CHAPTER 1

INTRODUCTION

1.1 Statement and significance of the problem

Traditional medicine is a way of healthcare by the traditional healer. Traditional medicine has a long history. It is the total sum of the knowledge, skills and practices based on the theories, beliefs and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health, as well as in the prevention, diagnosis, improvement or treatment of physical and mental illnesses (World Health Organization (WHO), 2000). Whole or parts of medicinal plants have long been used singly or together to prepare into herbal medicines by traditional healers for treatment of their patients with various degrees of success.

The World Health Organization estimates that presently, 4 billion people, 80 percents of the world population, presently use herbal medicine for some aspects of primary health care. The consumption of herbal medicines is significant and appears to be steadily increasing for a number of countries. In rural China, 35% of outpatients and 22% of inpatients are treated with traditional medicines. Herbal medicine sales accounted for 33.1% of the China drug market in 1995, and represented a greater than 200% increase on production levels of 1990. In Hong Kong, 60% of the populations have consulted traditional medicine practitioners. Japan had a 15-fold increase in herbal medicine sales between 1979 and 1989 in contrast to a 2.6 folds increase in sales of pharmaceutical during the same period. In Australia, a recent survey has

identified 48.5% of Australians as using alternative medicines, including herbal medicine. Furthermore, of the 119 plants-derived pharmaceuticals, about 74 percents are used in modern medicines in the ways that correlated directly with their traditional uses as plant medicines by native cultures (WHO, 1998).

Thai people have also adopted traditional medicines from the lifestyles and local wisdom including a cultural heritage that has cared people's health for a long time. However, the uses of Thai traditional medicines have been gradually reduced due to the popularity and easy accessibility of modern medicines. Nowadays, patient's access to Thai traditional medicine is one of the main problems in health care system. Thai traditional medicines have been called for its revival and encouragement of people's acceptance and also to make the service more available and accessible to all. Nevertheless, during the past decades, a rapid growth and development of sciences and technology have contributed to and been applied in the research and development of the re-emergence the Thai traditional medicine as an alternative to the modern medicine.

While four factors body, mind, society and environment were identified by Thai traditional medicine as contributing to the overall health, a stress was also made on a concept of three main causes of illness (supernatural power, power of nature and power of the universe). It can be seen that Thai traditional medicine deals with the people's way of life, beliefs, wisdom and environment. Several studies have shown that many Thai medicinal plant recipes contained plants with compounds of antiinflammatory activity, such as, Phra-Thammawarodom recipes, Lhuang Pu Suk recipes and Lanna medicinal plant recipes (Phra Thammawarodom, 1993; Luang Pu Suk, 1993; Manosroi and Manosroi, 1984).

Each region of the country has its own indigenous recipes made from medicinal plants which are claimed to have therapeutic efficacy. In addition, the plants and herbs also contain the biological constituents which not only provide nutrients but also can support and strengthen the action of the digestive system, encourage the rate of processing food and improve the absorption of nutrients (Taoprasert and Taoprasert, 2005). Using herbal medicine to prevent illness, restore health or treatment may vary from region to region depending their way of life, believe or culture. For people in the upper northern part of Thailand, the Thai Lanna traditional medicine is a living tradition with its roots stretching back hundreds of years. The folklore wisdom heritage is passed on from one to the others in the extent to which their relations are concerned. Recipes used in traditional medicine are normally prepared by healers using medicinal plants or herbs to provide care for the people's health. Parts or whole of locally found plants or herbs containing the active chemical constituents are used singly or combined for medicinal purpose. However, the environmental factors that influence secondary plant constituents including soil, climate, associated flora, and methods of cultivation (Tyler et al., 1988). Moreover, the life-cycle of a plant may also effect the high level of compounds in plant parts (Bohlin and Bruhn, 1998). Several chemical constituents in different parts of plant with their traditional indications are described as follows (Chevallier, 1996):

Mucilage is found in many plants. It is made up of polysaccharides producing a sticky jelly like mass. It lines the mucous membranes of the digestive tract, protecting against irritation, acidity and inflammation.

Phenols, includes salicylic acid are found in many plants, such as wintergreen (*Gaultheria procumbens*), and whiter willow (*Salix alba*), are antiseptic and anti-inflammatory agents.

Tannins are produced to a greater or lesser degree by all plants. Tannins contract the tissues of the body, hence their use to tan leather. They draw the tissues closer together and improve their resistance to infection. For example, oak bark (*Quercus robur*) and black catechu (*Acacia catechu*) both have high tannins. The latex of *Calotropis procera* containing high tannins showed potent of anti-inflammatory activity (Kumar and Basu, 1994).

Carotenoids are natural, fat-soluble pigments that provide bright coloration to plants and animals. A carotenoid found in tomatoes, watermelon, papaya, apricots, oranges, and pink grapefruit, has established anti-inflammatory activities. Lycopene, β -carotene and lutein are derivatives of carotenoid (Pan *et al.*, 2009).

Coumarins are found in many plant species and have widely divergent actions. The coumarins in melilot (*Melilotus officinali*) thin the blood. Bergapten, found in Celery (*Apium graveloens*) is used as a sunscreen. Khellin, found in visnaga (*Ammi visnaga*) is a powerful smooth muscle relaxant. The coumarin derivatives were found to present antioxidant and anti-inflammatory activities. (Kontogiorgi and Hadjipavlou-Litina, 2005).

Anthraquinones are the main active constituents in herbs such as senna (*Cassia senna*) and chinese rhubarb (*Rheum palmatum*), both of which are taken to relieve constipation. Anthraquinones have an irritant laxative effect on the large intestine, causing contractions of the intestinal walls and stimulation of a bowel movement.

Flavonoids are found in many plants with a wide range of actions. They are anti-inflammatory and especially useful in maintaining healthy circulation (Read, 1995). Rutin, a flavonoid found in plants, including buckwheat (*Fagopyrum esclentum*) and lemon (*Citrus limon*), strengthens capillary walls.

Anthocyanins, their pigments, which give flowers and fruits a blue, purple, or red hue, help to keep the blood vessels healthy. Blackberry (*Rubus fruticosus*) and grapes (*Vitis vinifera*) contain appreciable quantities of anthocyanins. It was found that the anthocyanins play significant role in anti-inflammatory activity (Konczak and Zhang, 2004).

Glucosilinates found exclusively in species of the mustard family have an irritant effect on the skin, causing inflammation and blistering. Glucosilinates reduce thyroid function. Both radish (*Raphanus sativus*) and mustard (*Sinapis alba*) contain significant quantities of glucosilinates.

Volatile oils are extracted from plants to produce essential oils. Some volatile oils contain sesquiterpenes, such as azulene, are found in german chamomile (*Chamomilla recutita*). These constitutes have an anti-inflammatory effect.

Saponins come in two types of compounds, triterpenoid and steroidal saponins. Many plants such as licorice (*Glycyrrhiza glabra*) containing steroidal saponins have a marked hormonal activity. Triterpenoid saponins, for example, found in cowslip root (*Primula veris*), are often strong expectorants and may also aid in the absorption of nutrients.

Cardiac glycosides can be found in various medicinal plants, most famously in common foxglove (*Digitalis purpurea*), yellow foxglove (*D. lutea*), and wooly foxglove (*D. lanata*). Cardiac glycosides such as digitoxin, digoxin, and gitoxin have

a strong, direct action on the heart, helping to support its strength and rate of contraction when it is failing.

Cyanogenic glycosides have a helpful sedative and relaxant effect on the heart and muscles in small doses. Both wild cherry bark (*Prunus serotina*) and elder (*Sambucus nigra*) contain cyanogenic glycosides, which contribute to both plants' ability to suppress and sooth irritant dry coughs.

For vitamins, some plants contain significant levels of vitamins. Watercress (*Nasturtium officinale*), for example, contains an appreciable quantity of vitamin E, and the hips of dog rose (*Rosa canina*) have particularly high levels of vitamin C.

Bitters are a varied group of constituents linked only by their pronounced bitter taste. The bitterness itself stimulates secretions by the salivary glands and digestive organs. The secretions can dramatically improve the appetite and strengthen the overall function of the digestive system. Many herbs have bitter constituents, notably wormwood (*Artemisia absinthium*) and chiretta (*Swertia chirata*).

Alkaloids, mostly contain a nitrogen-bearing molecule (-NH₂). Vincristine, derived from madagascar periwinkle (*Vinca rosea*), is used to treat some types of cancer.

Minerals are particularly rich in some herbs. For example, horsetail (*Equisetum arvense*) has high level of silica. Dandelion (*Taraxacum officinale*) has large quantities of potassium.

The conventional anti-inflammatory drugs such as steroidal anti-inflammatory drugs (SAID) and non steroidal anti-inflammatory drugs (NSAID) are used for the treatment of most of acute inflammatory disorders. Modern medicine has used NSAIDs to relieve mild to moderate pain such as headache, backache, toothache,

periodic pains, surgery and sports injuries. Since NSAIDs reduce inflammation and swelling, these drugs are often prescribed for the treatment of inflammatory conditions like arthritis and other rheumatic diseases. On the other hand, NSAIDs possess several side effects such as stomach discomfort, nausea, vomiting, heartburn, headache, diarrhea, constipation, drowsiness, and unusual fatigue. Some of which may cause further problems to uninformed users. Thailand has heavily relied on importing NSAIDs for treating anti-inflammation. The import of NSAIDs has increased almost up to three folds since 2000, from 950.633 million baht to 2,715.466 million baht in the year 2005 (FDA. Thailand, 2009). Its importing tendency is increasing continuously. To reduce the import and burden of high medical expenditures, Thai medicinal herbs recipes with confirmed and safe anti-inflammatory activity are needed as an alternative to modern medicines.

This study aims to search for medicinal plant recipes from Lanna medicinal plant textbooks database "MANOSROI II" and confirmed their anti-inflammatory activity in *in vivo* model. At least three recipes which showed potent *in vivo* anti-inflammatory activity will be selected and identified for their groups of active chemical compounds for further and wider use in treating inflammations.

1.2 Objectives

The purpose of this study is to select and test the Thai anti-inflammatory activity medicinal plant recipes for anti-inflammatory activity. The phytochemistry of the recipes will be also investigated.

1.3 Scope of study

1.3.1 Forty-nine recipes with anti-inflammatory activity both oral and topical administration will be selected from all Thai medicinal plant recipes appeared in the Lanna medicinal plant textbooks database MONOSROI II, which contained total of 11,130 recipes.

1.3.2 The anti-inflammatory recipes with both of oral and topical route will be collected for the study.

1.3.3 Seven medicinal plant recipes which have the high frequency of plants used in recipes, the ease of availability of plants in the local forest or market and the completeness of recipes, will be selected and tested for phytochemical and *in vivo* anti-inflammatory tests using rat hind paw and rat ear edema methods.

1.3.4 Results of the tests will be compared and reviewed to ensure significant evidence of anti-inflammation action.

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