CHAPTER 1

Introduction

1.1 Statement and significance of the problem

Air pollution is one of the serious public health problems in both developed and developing countries. Air pollutants have respiratory effects in children and adults, including increased respiratory tract illness (Anderson *et al*., 2012), asthma exacerbations (Migliaretti and Cavallo, 2004; Lee et al., 2006), and impaired lung function growth (Dockery and Brunekreef, 1996; Barraza-Villarreal *et al*., 2008; Dales *et al*., 2009). In adults, particulate air pollution is strongly associated with respiratory and cardiovascular hospitalizations (Peng *et al.*, 2008; Wang *et al*., 2012), cardiovascular mortality and lung cancer (Künzli and Tager, 2005; Brook and Rajagopalan, 2007; Pope *et al*., 2011; Rajarathnam *et al*., 2011). Air pollution also has effects on indirect health indicators such as health care utilization and school absences (Anderson *et al*., 2012; Le *et al*., 2012; Sram *et al*., 2013).

Air pollution is a complex mixture of thousands of pollutants. This mixture may consist of solid and liquid particles suspended in the air, and different types of gases such as ozone (O_3), nitrogen oxides (NO_2 or NOx), volatile organic carbons (VOCs), and carbon monoxide (CO) (Refs). While particles vary in number, size, shape, surface area and chemical composition, both particles and gases may vary in solubility and toxicity. Of all these pollutants, particulate matter (PM) is monitored in most urban settings as PM_{10} (particles with mean aerodynamic diameter less than 10 micrometer) and/or $PM_{2.5}$ (particles with mean aerodynamic diameter less than 2.5 micrometer). Size of particles indicates their potential for deposition and clearance in the respiratory tract, which is highly relevant for triggering deleterious health effects (Pope and Dockery, 2006; Sava and Carlsten, 2012). Health effects from PM are especially high for some susceptible groups such as the children and the elderly persons, and those with disease of lungs and heart (Liu and Zhang, 2009; Jia *et al*., 2009; Rodriguez-Villamizar *et al*., 2012). Children have increased exposure to PM compared with adults because of they generally spend more time and they are also more active outdoors than the adults, their smaller stature their breathing zone is lower, so they inhale air loaded with more particles and diameters of their airways are smaller (Trenga *et al*., 2006; Rodriguez-Villamizar *et al.*, 2012).

Some studied indicate that the mechanism of air PM-induced health effects involves an inflammation and oxidation stress both in lung, vascular, and heart tissue (Kelly, 2003; Anderson *et al*., 2012; Auerbach and Hernandez, 2012).Oxidative stress has been defined as an imbalance between pro-oxidants and antioxidant defenses in the organism with oxidant producing an increased presence of reactive oxygen species (ROS) at an intracellular level. The generation of ROS after PM exposure can induce cellular oxidative stress and biological effects, such as necrosis, apoptosis, DNA damage, inflammation, and mitochondrial damage. These biological effects can be directly induced by PM compositions that stimulating intracellular sources of ROS or indirectly from ROS produced by proinflammatory mediators released by PM-stimulated macrophages (González-Flecha, 2004). Oxidative stress can arise for many reasons, including air pollutant (Kelly, 2003). Oxidative stress can be assessed and monitored through the determination of the levels of biomarkers, such as hydrogen peroxide, lipid peroxidation-derived products, namely aldehydes and isoprostanes, and protein carbonyl groups (Gillissen *et al*., 2009; Hoffmeyer *et al.*, 2009a; Hoffmeyer *et al*., 2009b; Taylor, 2011; Davis *et al*., 2012). Induction of oxidative damage by PM has been extensively studied in controlled exposure, but little evidence on general population especially in children exposed to ambient PM. Alteration of the antioxidant response are available, partly because of non-invasive biomarkers assessing oxidative stress and tissue injury. Recently the interest in the analysis of biomarkers in exhaled breath has been explored. Exhaled breath condensate (EBC) is a new tool for monitoring airway inflammatory and oxidative stress markers involved in the pathogenesis of various respiratory conditions (Montuschi and Barnes, 2002). EBC is collected by cooling or freezing exhaled air which contains a number of volatile and non-volatile compounds derived from respiratory surface. EBC collecting is simple, non-invasive, safely applied to children and suited for repeating measurements (Grob *et al*., 2008; Gillissen *et al*., 2009; Davis *et al*., 2012;). Previous studies have used a variety of devices to collect EBC samples. These devices include the RTube^{TM} (Respiratory Research Inc., USA), the ECoScreen (Jaeger GmbH, Germany) and developed collection devices (Montuschi, 2007; Grob *et al*., 2008).

Chiang Mai is the second largest province of Thailand and situated down near Ping river valley near the foothill of Suthep Mountains. It is situated approximately 700 km from Bangkok in the upper north region of the country. The Pollution Control Department (PCD), Ministry of Natural Resources and Environment provides the information on air quality parameters including PM_{10}, NO_X, O_3, SO_2, CO from two air quality monitoring stations in Chiang Mai province. The first station is located at Yupparaj Wittayalai School (YP) in central Chiang Mai city and the second one is located at Chiang Mai city hall (CM) which is in suburban area of Chiang Mai city. The level of PM_{10} had become a serious air pollutant problem in Chiang Mai. Trend of PM_{10} levels in Chiang Mai is likely to increase in dry season, especially in January to March that the level of PM_{10} in Chiang Mai is high and exceeding the standard limit as shown in Figure1.1. The major sources that contribute to high levels of PM_{10} is agricultural burning settings (Pengchai *et al*., 2009; Chantara *et al*., 2012; Wiraya *et al*., 2013).

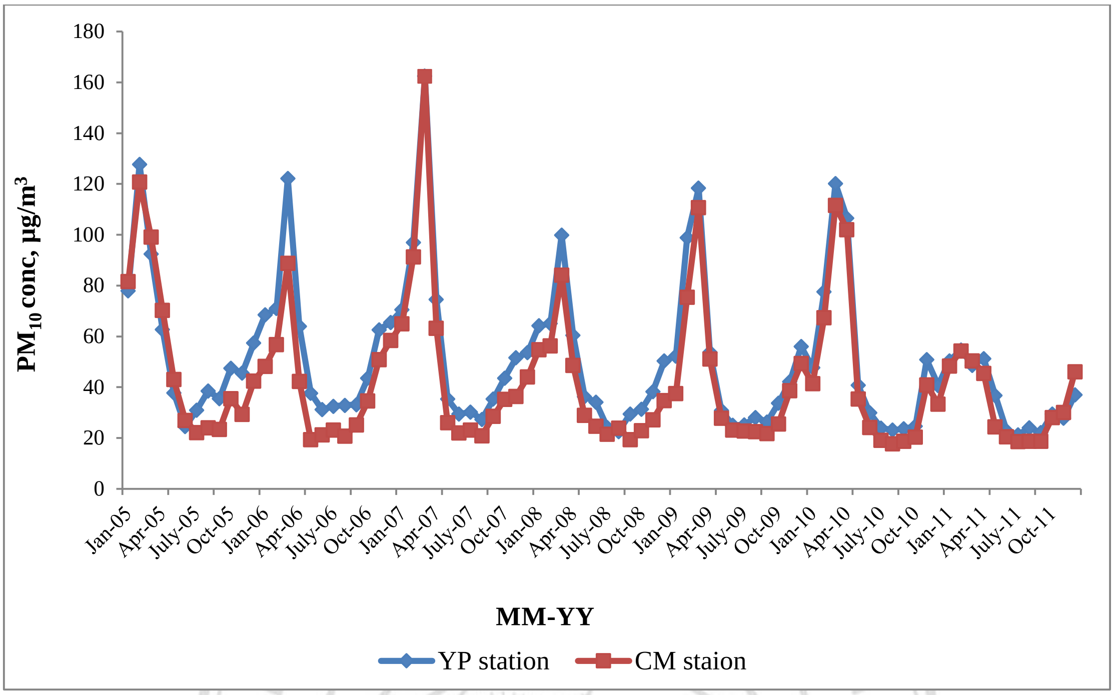

Figure 1.1 Monthly mean concentration of PM_{10} (µg/m^3) from 2005-2011 by air quality monitoring stations in Chiang Mai province. (Source: The Pollution control Department, Ministry of Natural Resources and Environment)

Chiang Mai Provincial Public Health Office reported respiratory system diseases are the major cause of illness in Chiang Mai province. The incidence of respiratory system diseases were raised from 438 per 1,000 in 2004 to 510 per 1,000 of populations in 2008 (http://www.chiangmaihealth.com/ict/stat.php, October, 19, 2014). The major causes of illness in Chiang Mai province are shown in Figure 1.2.

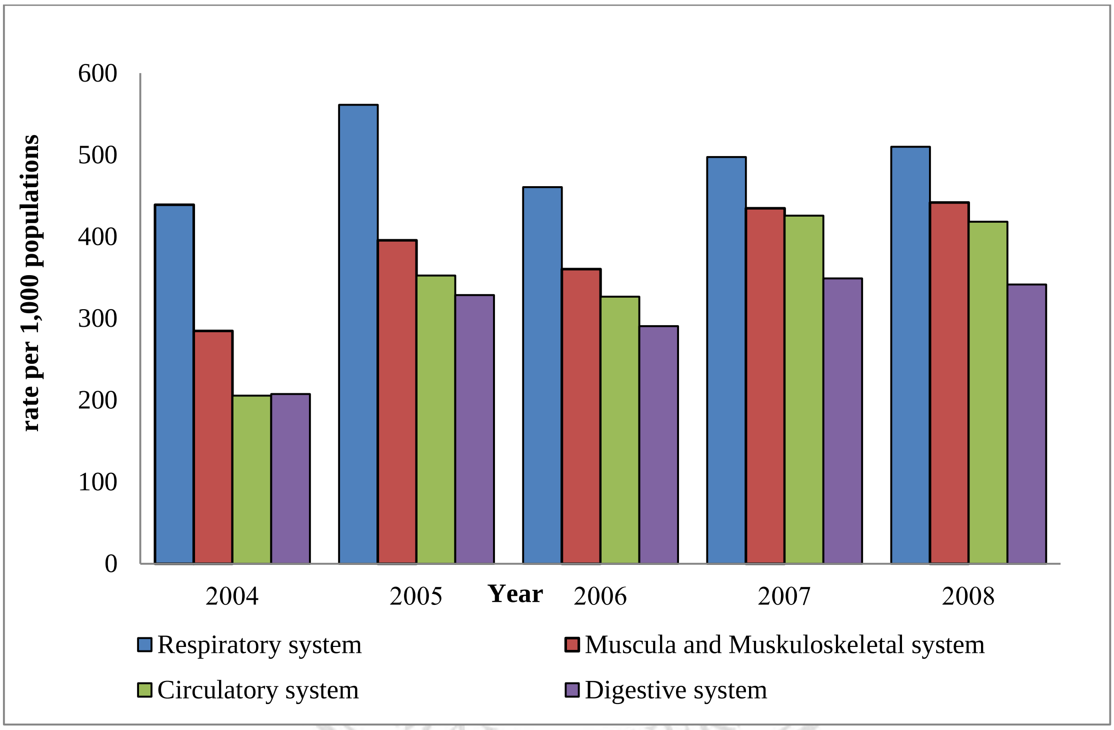

Figure 1.2 Major causes of illness, Chiang Mai populations, 2004-2008

(Source: Chiang Mai Provincial Public Health Office)

EBC has been studied widely to identify inflammatory and oxidative stress markers implicated in the pathogenesis of various respiratory conditions (Antczak and Górski, 2002). Although the collection of EBC is non-invasive, easy to perform and able to repeat, knowledge of the usefulness of EBC samples for investigation the effects of PM_{10} among children are limited. Therefore, this study had developed a simple and portable EBC collecting device and then used to collect EBC samples from the school children who supposedly exposed to airborne PM_{10}. The questionnaire was also collected to determine other factors associated with respiratory health, such as smoking in family, household cooking fuel types and traffic volume in the neighborhood. Then the association of exposure to PM_{10} and respiratory health in school children by measuring the pulmonary function, exhaled H_2O_2 and exhaled MDA concentrations, and recording respiratory symptom were statistically performed.

1.2 Objectives of the study

The specific objectives of the present study were as following:

1.2.1 To develop a simple and portable EBC collecting device for collecting EBC samples from the school children.

1.2.2 To evaluate the effects of PM_{10} air pollution on respiratory health among children from an urban school in Chiang Mai city compared to those children from rural school in a highland area of Chiang Mai province.

To achieve these, two research parts were focused as following:

Part 1: To develop a simple and portable EBC collecting device and evaluate the use of developed device with a group of volunteers.

Part 2: To apply the developed EBC collecting device to collect EBC samples of school children who exposed to PM_{10}. After that, to evaluated the effects of PM_{10} exposure to respiratory health as well as pulmonary function, H_2O_2 and MDA concentrations in EBC of children in an urban and a highland school in Chiang Mai province during different seasons.

The working diagram of this study is shown in Figure1.3.

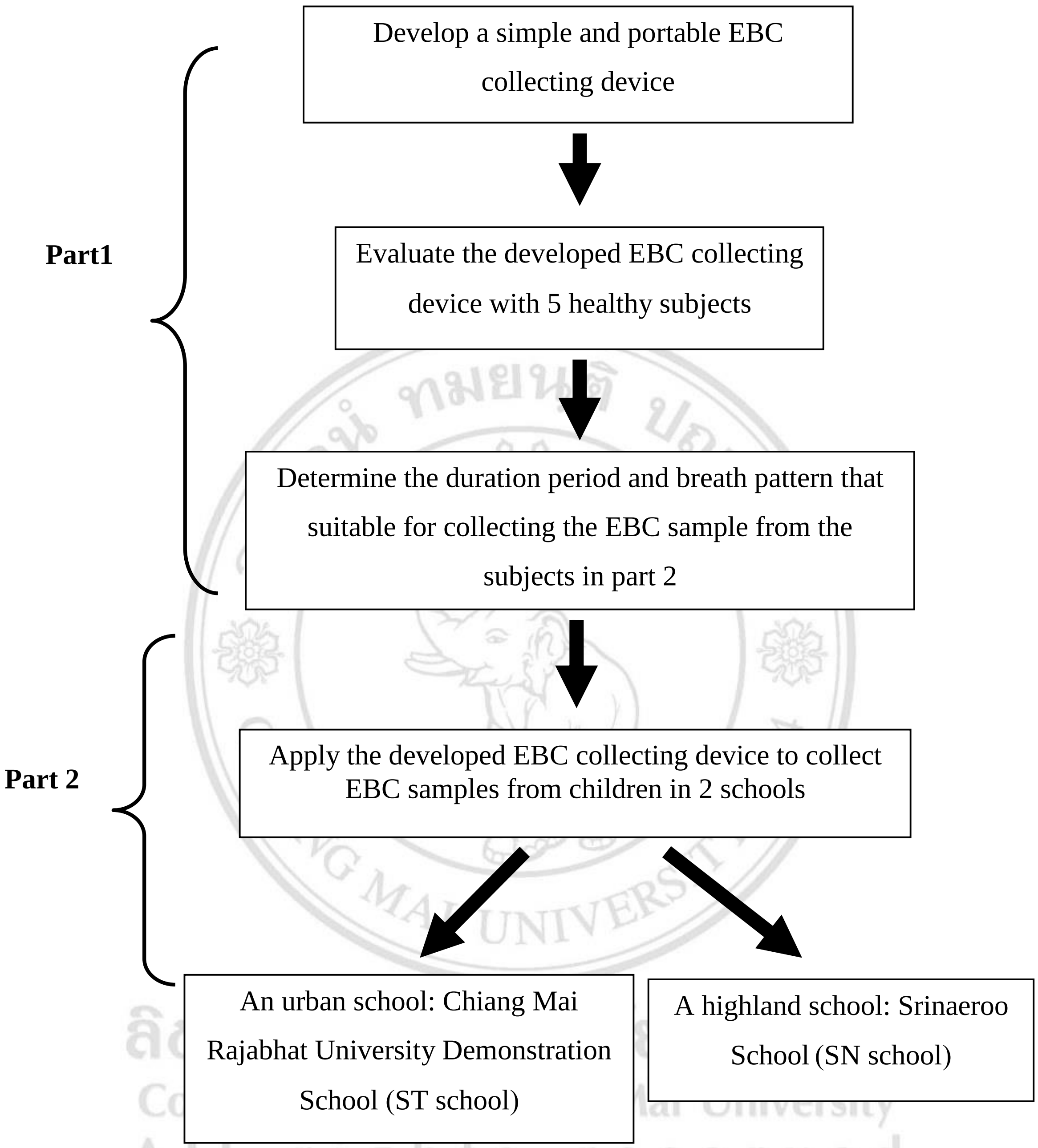

Figure 1.3 Working diagram of the study

1.3 Conceptual framework

The dependent variable in the present study was respiratory health of school children such as the concentration of H_2O_2 and MDA in EBC, pulmonary function indices and respiratory symptoms. The independent variables were child factors and environmental factors. The conceptual framework as shown in Figure 1.4

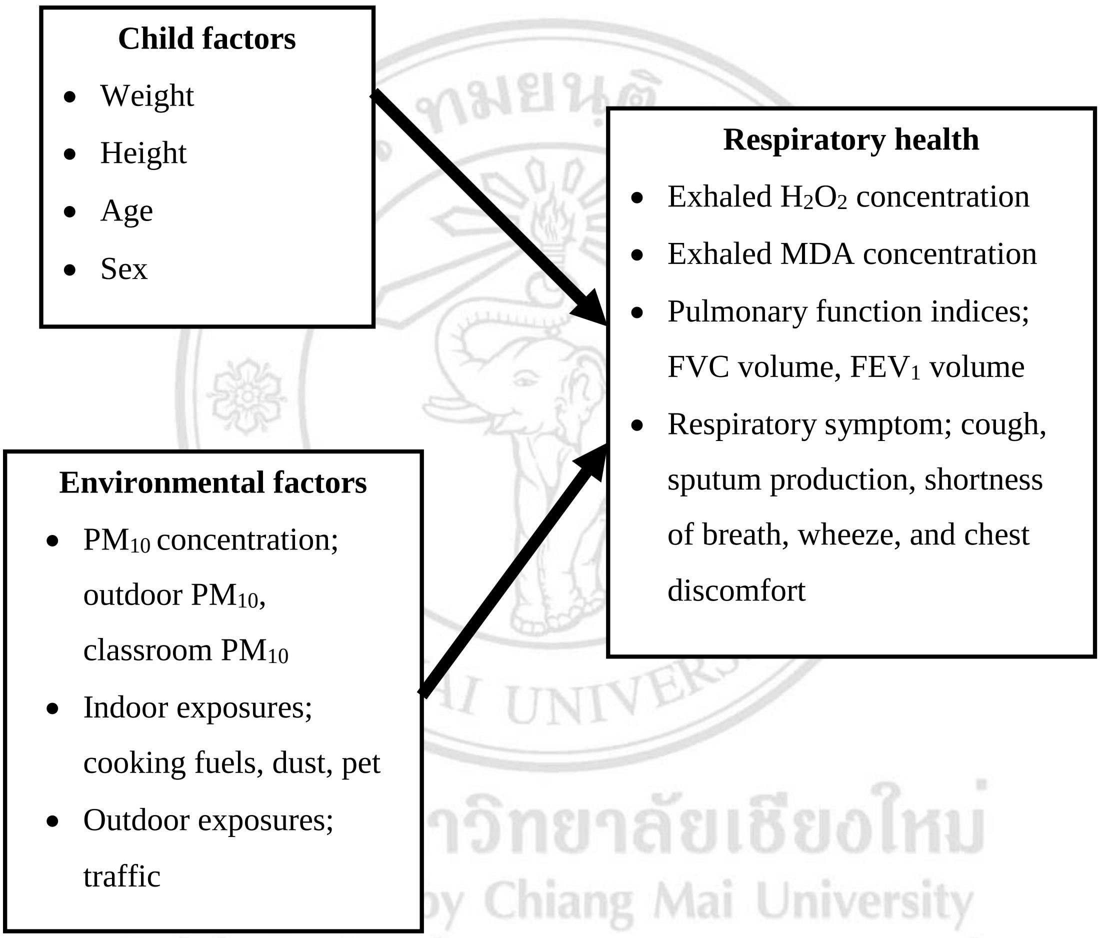

Figure 1.4 Factors affecting respiratory health of school children

1.4 Definition of terms in this study

1.4.1 Outdoor PM_{10} is the level of PM_{10} in the surrounding environment. The PM_{10} levels from the nearest air quality monitoring station were used to represent the subject's exposure to outdoor PM_{10}. The exposure from PM_{10} pollution of ST children was obtained daily ambient concentration from the YP station which locating within 2.5 kilometers radius of the ST school. However at the highland area was lacked of the air quality monitoring station; therefore the portable air monitor (E-sampler, Met One Instruments Inc., USA) was used to operate at SN school to represent the exposure from PM_{10} of SN children during the study period.

1.4.2 Classroom PM_{10} is the level of PM_{10} in each classroom of the subjects. Each sample was collected for 7-8 hours using single-stage impactor (Personal Environmental Monitor-PEM; SKC Inc., USA). The sampling position in each classrooms were opposite to the black board, about 1 meter above the floor level, the level at which the subjects would normally inhale, and away from the door.

1.4.3 Urban school children are those children studying at Chiang Mai Rajabhat University Demonstration School.

1.4.4 Highland school children are those children studying at Srinaeroo school.

1.4.5 Exhaled breath condensate (EBC) is the exhalation from breath that has been condensed, typically having a cooling part of collecting device. EBC reflects the change in respiratory fluid that lines the airways. EBC is mainly formed by water vapor, but also contains aerosol particles in which several biomolecules. Analysis of EBC is a noninvasive method for studying the composition of airway lining fluid and has the potential for assessing lung inflammation.

1.4.6 Biomarkers of effect are biological indicators of the body's response to exposure and indicate sub-clinical changes, which if prolonged, may go on to have pathological consequences.

1.4.7 Hydrogen peroxide (H_2O_2) is produced by inflammatory and vascular cells and induces oxidative stress, which may contribute to vascular disease and endothelial cell dysfunction. In respiratory system, H_2O_2 can be released from both inflammatory and structural cells including neutrophils, eosinophils, macrophages and epithelial cells. H_2O_2 is an important reactive oxygen species.

1.4.8 Malondialdehyde (MDA) is a highly reactive three carbon dialdehyde produced as a by-product of polyunsaturated fatty acid peroxidation and also during arachidonic acid metabolism for the synthesis of prostaglandins. MDA can combine with several functional groups on molecules including proteins, lipoproteins, RNA and DNA. The monitoring of MDA levels in biological materials can be used as an important indicator of lipid peroxidation in vitro and in vivo for various diseases.

1.4.9 Pulmonary function tests (PFTs) are noninvasive diagnostic tests that provide measurable feedback about the function of the lung. By assessing lung volumes, capacities, rates of flow and gas exchange. The primary purpose of pulmonary function testing is to identify the severity of pulmonary impairment. Pulmonary function testing has diagnostic and therapeutic roles and helps clinicians answer some general questions about patients with lung disease.

1.4.10 FEV_1 is the volume exhaled in the first second of the forced expiration after a maximal inspiration.

1.4.11 FVC is the maximum volume of air that can be exhaled or inspired during a forced maneuver.