaloids, cyanogenic glycosides (traces), flavonoids, tannins, glucosinolates, sterols and/or triterpenes (Al-Yahya *et al.*, 1994).

Figure 2.28 *Lepidium sativum* L. (Sinchai, 2006)

23) *Nigella sativa* L. Ranunculaceae. (Figure 2.29)

Local name: Black Cumin (Thai name - Thien dam)

Collecting location: Obtained from a local market (dried seed)

Description: Annual flowering plant, native to southwest Asia. It grows to 20-30 cm tall, with finely divided, linear (but not thread-like) leaves. Flower is delicate, and usually coloured pale blue and white, with 5-10 petals. Fruit is large and inflated capsule composed of 3-7 united follicles, each containing numerous seeds. Seed is as a spice (Bunyapraphatsara and Chokechaicharoenporn, 1998).

Uses in traditional medicine: The traditional system of medicine practised in the Arabian Gulf region, black seed is used for cough, bronchitis, asthma, chronic headache, migraine, dizziness, chest congestion, dysmenorrhea, obesity, diabetes, paralysis, hemiplagia, back pain, infection, inflammation, rheumatism, hypertension, and gastrointestinal problems such as dyspepsia, flatulence, dysentery, and diarrhea. It has been used as a stimulant, diuretic, emmenagogue, lactagogue, anthelmintic, and carminative. Black Seed has also been used externally where it is applied directly to abscesses, nasal ulcers, orchitis, eczema, and swollen joints (Nadkarni, 1976).

Chemical constituents: Thimoquinone: From the data review, it was found to inhibit the eicosanoid generation and membrane lipid peroxidation through the inhitbition of cycloxygenase and 5-lipoxygenase pathways of arachidonate metabolism which is responsible for the anti-inflammatory activity (Gilani *et al.*, 2004). Nigellone; Black cumin oil and its derivative inhibit eicosanoid generation in leukocytes and membrane lipid peroxidation (EI-Dakhakhny *et al.*, 2002). The alkaloids as nigellidine, nigellimine and nigellicine was extract from the seeds of Black cumin for many pharmacological activity such as anti-inflammatory, anitidiabetic and bronchodilatory (Mehta *et al.*, 2008).

Figure 2.29 *Nigella saiva* L. (Sinchai, 2006)

24) *Oryza sativa* L. Poaceae (Figure 2.30)

Local name: Paddy Plant, Rice Plant (Thai name - Khao)

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailand.

Description: It is an erect annual grass, growing to 1.2 m tall; culms angled, smooth, nearly enclosed in glabrous, strongly-nerved leaf-sheaths; leaf-blades long, flat, 1.2 cm broad, more or less scabrous; panicle terminal, narrow, curved or nodding to one side, 15-30 cm long, with many long, ascending branches; spikelets strongly flattened sidewise, perfect, ribbed pubescent, awned or awnless; palea with 2 nerves near margin; kernel free-threshing, oblong, flattened on the sides, with long hilum, straw-colored or yellow, from 28,000 to 44,000 per kg, depending on the variety (Reed, 1976).

Uses in traditional medicine: There is various use of the plant in each country. In China, hot water extract of the dried straw is taken orally for hepatitis while in India, hot water extract of the grain is taken orally for jaundice and the powdered grain is

taken orally for the typhoid fever. In Thailand, hot water extract of the fresh seedling is taken orally as a tonic (Ross, 2003).

Chemical constituents: Many types of constituents of each plant part have been reported. Its leaf contains 15-16-Epoxy-3-oxa-kauran-2-one, oryzalexin A-F,S, cyanidine diglycoside (Anthocyanin group), alanine, aluminum; the root contains asparagines; the straw contains tyrosin, tricin and the seed contains thiamine (Ross, 2003). The compounds, proanthocyanidin and cyanidin 3-glucoside are found from the glutinous rice bran (Punyatong *et al.*, 2008) which have anti-inflammatory, anticarcinogenic, antiallergic, antibacterial, antiviral and vasodilatory actions (Anne, 2000). The oryzadine (new alkaloid) was found from the seeds of the rice plant which have the antioxidant action (Kang *et al.*, 2009).

Figure 2.30 *Oryza sativa* L. (Sinchai, 2006)

25) *Passiflora foetida* L. Passifloraceae (Figure 2.31)

Local name: Stinking Passion Flower (Thai name - Ka-Tog-Log)

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailnd.

Description: A perennial herbaceous vine stem thin, wiry and woody covered with sticky yellow hairs. Leaves have three to five lobes and viscid-hairy. Flowers are

white to pale cream coloured, about 5-6 cm diameter. Fruits are edible, globose yellowish-orange to red when ripe, seeds are black colour and in pulp (Nellis, 1997).

Uses in traditional medicine: The leaf tea is used to treat stomach upset, vomiting, inflammation of the kidney or bladder and female problems. Tea prepared from the vine has been used to treat eczema, eye inflammation, kidney problems, measles, rash, skin ulcers, urinary burning and wounds (Nellis, 1997).

Chemical constituents: It is found the flavonoid ermanin and alkaloid methyl-beta-carboline (Nellis, 1997). Passifloricins have been reported in *Passiflora foetida* resin (Echeverri *et al*., 2001).

Figure 2.31 *Passiflora foetida* L. (Sinchai, 2006)

26) *Phyllanthus emblica* L. Euphorbiaceae (Figure 2.32)

Local name: Emblic Myrobalan (Thai name - Ma-Kham-Pom)

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailnd.

Description: Tree is a deciduous, small or middle-sized with a crooked trunk, and spreading branches. Leaves are subsessile 10-13 by 2.5-8 mm closely set along the branchlets, distichous, light green, glabrous, narrowly linear obtuse, imbricate when

young. Flowers have greenish yellow inaxillary, fascicles on the leaf-bearing branchlets often on the naked portion below the leaves. Fruits are 1.3-1.6 cm, fleshy, glabrous and pale yellow of three 2 seeded crustaceous cocci (Panda, 2000).

Uses in traditional medicine: In Thailand, the fruits are traditionally used as an expectorant, antipyretic, diuretic, antidiarrhoeal and antiscurvy (Saralamp, 1992).

Chemical constituents: It contains ascorbic acid (Prakash *et al.*, 2000) astragalin-flavonol, kaempherol-3-O-ß-D-glucoside from the fruit (EI-Mekkawy *et al.*, 1995), gallic acid–benzenoid, emblicol, phyllemblic acid (Iyer and Pillay, 1958), emblicanin A, emblicanin B, pedunculagin, punigluconin–tannin (Bhattacharya *et al*, 2000), ellagic acid, coumarin (Jamwal *et al*., 1959). The alkaloid (phyllantine and phyllantidine) was found from the leaves and fruits *in vitro* study (Khanna and Bansal, 1975). Further report found tannins like glucogallia, corilagin, chebulagic acid and 3,6-digalloyl glucose from the fruit. Root yields ellagic acid, lupeol, quercetin and β-sitosterol (Thakur *et al*., 1989). The report from Thai herbal pharmacopoeia found ascorbic acid, rutin, mucic acid gallic acid, phylemblic acid and protein.

Figure 2.32 *Phyllanthus emblica* L. (Sinchai, 2006)

27) *Piper chaba* Hunt Piperaceae (Figure 2.33)

Local name: Java Long Peper (Thai name - Dee Plee)

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailnd.

Description: It is a climber witth stems of 2 mm thick, terete, and striated with 1.8-4.2 cm long internodes. Leaves are simple, exstipulate and spiral; petiole of lower leaves 9 mm long, blade with narrowly elliptic, ovate-oblong, papery, glaucous and showing four pairs of secondary nerves and a few tertiary nerves; inflorescences, spikes, attached to em-long pedicels (Wiart, 2006).

Uses in traditional medicine: Cambodia, Laos and Vietnam, the plant is used to treat fever, jaundice, rheumatism, neuralgia and boils. In the Philippines, the roots are chewed to promote digestion and externally used to heal wounds (Wiart, 2006).

Chemical constituents: Chabamide from the stem of *Piper chaba* Hunt has shown antimalarial and antituberculosis activities (Rukachaisirikul *et al*., 2002). The crude extract found four compounds: piperine, pipernonaline, guineensine, and the isobutylamide of 11-(3,4-methylenedioxyphenyl) undeca-2,4,10-trienoic acid (Dagli, 2004). The pharmacological study showed the stem bark of *Piper chaba* gave the induced diarrhoeal effect and decreased gastrointestinal motility in mice (Taufiq-Ur-Rahman *et al*., 2005). The methanol extracts of *Piper chaba* stem bark was found the anti-inflammatory activity on the acute inflammation (Rahman *et al*., 2005) and chronic inflammation (Begum *et al.*, 2008). The fruit extract was found piperanine C; a new amide constituent named piperchabamide F, and two new phenylpropanoid glycosides, piperchabaosides A and B (Morikawa *et al*., 2009).

Figure 2.33 *Piper chaba* Hunt. (Sinchai, 2006)

28) *Piper nigrum* L. Piperaceae (Figure 2.34)

Local name: Black Pepper, White Pepper, (Thai name - Prik-Thai)

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailnd.

Description: The plant is a stout climber, rooting at nodes. Petiole grooved, 0.8-1.5 cm long; leaf blade fleshy coriaceous, ovate to elliptic, 4-6 cm wide, 9-11 cm long; apex acuminate, base rounded to oblique; veins 7, two pairs basal, one pair arising 1-2 cm apart from base, reaching leaf apex. Spikes with male and female flowers together, 5-13 cm long, 0.3-0.5 cm in diameter; peduncle 1-1.5 cm long; stamens 2; stigmas 3. Fruiting spike 7-10 cm long; drupe globose, sessile, arranged loosely on rachis. Flowering and fruiting on year round (Ghazanfar, 1994).

Uses in traditional medicine: It is considered to be an aromatic, carminative, febrifuge, rubefaccient and stimulant. Peperine in its leaf can be used for synthesizing heliotropin which is an antiseptic and antipyretic (Rocha and Ming, 1999). In Ayurveda, uses for treat the digestive and repiratory order (Heinrich *et al.*, 2004).

Chemical constituents: It contains piperine 2-6% which useful as an analeptic in barbiturate poisoning (Duke and Ayensu, 1985). The isolation from berries of *Piper*

nigrum has been found isopiperolein B: an alkamide (Srinivas and Rao, 1999). Piperine (1-Piperoyl piperidine) was found in *Piper nigrum* (Khajuria *et al*., 2002) which gave the anti-inflammatory activity (Bang *et al*., 2009).

Figure 2.34 *Piper nigrum* L. (Sinchai, 2006)

29) *Plumbago indica* L. Plumbaginaceae (Figure 2.35)

Local name: Rose Colour Leadwort, (Thai name - Chetta Mun Phloeng Daeng)

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailand.

Description: Stem is an erect or spreading, more or less branched, herbaceous or half-woody plant 1.5 meters or less in height. Leaves are ovate to oblong-ovate, slightly drooping, and smooth, with entire, undulate or wavy margins, pointed or blunt tip, and pointed base; calyx, tubular, covered with stalked, sticky glands; corolla, bright red (Schmelzer and Gurib-Fakim, 2008).

Uses in traditional medicine: In eastern Africa, its root has many uses; it is acrid, vesicant, digestive; an infusion of roots is taken to treat dyspepsia, colic, cough and bronchitis. Moreover, small doses of compound can stimulate the central nervous system but the large doses may cause death from respiratory failure (Schmelzer and Gurib-Fakim, 2008). From the *in vivo* study of anti-inflammatory activity of

medicinal plants selected from the Thai/Lanna medicinal plant recipe database found the *Plumbago indica* L. extract which gave the anti-inflammatory activity (Monosroi *et al*., 2009).

Chemical constituents: The chemical constituents include plumbagin and sitosterol glucoside. Clinical trials have demonstrated that plumbagin oil from *P. indica* is useful in common wart (Satyavati *et al*, 1987). The root contains naphthoquinone plumbagin (2-methyl juglone), the aerial parts include 6-hydroxyplumbagin, plumbaginol, (a flavonol), leucodelphinidin and steroids (e.g. β-sitosterol, campesterol). Regarding its pharmacological activities, it has antimicrobial, anticancer, cardiotonic and antifertility actions (Schmelzer and Gurib-Fakim, 2008).

Figure 2.35 *Plumbago indica* L. (Sinchai, 2006)

30) *Plumbago zeylanica* L. Plumbaginaceae (Figure 2.36)

Local name: Wild Leadwort, Wild White Plumbago, (Thai name - Chetta Mun Phloeng Khao)

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailnd.

Description: It is a staggling shrub of up to 3 m tall, stems erect, trailing or climbing, wiry, diffusely branched, glabrous, with prominent longitudinal ridges and often with white waxy dots, leaves alternate, simple and entire, stipules absent, petiole 0-5 mm long with small auricles present in young leaves; blade ovate, ovate-lanceolate, elliptical or oblong, base cuneate, apex acute, acuminate or obtuse, with white waxy dots underneath. Inflorescence a terminal raceme, sometime paniculate, many flowered, bracts ovate to lanceolate, peduncle 1-1.5 cm long, with prominent sessile glands. Flowers bisexual, regular, 5 merous, sweet scented; pedicel 1-2 mm long; calyx tubular, 7-11 mm long, 5-ribbed, with stalked glands along ribs, lobes up to 1.5 mm long; corolla tube 15-30 mm long, lobes oblong to ovate, 5-12 mm long, spreading, mucronate, shite; stamens free, included; ovary superior, 1 celled, style filiform, with 5 elongated stigma lobes. Fruit an oblong capsule 7.5-8 mm long, apex acute with 5 furrows, 1 seeded. Seed oblong, 5-6 mm long, reddish brown to dark brown (Schmelzer and Gurib-Fakim, 2008).

Uses in traditional medicine: In African and Asia has used as a remedy using all the plant parts for skin deseases, infections and intestinal worms, leprosy, scabies, ringworm, dermatitis, acne, sores, ulcers of the leg, haemorrhoids and hook worm (Schmelzer and Gurib-Fakim, 2008).

Chemical constituents: The root and leaves contain the naphthoquinone plumbagin. Other compounds isolated are mainly the plumbagin derivatives, bi-plumbagin-derivatives and coumarins (Schmelzer and Gurib-Fakim, 2008). For pharmalogical activities, plumbagin also possesses the antimicrobial, antiplasmodial, anticancer and antifertility actions (Schmelzer and Gurib-Fakim, 2008). The anti-inflammatory activity has been reported from the roots extract of *Plumbago zeylanica* L. (Aparanji

et al., 2005). The study of induction of anti-inflammatory and altered T-cell proliferative responses by the ethanol root extract of *Plumbago zeylanica* in adjuvant-induced arthritic rats has been found the anti-inflammatory activity and anticancer action (Aparanji *et al.*, 2005). Plumbagin compound in the *Plumbago zeylanica* also inhibited NF-kB activation induced by TNF, and other carcinogens and inflammatory stimuli (Sandur *et al.*, 2006).

Figure 2.36 *Plumbago zeylanica* L. (Sinchai, 2006)

31) *Psophocarpus tetragonolobus* DC. Leguminosae-Papilionoideae (Figure 2.37)

Local name: Winged Bean, Goa Bean (Thai name - Thua Phu)

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailand.

Description: It is a perennial climbing or twining herb usually grow as an annual crop. Roots are numerous, long and lateral, stems up to 4 m long, ridged stipules ovate-lanceolate, spurred and glabrous. Leaves are alternate, 3 foliage with persistent, petiole 3-12 cm long, rachis 1.5-5.5 cm long; leaflets ovate-trianular, truneae to round at base, acute at apex, glabrous or glabrescent on both surfaces. Inflorescence 2-3 flowered pseudoraceme, peduncle 5-15 cm long, rachis 1-10 cm long. Flowers are

bisexual, papilionaceous, calyx with tube 4-6 mm long, obes unequal, green to dark red-purple corolla blue, mauve, creamy or reddish, wing and keel slightly shorter, ovary superior, oblong, style bent, with a row hairs below the stigma. Seeds are almost globose, yellow, brown or black or white (Grubben and Denton, 2004).

Uses in traditional medicine: In Thai traditional medicinal, all parts of the plant is used mainly for nutritive and treatment purposes, namely, roots are for boils and stomachic, tubers for weakness and food supplement for pregnant women, leaves for boils and promote digestive system, pods for asthma (Bunyapraphatsara and Chokechaicharoenporn, 1998). In Thai Lanna recipes, it is used as the treatment of cancer, febrile, boils, abdominal disturbance (Manosroi and Manosroi, 1984).

Chemical constituents: The pharmacological acitivitis showed the antimicrobial action of the extract of *Psophocarpus tetragonolobus* pods (Latha *et al*, 2007); antioxidant property (Latha *et al*., 2005; Amin *et al.*, 2009). It has been reported of lectin in the tuberous roots of winged bean (Kortt and Caldwell, 1987); palmitic acid of the seed oil of winged bean (Murgiswany *et al*., 1981).

Figure 2.37 *Psophocarpus tetragonolobus*. (Sinchai, 2006)

32) *Quisqualis indica* L. Combretaceae (Figure 2.38)

Local name: Rangoon Creeper (Thai name - Leb Muoe Nang)

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailnd.

Description: The plant is a large, climbing, woody shrub reaching a length of from 2 to 8 m, younger parts with a rusty appearance on account of brown hairs. Leaves are oblong to elliptic, 7-15 cm long, with pointed tip and rounded base. Flowers are fragrant, showy, first white and then rose colour, reddish-purple, or orange, exhibiting all these different stages on one and the same flower stalk. Fruits are narrowly ellipsoid and 2.5 to 3 cm long, with five, sharp, longitudinal angles or wings, seeds, pentagonal and black (Eewards and Lindley, 1820).

Uses in traditional medicine: In China, its fruit is mainly used as vermifuge, decocted alone or with other herbs, also for abdominal distention, dyspepsia, and marasmus, leucorrhea. When macerated in oil, it can be used to apply to skin ailments due to parasites. Ripe seeds are roasted and given in diarrhea and fever cases. Its extract shows antitumor and cathartic action. In the Mongolian use, fruits and seeds are used to sustain the spleen, causing obstructions to disappear. In Malayan use, the juices of its leaves are for boils and ulcers. (Duke and Ayensu, 1985)

Chemical constituents: Quisqualic acid which gave the anthelmintic action can be found (Fabrican and Farnsworth, 2001). The seeds gave 10% tannin and 22% fixed oil (Tan, 1980). The dried flowers and crude extract of *Quisqualis indica* indicated the highest phenol contents of and antioxidant activity (Wetwitayaklung *et al.*, 2007).

Figure 2.38 *Quisqualis indica* L. (Sinchai, 2006)

33) *Sauropus androgynus* L. Merr. Euphorbiaceae (Figure 2.39)

Local name: Star Gooseberry, (Thai name- Phak Wan Ban)

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailnd.

Description: The shrubs are grown to treelets up to 4 m high, with glabrous, young branches with 2 or vaguely 4 ribs, without asperities, stipules triangular. Leaves, petiole c. 2 mm long, flattened above, blade ovate, papery (to pergamentaceous), drying greenish, base rounded to truncate, margin flat to recurved, gradually tapering (usually without a sinus) into the obtuse to acute apex, often mucronulate, green above, grey-green underneath; nerves usually distinct on both sides, 6-10. Flowers in axillary fascicles, in small groups or on short, up to 8 mm long inflorescences, greenish to yellowish to (partly) red; staminate flowers 3-18.5 mm in diameter, pedicel 4.5-13 mm longm calyx flat, small and lobed to wide, reflexed and hardly lobed, lobes indistinct to ovate, apices rounded, scales present, stamens, androphore 0.1-0.3 mm long, stamens 0.4-0.6 by 0.4-0.6 mm; pistillate flowers 5.5-10 mm in diameter, pedicel, calyx lobes usually obovate, ovary 1.1-1.5 by 1-2 mm, stigmas up to 1.2 mm long, flat, split till halfway, bend, forming less than a circle. Fruits are

white, inflated, fleshy, column with apically heart-shaped remnants of the septae, seeds triangular in transverse section, hollow, 7-8 by 4.5-5 by 4-4.5 mm, white and black ; key to species, leaves papery (to pergamentaceous), usually drying greenish, nerves 6-10 per side, staminate flowers 2.5-18.5 mm in diameter, pistillate pedicel 3.2-14 mm long, fruits fleshy, inflated, 14-16 by 9-15 mm (Welzen and Chayamarit, 2009).

Uses in traditional medicine: The dried and crushed root is used medicinally in Chiang Mai province of Thailand against headache, fever or urinary problem. Leaves are used as stimulating the milk production and to cover the womb after childbirth (Welzen and Chayamarit, 2009). In China, its leaves are used as a medicine for coughs and to soothe the lungs, as a tonic, and as a febrifugal to relieve in terna fever. They are also used as a vegetable (Shu *et al.*, 2008).

Chemical constituents: For pharmacological activities, its antioxidant capacities are found in its *Sauropus androgynus* (Tangkanakul *et al.*, 2006). The alpha-tocopherol content is in the leaves (Ching and Mohamed, 2001). The research on content an distribution of flavonoid among 91 edible plant species found flavonoid in the shoots of *Sauropus androgynus* (Miean and Mohamed, 2001; Yang *et al*., 2008).

Figure 2.39 *Sauropus androgynus* L. Merr. (Sinchai, 2006)

34) *Sesamum indicum* L. Pedaliaceae (Figure 2.40)

Local name: Sesame, Beni, Baniseed, Sem-Sem, Til (Thai name - Nga)

Collecting location: Obtained from a local market (dried seed)

Description: The stem is erect, normally square, flat shapes, smooth, slightly hairy or very hairy, stem light green to purple. Its leaves are broad, lower leaves, margins prominently toothed with the teeth deiverted outwards, narrow and lanceolate of upper leaves, glabrous, darkish-gree. Flowers arise in the axils of leaves, singly on the lower leaf axils with multiple flowers on the upper stem or branches, calyx, with the short of calyx lobes, velvety, narrow acuminate and united at the base, corolla, white or pale pink, stamens, attached to the tube of corolla with five ovary, superior and 2 celled. Fruits are capsule, rectangular and deeply grooved, 2.5-8 cm long, hairy; seeds, small, ovate, slightly flattened, colour varying from black, white yellow, reddish brown, grey , dark grey, olive green and dark brown (Peter, 2004).

Uses in traditional medicine: In China, the plant is used as lenitive in scybalous constipation, a nutrient tonic in degenerative neuritis, neuro-paralysis, aneuria, cachexia, constipation, hypertention, impotency, uteritis and vertigo (Duke andAyensu, 1985).

Chemical constitutes: Investigation of flowers of *Sesamum* indicum showed six flavones; apigenin, ladanetin, ladanetin-6-O-beta-D-glucosice, apigenin-7-O-glucoronic acid, pedalitin, and pedalitin-6-O-glucoside (Hu *et al*., 2007). Dried flowers extracted which elucidated as latifonin indicated ten compounds (Hu *et al.*, 2007). Other chemical compounds are arginin, choline, globulin, lecithin, phytin and sesamin (Duke and Ayensu, 1985). For pharmalogical action, the seeds and oil treat

various types of wounds (Kiran and Asad, 2008). The sinapic acid from the sesamum seeds is responsible for the anti-inflammatory activity (Yun *et al.*, 2008).

Figure 2.40 *Sesamum indica* L. (Sinchai, 2006)

35) *Siphonodon celastrineus* Griff. Celastraceae (Figure 2.41)

Local name: Ma Duk (Thai name)

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailnd.

Description: The tree is 20-30 m long. Simple Leaf; alternate, elliptic shade to lanceolate with 3-6 cm wide and 7-13 cm long, serrate marginal leaf. Inflorescence; umbel in leaf axil with 2-6 florets, short peduncle, yellow petal with red dot or red line. Fruit; ovate shape and yellow-orange when ripe (Chayamarit, 2007).

Uses in traditional medicine: In Thai traditional medicine, it is used to cure boils which occurred in liver, lung, bone and for skin disease (Wuthithummavej, 1998).

Chemical constituents: A new oleanane-triterpene, 3β-acetoxy-11α-benzoyloxy-13β-hydroxyolean-12-one was isolated from the root bark of *Siphonodon celastrineus* Griff (Niampoka *et al.*, 2005). In the review of cytotoxic against cell line, high

cytotoxic activity is exhibited, showing a certain degree of selectivity against the different cell types (Itharat and Ooraikul, 2007).

Figure 2.41 *Siphonodon celastrineus* Griff. (Sinchai, 2006)

36) *Terminalia chebula* Retz. Combretaceae (Figure 2.42)

Local name: Myrobalan Tree,(Thai name - Sa Maw Thai)

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailand.

Description: It is a medium sized plant up to 30 m high, deciduous tree with a cylindrical bole, rounded crown, spreading branches with dark brown bark and brownish gray heartwood; leaves are simple, alternate or subopposite, ovate or elliptic ovate with short petioles bearing 2 glands below the blades; flowers pale yellow or white in 4-10 cm long axillary spikes; calyx tube hairy pale yellow and 5 lobed, no petals; stamens consist of 10 filaments subulate, anthers small; ovary inferior, 1-celled with 2-3 pendulous ovule; fruit is a drupe, ovoid glossy, glabrous, faintly angled and yellow to orange brown in colour; seeds are hard and pale yellow (Thai herbal pharmacopoeia, 2000).

Uses in traditional medicine: In unani system, it is used as a blood purifier; the pulp of the fruit is given to treat piles, chronic diarrhoea, dysentery, costiveness, flatulence,

asthma, urinary disorders, vomiting, hiccup, intestinal worms, ascites and enlarged spleen and liver; powdered fruit is used in chronic ulcers and wounds, carious teeth and bleeding ulceration of the gums; the bark is a good cardiac tonic (Joy *et al*., 1998). Its activities of laxative, carminative, astringenn and expectorant are used in Thai traditional medicine (Thai herbal pharmacopoeia, 2000).

Chemical constituents: The tannin is found in the plant (Shyamkumar, 2007). Its kernel oil of Chebulic myrobalan contains 6 fatty acids viz. Palmitic, stearic, oleic, linoleic, arachidic and behenic acid; its fruits contain chebulinic acid, tannic acid, gallic acid, chebulin an anthraquinone glycosides and tannin; the leaves contain terpenes and saponins. β-sitosterol is present in the bark. Fruits are astringent, purgative, tonic, carminative, alternative and antispasmodic. Flowers and fruits are antiviral and hypoglycaemic; Wood is oxytocic and hypothermic (Joy *et al*., 1998). The antioxidant activity is found in *Terminalia chebula* (Aqil, 2006). The leaves of *Terminalia* species have potential in antidiabetic activity (Anam *et al*., 2009). Tannin; chebulinic acid, tannic acid, gallic acid are also found in the plant. It contains the β-sitosterol, saponins and fixed oil containing principally esters of palmitic, oleic and linoleic acids (Thai herbal pharmacopoeia, 2000).

Figure 2.42 *Terminalia chebula* Retz. (Sinchai, 2006)

37) *Tiliacora triandra* Diels. Menispermaceae (Figure 2.43)

Local name: Yanang (Thai name)

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailnd.

Description: This is a plant of twining shrub with a lot of branches with green and climb 7-13 m long, young stem of a vine with soft grey ciliate and disappear when old; leaf simple alternate, lanceolate-ovate 2-4 cm wide and 5-12 cm long, cordate leaf base, little crenate leaf margin, thick and smooth leaf with strong green colour; inflorescence, in axillary or cauliflorous panicle, unisexual with 3.5-7 cm long, dioecious, apetalous; fruit, aggregate, composed of ovoid drupelets and orange colour when old (Chayamarit and Pupattanapong, 1992).

Uses in traditional medicine: In addition to using the plant leaves mainly in cooking. Traditional medicine uses it for treatment of diarrhea and the root infusion for fever relieve (Chayamarit and Pupattanapong, 1992).

Chemical constituents: The three known alkaloids; tiliacorinine (1), tiliacorine (2) and nortiliacorinine A (3), together with a new alkaloid, tiliacorinine 2'-*N*-oxide (4), have been isolated from the roots of *Tiliacora triandra* Diels (Wiriyachitra and Phuriyakorn, 1981).

Figure 2.43 *Tiliacora triandra* Diels. (Sinchai, 2006)

38) *Vitex trifolia* L. Verbenaceae (Figure 2.44)

Local name: Indian Wild Pepper (Thai name - Kon Tee Soe)

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailnd.

Description: Its Shrub or a small tree grows up to 5 m tall. Leaves are opposite, palmately compound with 2-5 elliptic leaflets up to 10 cm long, greyish below and dark green above. Flowers are relatively small, bilateral, and purple. Fruits are small globose, 4-seeded capsule. Flowers and fruit are available throughout the year. (WHO, 1998).

Uses in traditional medicine: In China, the plant parts are used as treatment, namely, leaves are for fever; fruits for analgesic, sedative and also for breast cancer, seeds for analgesic, sedative; plant for parasitic ailments (Duke and Ayensu, 1985), expectorant, anthelmintic, and antiasthmatic. In Fiji, liquid from the leaves is used to treat stomach pains where one side of the stomach feels hard. In Tonga, an infusion of the leaves is used in treating mouth infections in children and is used to treat stomachache. The leaves are also used to treat diseases thought to be brought on by spirits. Tongans also use the plant to treat inflammations. Samoans use an infusion of the leaves or bark to treat fevers and respiratory problems. Futunans use an infusion of the plant to treat toothaches. In the Cook Islands, women who have given birth use an infusion of the leaves in their bath water. It is believed that this helps to remove any remaining blood from the uterus (WHO, 1998). In Thailand, the fruits are used to treat asthmatic cough and haemorrhoids, and the root is applied in the treatment of liver diseases (Orwa *et al.*, 2009).

Chemical constituents: Leaf extracts inhibit the tuberculosis and anticancer activity and the oil yields camphene, pinene, terpenylacetate, moreover, the leaves contain aucubin, agnuside, casticin, orientin, isoorientin, luteolin-7-glucoside (Duke and Ayensu, 1985). The fruits of *Vitex trifolia* were isolated and five compounds; rho-hydroxybenzoic acid, β-sitosterole, β-sitosterol-3-O-glucoside, casticin and 3, 6, 7-trimethylquercetagetin were identified (Zeng *et al*., 1996). There are aucubin, agnuside, casticin, orientin, iso-orientin, luteolin glucoside, fridelin, daucosterol, sitosterol, artemetin, alpha-pinene, camphene and other terpenes, dulcitol, vanillic acid, fatty acids, vitricine sesquiterpenoids in leaf oil (WHO, 1998). The Six flavonoids, persicogenin (1), artemetin (2), luteolin (3), penduletin (4), vitexicarpin (5) and chrysosplenol-D (6), have been isolated for the first time as new cell cycle inhibitors from *Vitex trifolia* L., a Chinese folk medicine used to treat cancers, through a bioassay-guided separation procedure (Wen-Xin *et al*., 2005). Pharmacological activity of the flowers extraction showed the hepatoprotective activity in rats (Anandan *et al*., 2009). The leaves extract of *Vitex trifolia* was found anti-inflammatory activity (Matsui *et al*., 2009; Goverdhan and Bbbala, 2009)

Figure 2.44 *Vitex trifolia* L. (Sinchai, 2006)

39) *Zingiber officinale* Roscoe. Zingiberaceae (Figure 2.45)

Local name: Ginger (Thai name - Khing)

Collecting location: The scrub forest, Mae Tang District, Chiang Mai Province, Thailand.

Description: A herbaceous rhizomatous perennial; reaching up to 90 cm in height under cultivation; rhizomes, aromatic, thick lobed, pale yellowish, bearing simple alternate distichous narrow oblong lanceolate leaves; herb, several lateral shoots in clumps, dry when the plant matures; leaves, long and 2-3 cm broad with sheathing bases, the blade gradually tapering to a point; inflorescence, solitary, lateral radical pedunculate oblong cylindrical spikes; flowers, rare, rather small, calyx superior, gamosepalous, three toothed, open splitting on one side, corolla of three subequal oblong to lanceolate connate greenish segments (WHO, 1999).

Uses in traditional medicine: In Asia, ginger root is widely used as a digestive aid for mild dyspepsia and to treat or prevent nausea, motion and morning sickness; to relieve sore throat; and to treat migraine headaches. Known since ancient times, ginger has also been used for arthritis, colic, diarrhea, heart disease and as a general "worming" herb (WHO, 2007).

Chemical constituents: Gingerol, zingerone, shogoal, bisabolene, zingiberene, zingiberol and pharmalogical activities are found ; antiemetic and antinausea, anti-inflammatory, improved digestive function, antiulcer effects due to gingerol and gingesulphonic acid, antiplatelet action as a result of the inhibition of thromboxane formation, antiinfective action against both gram-positive and gram-negative bacteria, antioxidant action due to gingerol and zingerone which inhibit lipoxygenase and eliminate superoxide and hydroxyl radicals, hypoglycemic effect, positive inotropic

action and rise in blood pressure, its metabolites are known to be eliminated via urinary excretion within 24 hours, and it is 90% bound to plasma proteins (WHO, 2007). The 6-gingerol (Young *et al*., 2005) and (6)- shogal (Suekawa *et al*., 1986) have found from dried ginger which have the anti-inflammatory activity.

Figure 2.45 *Zingiber officinale* Roscoe. (Sinchai, 2006)

2.1.7 *In vivo* study for the anti-inflammatory activity

There are many types of methods aiming to measure the inflammation incidence, for examples, rat paw edema, rat pleural model of inflammation, models of acute inflammation in the ear. These methods are specific in the purposes and procedures. For this study, the rat paw model and rat ear model, which are not complicated in procedures, less time consuming as well as accuracy in the results (Winyard and Willoughby, 2003).

2.1.7.1 Rat paw edema model (Winter *et al.*, 1962)

This model is based on the principle of the release of various inflammatory mediators by carrageenan. Edema formation due to carrageenan in the rat paw is biphasic event. The initial phase is attributed to the release of histamine and serotonin. The second phase of edema is due to the release of prostaglandins,

protease and lysosome. Subcutaneous injection of carrageenan into the rat paw produces inflammation resulting from plasma extravasation, increased tissue water and plasma protein exudation along with neutrophil extravasation, all of which are due to the metabolism of arachidonic acid. The first phase begins immediately after injection of carrageenan and then diminishes in two hours. The second phase begins at the end of the first phase and remains through third hour up to five hours.

Procedure: Animals are divided into three groups of six each, (n=6) starved overnight with water ad libitum prior to the day of experiment. The control group receives vehicle orally, while other groups receive the test drug and standard drug respectively. The animals' left hind paw is marked with ink at the level of lateral malleolus. Basal paw volume is measured plethysmographically by volume displacement method using Plethysmometer (UGO Basile 7140, Italy) by immersing the paw to the level of lateral malleolus. The animals are then given the drug treatment. One hour after dosing, the rats are challenged by a subcutaneous injection of 0.1 ml of 1% solution of carrageenan into the sub-plantar side of the left hind paw. The paw volume is measured again at 1, 2, 3, 4 and 5 hours after the challenge. The increase in paw volume is calculated as percentages compared with the basal volume. The difference of the average values between the treated animals and the control group is calculated for each time interval and evaluated statistically. The percentages of inhibition are calculated using the following formula:

$$\% \text{ edema inhibition} = (Vt-Vc)/Vt \times 100$$

where Vt and Vc are edema volume in the control groups and treated drug respectively (Palanichamy and Nagarajan, 1990).

2.1.7.2 Rat ear edema model (Brattsand *et al*., 1982)

The use of topical glucocorticosteroid therapy on large skin areas or in the lung is sometimes restricted by the occurrence of unwanted, general corticoid actions owing to a profound systemic absorption. To decrease this risk, potent glucocorticoids with an enhanced ratio between their topical and their systemic glucocorticoid potencies are needed. Therefore, structure-activity studies were performed in rat models to investigate what influences the type of substitution in the 16 alpha, 17 alpha-acetal group and the introduction of fluorine in the 9 alpha- or the 6 alpha, 9 alpha-positions have on the topical and the systemic activities, respectively. The introduction of an unsymmetrical 16 alpha, 17 alpha-acetal group (named acetal type B) markedly enhanced the topical anti-inflammatory potency compared with that of the conventional 16 alpha, 17 alpha-acetonide group (named acetal type A). Both acetal types had similar systemic glucocorticoid potency. However, 9 alpha-Fluoro and especially 6 alpha, 9 alpha-difluoro substitution, on the other hand, enhanced the systemic glucocorticoid activity more than they raised the topical anti-inflammatory potency. Optimal topical to systemic activity ratio was obtained with a nonhalogenated corticoid of acetal type B structure. This compound, budesonide, had at least the same high topical anti-inflammatory potency as fluocinolone acetonide but was about 10 times less potent than this reference to induce systemic glucocorticoid actions. Its lower systemic activity is probably due to the more rapid biotransformation in the liver.

Procedure: The method of using ethyl phenylpropiolate-induced ear inflammation is as follows (Winyard and Wiloughby, 2003):

A. Male rats weighing 90-100 gm are used.

B. Dissolve ethyl phenylpropiolate (EPP) in acetone (50 mg EPP/ml) and apply topically to both ears at the volume of 20 µl/ear side.

C. Measure the ear thickness before induction and after 2 h with a special micrometer (Oditest). Ear thickness is measured at the tip of the pinna with a spring-loaded micrometer at different time intervals after elicitation of the inflammation. Thickness measurements with calipers are subject to operator error, and care must be taken not to leave the calipers in contact with the ear for too long because it is possible to squeeze substantial amounts of edema fluid out of the ear tissue. To minimize variation due to technique, measurements throughout any one experiment are performed by a single investigator.

D. Express the extent of the edema as the individual gain in ear thickness. The difference of the average values between the treated animals and the control group is calculated for each time interval and evaluated statistically. The percentages of inhibition are calculated using the same formula of the rat hind paw assay.