CHARPTER I

INTRODUCTION

Rationale and significance of the study

The development of obesity is most commonly caused by consumption of excessive carbohydrates such as sucrose and fructose, as well as fat (Lutsey, et al., 2008). Nowadays, most people often consume a Western-style diet which contains a lot of fat and sugar. Western-style diet was correlated with an increased incidence of diabetes mellitus type 2 (Halton, et al., 2006), cardiovascular disease and obesity (Fung, et al., 2001). Consumption of high fat and high sucrose diet can lead to the development of central obesity, body weight gain (Lin, et al., 2000), increasing of triglyceride, blood glucose and free fatty acids levels (Coelho, et al., 2010), impaired glucose tolerance and hyperinsulinemia (Lombardo, et al., 1996). Nowadays, obesity has been cited as a major health issue. Obesity is a metabolic disorder caused by an imbalance between caloric intake and expenditure, lead to the increase of visceral fat deposition especially in abdomen (Voshol, et al., 2009). An excess fat deposition in abdominal cavity will lead to the onset of metabolic syndrome (MetS) (Grundy, et al., 2005). The progression of the onset of MetS has been linked to obesity (Karmelic, et al., 2012). Metabolic syndrome is a cluster of metabolic disorder which includes abdominal obesity, insulin resistance, high fasting blood glucose, impaired glucose tolerance, hypertension (Simmons, et al., 2010), elevated plasma triglyceride (Spranger, et al., 2003) and decreased high-density lipoprotein cholesterol (Sorrentino, 2005). These risk factors are accepted to increase the incidence of diabetes mellitus type 2, cardiovascular disease (Rosenson, 2005), cancer and non alcoholic fatty liver disease (Angela, 2007).

The prevalence of MetS is growing rapidly. In a previous study has found that adults in worldwide approximately 20-25% have symptoms of MetS (Alberti KG, 2006). In 2011, it has been reported about the prevalence of MetS found in several areas, for example Antarctica (20%), Africa (26.6% in males and 32.2% in females), Europe (30-80% in adults), North America (35%), South America (34%), Australia

(48.2% in males and 29.9% in females) and Asia (31%) (Pudata and Konduru, 2011). The prevalence of MetS in Thai adults were 15.2% in 2007 (Lohsoonthorn, et al., 2007) and increased to 32.6% in 2011 (Aekplakorn, et al., 2011). It is foreseeable that the number of MetS in adults is substantial issue and the prevalence rapidly increases throughout the world (Zimmet, et al., 2005).

MetS induces pathophysiological changes all over the body and increasing the risk of mortality from cardiovascular disease (Lakka, et al., 2002) and type 2 diabetes mellitus (Ford, 2005b). Epidemiology of type 2 diabetes around the world is predicted to rise from 289 million in 2003 to 324 million in 2025. The world mortality rate from diabetes was 1.3 million deaths (World Health Organization, 2008). In Thailand mortality from diabetes has increased every year and rised to 7,749 deaths in 2012 (Ministry of Public Health, 2013). It would be great if there is a way to prevent the MetS at the early stages, mortality rates around the world will be reduced.

Kaempferia parviflora Wall. ex Baker (*K. parviflora*), a plant in the family of Zingiberaceae which has a black rhizome, is native to Southeast Asia, and found mainly in the North and Northeast of Thailand. *K. parviflora* has been known in Thai as krachai-dam. In Thailand, the rhizome of *K. parviflora* is used as a traditional medicine to treatment various diseases such as improving of blood flow and impotence, increase vitality, decrease pain, muscle fatigue and numbness (Department of Agriculture, 2009). Additionally, *K. parviflora* extract has many benefits such as treated of gastric ulcer (Rujjanawate, et al., 2005), used against *Plasmodium falciparum* (Yenjai, et al., 2004), inhibited cholinesterase activity (Sawasdee, et al., 2009), improved vascular endothelial function (Wattanapitayakul, et al., 2007), protected cardiovascular disorder (Malakul, et al., 2011a), inhibited nitric oxide synthase and prostaglandin E_2 (Sae-wong, et al., 2009) as well as anti-inflammatory property (Chien, et al., 2008). Therefore, the *K. parviflora* should have properties and capabilities for the treatment of various diseases. Moreover, it was used as an herbal for alternative medicine rising.

In recent times, previous study reported that in Obese Diabetes (TSOD) mice which is a genetic disease animal model in spontaneously obese type 2 diabetes, *K. parviflora* was able to reduce body weight gain and improving insulin resistance, glucose and lipid metabolism abnormalities (Akase, et al., 2011). Nonetheless, there is

less scientific data explains about the *K. parviflora* action on the improvement of metabolic disease that caused by consumption of high fat and high sucrose diet for a long time. The most incidence of metabolic syndrome is caused by the consumption of high fat and high glycemic index carbohydrate diets. For these reports demonstrated that in mice induce by high fat and high sucrose diet had body weight gain, unusual fat accumulation, increasing of insulin, leptin and blood glucose levels and progressed to dyslipidemia (Murase, et al., 2001).

Therefore, it is interesting to examine the effect of *K. parviflora* extract on mice that induce by high fat and high sucrose diet.

Objectives of the study

A general experiment objective

The present study aims to examine the effects of *K. parviflora* extract on improving of the symptoms of various disorders in mice fed with high fat and high sucrose diet.

Specific objective

To investigate the effect of KPE on body weight, blood glucose, blood pressure, oral glucose tolerance test, serum lipid profile, visceral fat deposition and structural adaptations of adipocytes in mice fed with high fat and high sucrose diet.

The scope of the study

Male C57BL/6Mlac mice were used in present study to examine the effects of KPE on the improving of abnormalities that found in mice fed with high fat and high sucrose diet. They were induced to be MetS by feeding high fat high sucrose diet for 20 weeks. After that KPE at the dose 10 and 100 mg/kg BW were orally administered for 8 weeks before determining of body weight, blood glucose, blood pressure, oral glucose tolerance test (OGTT), serum cholesterol, triglycerides and high-density lipoprotein cholesterol (HDL-C) concentration, visceral fat accumulation and an alteration in the structure of adipocytes were also examined. Blood glucose and OGTT were determined by using an Accu-Chek glucometer test. Blood pressure was investigated by tail cuff method. The serum cholesterol, triglycerides and HDL-C concentration were measured by using the enzymatic colorimetric test kits. The body

weight and visceral fat deposition were determined by weighing. The adipocytes alteration was evaluated by histological analysis.
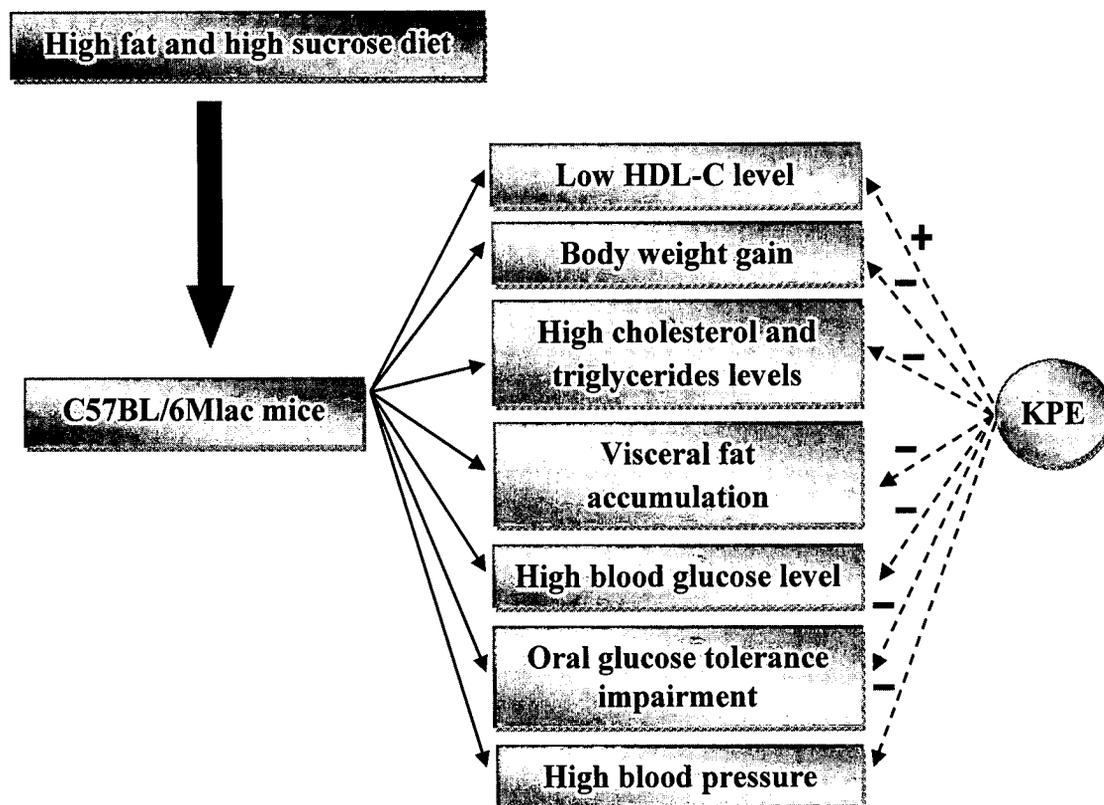

Figure 1 Conceptual framework

Hypothesis

KPE may restore the body weight gain, the high blood glucose and blood pressure, the increase cholesterol and triglycerides levels, the low level of HDL-C, the oral glucose tolerance impairment and the visceral fat deposition, which found in mice fed with high fat and high sucrose diet.

Keywords

Kaempferia parviflora, obesity, metabolic syndrome, triglycerides, high fat and high sucrose diet

The anticipated outcomes of the study

The results from this study will be anticipated to show the effects of KPE on body weight, blood glucose concentration, blood pressure, visceral fat deposition, adipocytes diameter and lipid profile in the mice model of MetS induced by high fat and high sucrose diet. It may provide an important basic knowledge that is useful for the clinical studies in the future to develop a drug for anti-MetS or supplement for health care.