CHAPTER I

INTRODUCTION

1.1 Background and Rationale

Type 2 diabetes mellitus (type 2 DM) is a chronic disorder that is characterized by high blood glucose (hyperglycemia) resulting from defects in insulin resistance and relative insulin deficiency (β-cell failure). It is the most common form of diabetes which affects 90 to 95% of all people with diabetes (Franz, 2007). Type 2 DM has become a significant public health concern because the prevalence of type 2 DM is increasing rapidly worldwide due to increasing obesity, reduced physical activity, and aging as countries become more industrialized. The total number of people with diabetes worldwide is estimated to rise from 171 million in 2000 to 366 million in 2030 (Wild et al., 2004). In Thailand, the number of people with diabetes is projected to increase almost twice over this time period from 1.54 to 2.74 million (World Health Organization, 2008). Furthermore, type 2 DM is an important cause of hospitalization, premature morbidity and mortality, particularly from its complications including increased risks of cardiovascular disease (CVD) and stroke, hypertension, retinopathy and blindness, renal disease, and neuropathy. The risk of death for people with diabetes is twice compared to people without diabetes (Fonseca, 2003).

The important goal of diabetic treatment is to achieve the best possible control of blood glucose and the risk factors of CVD such as dyslipidemia, hypertension, insulin resistance, and obesity (Asian-Pacific Type 2 Diabetes Policy Group, 2005). The initial recommended treatment for patients with type 2 DM are lifestyle

modifications including diet therapy, weight reduction and increasing physical activity. Medications are typically needed as the disease progresses. Nutrition is an essential component of overall healthy lifestyles that plays role in preventing and controlling diabetes and its complications (Fonseca, 2003; Powers, 2008). Numerous studies have attempted to identify the foods that have beneficial effects for individuals with diabetes. A number of studies reported that whey protein may have beneficial effects for individuals with diabetes and CVD (Morris and FitzGerald, 2008; Smithers, 2008).

Whey protein is natural ingredient found in any type of milk. Most of commercial whey protein products are produced from bovine whey, which is a liquid by-product of cheese production. When pasteurized whey is processed by various procedures to increase protein content, several whey products such as delactose whey, whey protein concentrate (WPC), whey protein isolate (WPI), and whey protein hydrolysate (WPH) are obtained (Miller et al., 2006; U.S. Dairy Export Council, 2004). When compared with other typical food proteins, whey protein is an excellent source of the essential amino acids (EAAs), particularly the branched-chain amino acids (BCAAs), which play a role as metabolic regulators in protein and glucose homeostasis and lipid metabolism. Moreover, whey protein contains a high content of sulfur-containing amino acids, which are important for the biosynthesis of glutathione, a tripeptide with antioxidant and immune stimulating properties (Smithers, 2008; Walzem, 2004). Beyond providing essential nutrients, findings from in vitro, animal, and human studies suggest that whey protein may reduce postprandial blood glucose, cholesterol, blood pressure, body weight, and may

increase postprandial insulin secretion and insulin sensitivity (Marshall, 2004; Yalcin, 2006; Morris and FitzGerald, 2008; Smithers, 2008).

A study on insulin resistance in rats showed that 6 weeks after feeding rat with a diet containing WPC (320 g/kg diet) significantly reduced energy intake, visceral and subcutaneous fat, and weight. The WPC diet also reduced fasting blood insulin concentration and increased insulin sensitivity, compared to a diet containing red meat (Belobrajdic et al., 2004). Nilsson et al. (2004) determined insulinotropic properties of whey protein. Twelve healthy volunteers were served test meals consisting of reconstituted milk, cheese, whey protein, cod, and wheat gluten with equivalent amounts of lactose using white bread as reference. The results indicated that postprandial blood glucose response was lower but postprandial blood insulin was higher after whey protein consumption than the bread consumption. A similar study was conducted in a group of 14 subjects with type 2 DM. Whey protein was supplemented with breakfast and lunch on day 1 and was exchanged for lean ham on day 2. The results showed that 4 hours after breakfast and 3 hours after lunch, the levels of insulin and glucose-dependent insulinotropic polypeptide (GIP) were significant higher under meals supplemented with whey protein (Frid et al., 2005).

Furthermore, several studies revealed that whey protein may have positive effects on cardiovascular health such as lowering blood pressure, body weight, and improving lipid profile. Kawase et al. (2000) conducted a study in a group of 20 healthy adult males. The subjects consumed 200 ml of fermented milk supplemented with WPC or placebo twice daily for 8 weeks. After 8 weeks, the fermented-milk group showed significantly higher HDL-cholesterol and lower triglyceride and systolic blood pressure than did the placebo group. In a study by Pins and Keenan

(2002), daily supplementation of 20-g WPH for 6 weeks in borderline hypertensive adults significantly reduced both systolic and diastolic blood pressure levels compared to the control. Consistently, a study in 90 overweight and obese subjects indicated that consuming 60 g of whey protein daily for 6 months could decrease body weight, body fat and waist circumferences (Baer et al., 2006). In a long-term clinical study, overweight and obese subjects (n = 127) who consumed 30 g daily of glycomacropeptide-enriched whey protein isolate for 6 months and 15 g daily for a further 6 months showed significantly decrease in total cholesterol, LDL-cholesterol, triglyceride, blood glucose, insulin, systolic blood pressure, diastolic blood pressure, and body weight at months 6 and 12 compared to those who consumed skim milk powder (Keogh and Clifton, 2008).

Currently, there is not enough documented information about the adverse effects of whey protein. According to clinical studies, whey protein products were generally well tolerated. No serious adverse events have been noted in participants who consumed 20-60 g daily of whey protein (Bounous et al., 1993; Frestedt et al., 2008. Grey et al., 2003; Kasim-Karakas et al., 2009; Kennedy et al., 1995; Keogh and Clifton, 2008; Micke et al., 2002; Pins and Keenan, 2002; Tienboon et al., 2009).

Research findings suggest that whey protein may be advantageous for individuals with type 2 DM. However, clinical studies documenting the beneficial and adverse effects of whey protein supplementation in type 2 diabetic patients are limited. Additional clinical studies are necessary. Therefore, this study was designed to investigate clinical outcomes, insulin resistance and adverse effects of whey protein supplementation in type 2 diabetic patients.

1.2 Objectives of the Study

The main objective of this study was to evaluate effects of whey protein supplementation on clinical outcomes and insulin resistance in type 2 diabetic patients at public health center 66, Health Department, Bangkok Metropolitan Administration. The further objective was to investigate the adverse effects of whey protein supplementation in type 2 diabetic patients.

1.3 Benefits of the Study

This study provides the information about insulin resistance, clinical outcomes and adverse effects of whey protein supplementation in type 2 diabetic patients. The study results may be helpful for consideration of whey protein supplementation in type 2 diabetic patients.

1.4 Operational Definition of Terms

Whey protein isolate: a dry powder form of whey protein that contains at least 90% protein on a moisture-free basis and little, if any, lactose or fat (U.S. Dairy Export Council, 2008).

Insulin resistance: an impaired biologic response (sensitivity) of body cells to the action of insulin that results in hyperglycemia and other metabolic abnormalities (Franz, 2007).

Clinical outcomes: clinical outcomes of the present study consist of the following parameters: fasting plasma glucose (FPG), fasting serum insulin, hemoglobin A1c (HbA1c), triglyceride, (TG), total cholesterol (total-C), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C),

uric acid, albumin, blood urea nitrogen (BUN), serum creatinine (SCr), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), and electrolytes including sodium (Na), potassium (K), chloride (Cl), and carbondioxide (CO_2), anthropometric parameters, and systolic (SBP) and diastolic blood pressure (DBP).