Chapter 2

Review of Literature

During the past few years, interest has been paid on the use of diet and lifestyle modification rather than drugs for the prevention and management of diabetes. Most of the early studies were focused on the possible role of dietary fiber in ameliorating the metabolic abnormalities of the diabetic state. Several epidemiologic studies reported that diet high in soluble fiber and insoluble fiber like grains was able to decrease blood cholesterol (Behall et al., 2004) and reduced the risks of CVD (Rimm et al., 1996; Hu et al., 2000). These fibers were able to reduce blood glucose (Hallfrisoh et al., 2000) and improve insulin sensitivity (Weickert et al., 2006) as well. Whole grain cereals, fruits and vegetables are the preferred sources of non-starch polysaccharides (NSP), recognized as resistance starch which give benefit to health. The consumption of fruits, vegetables and whole grain cereals as recommended by WHO/FAO expert can provide more than 20 g per day. This amount of NSP was derived from approximately 25 g of total dietary fibre.

2.1 Rice

Rice is one of the most important food cereals. Rice is from the genus *Oryza* and is comprised of 21 species, only two of which are cultivated: *Oryza sativa* and *Oryza glaberrima* (Juliano, 1985). *Oryza sativa* is believed to have originated in Southeast Asia, while *Oryza glaberrima* originated in West Africa (Kennedy & Burlingame, 2003). In Thailand, Khao Dawk Mali 105, commonly known in food markets as ‘‘Jasmine Rice’’ or ‘‘Thai Hom Mali Rice’’ is the most popular aromatic rice variety grown.

2.2 Rice bran

Rice bran (RB) is the hull and germ of the seeds and constitutes about 8-10% of rough rice grain (Shih et al., 1997)

Rice bran is a by-product of the rice milling industry. It is the portion of paddy between the hull and white rice grain. The hull is removed in the first stage of milling, yielding brown rice. In the second stage of milling, the outer brown layer is removed to produce white rice. The outer brown layer, called **“rice bran**”. The kernel is also removed in the second polishing step. During the process of polishing brown rice, phytochemically rich rice germ also gets mixed into the bran. About 10% weight of rough rice grain contains essential nutrients (Cheruvanky, 2000).

Rice bran is a rich source of hypoallergenic protein, oil, dietary fiber, and nutrients essential to life. Rice bran containing 34-62 % starch,15-22% oil, 24-29% dietary fiber and 6.6-9.9% minerals (Cheruvanky, 2000; Fuh & Chiang, 2001). Rice bran oil is high in polyunsaturated and monounsaturated fatty acid in their glyceride moiety and it is extraordinary heat stable. Major carbohydrate in rice bran are hemicellulose (8.7-11.4%) and cellulose (9-12.8%). Rice bran is rich in B-complex vitamin.

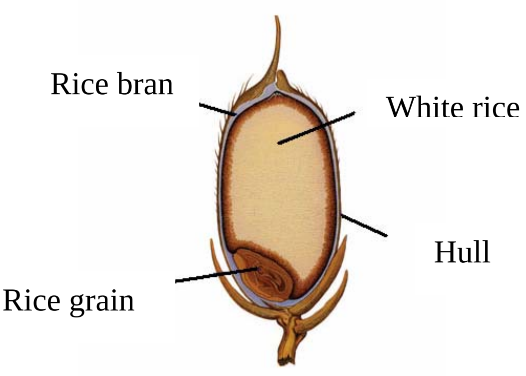


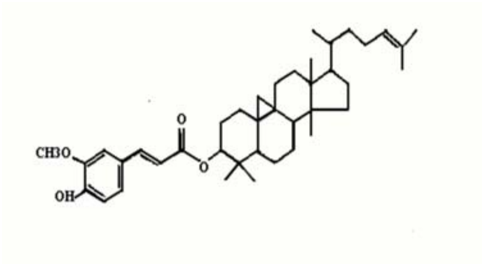
Figure 2.1

Characteristic of rice bran (http://www. products.mercola.com)

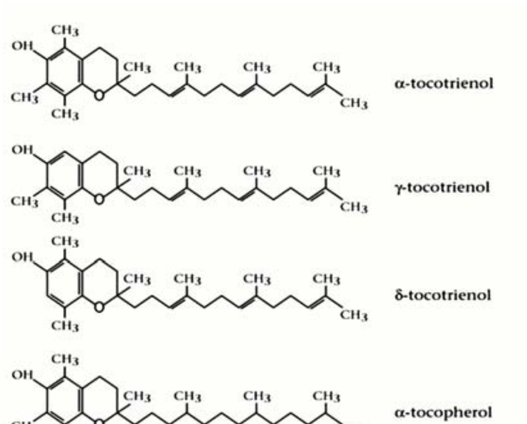
Rice bran oil is obtained from stabilized rice bran. It is considered to be a high quality health oil. Rice bran oil contain about 0.1-0.14% vitamin E and 0.9-2.9% oryzanol. The concentration can vary substantially according to the origin of the rice bran (Hu et al., 1996; Lloyd et al., 2000)

Oryzanol is a mixture of esters of ferulic acid with sterols and triterpene alcohols and has similar antioxidant properties with vitamin E (Shin et al., 1997). The 10 components of γ-oryzanol were identified as Δ7-stigmastenyl ferulate, stigmasteryl ferulate, cycloartenyl ferulate, 24-methylenecycloartanyl ferulate, Δ7-campestenyl ferulate, campesteryl ferulate, Δ7-sitostenyl ferulate, sitosteryl ferulate, campestanyl ferulate, and sitostanyl ferulate. Three of these, cycloartenyl ferulate, 24-methylenecycloartanyl ferulate, and campesteryl ferulate, was the major components of γ-oryzanol (Xu & Godber, 1999).

Cycloartenyl-ferulate



Tocotrienols



β-sitosterol

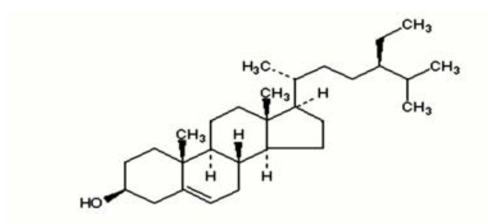


Figure 2.2

Main rice bran active components formulas: cycloartenyl-ferulate, γ-tocotrienol, β-sitosterol (Cicero & Derosa, 2005)

Table 2.1

Composition of stabilized rice bran, rice bran water soluble, and rice bran fiber concentrates

Ingredients	Stabilized rice bran (%)	Rice bran water soluble (%)	Rice bran fiber concentrates (%)
Carbohydrates	51.0*	57.5**	52.5**
Protein	14.5	7.5	20.5
Dietary fiber	29.0	6.0	42.0
Fat	20.5	26.5	13.5
Tocols (>90% tocotrienols)	350 ppm	270 ppm	30 ppm
γ-Oryzanol	3000 ppm	2600 ppm	2400 ppm
Microcomponents (γ-oryzanol, tocols, polyphenols, terpenes)	<1.1%	<0.77%	<0.92%

Source: "Effects of stabilized rice bran, its soluble and fiber fractions on blood glucose levels and serum lipid parameters in humans with diabetes mellitus Types I and II," by Qureshi et al.,2002, *The Journal of Nutritional Biochemistry*, 13,175-187.

* Complex carbohydrates (starch).

** Starch is converted to dextrins after enzyme treatment of stabilized rice bran.

Rice bran contains high level of several phytochemicals that have antioxidant activity. Since oxidative stress is considered to be a key factor in the development of DM and its complications, so rice bran was supposed to have an effect on DM. Kanaya et al. in 2004 found that rice trienol is another antioxidant which have beneficial effect on diabetic mice. Ardriansyah et al. in 2006 demonstrated that Driselase and ethanol treated fractions of rice bran contained components which have beneficial effect in lowering blood pressure and improving metabolic parameters such as lipid profile and serum glucose in stroke-prone spontaneously hypertensive rats. γ-Oryzanol from rice bran has been suggested to reduce blood cholesterol (Rukmini & Raghuram,1991; Nicolosi et al.,1991) and inhibit platelet aggregation (Eitenmiller,1997).

Kestin et al. in 1990 compared the effects of three kinds of cereal bran on metabolic profile in hypercholesterolemic men where they found rice bran and oat bran to be more superior in lowering plasma triglyceride and increasing HDL-C to total cholesterol ratio. According to Framingham Study, HDL-C to total cholesterol ratio was the best predictor of coronary heart disease. Likewise, randomized double blind study of Gerhardt et al. in 1998 demonstrated the decrease in LDL-C to HDL-C ratio when rice bran was consumed by subjects with hypercholesterolemia.

Kahlon et al. in 1992 found that full-fat rice bran (FFRB) significantly reduced plasma and liver cholesterol in hamsters, whereas defatted rice bran (DFRB) had no effect on plasma cholesterol. This was inconsistent with Newman et al. in 1992 who study in Leghorn cockerel chicks and found that DFRB increased cholesterol in all forms of lipoprotein as well as triglyceride. These results suggested the response to DFRB was either species difference or depending on the structure of DFRB during the defatting and stabilizing processes.

Rice bran and fraction from rice bran, unsaponifiable matter, appeared to reduce plasma and liver cholesterol in a dose-dependent manner in hamsters while maintaining the ratio of HDL-C to LDL-C (Kahlon et al. 1996). The possible mechanism was to increase fecal excretion of sterols. In 2007, Wilson et al. found that Oryzanol, one of the two major unsaponifiables of RBO, reduced plasma LDL-C and increased HDL-C in hamsters through the same mechanism. The study of Juliano et al. in 2005 also demonstrated that gamma-oryzanol extract from RBO is a free radical scavenger which improved the oxidative stability of oils by preventing lipoperoxidation. Indeed, an unsaponifiable component of RBO was able to reduce blood cholesterol level in healthy and moderately hypercholesterolemic humans (Most et al. 2005).

Sugano et al. in 1997 discovered that blending RBO with safflower oil at a definite proportion (7:3 wt/wt) magnified the cholesterol lowering effect in rats as compared with the effect of either oil alone.

Qureshi et al. in 2002 found that tocotrienol-rich fraction (TRF-25) of rice bran reduced the level of various parameters of lipid profile in hypercholesterolemic humans in a dose- dependent manner. Similarly, Minhajuddin et al. (2005) found that TRF from rice bran exhibited a dose-dependent decrement in blood lipid profile as well as possessing an antioxidant effect in experimentally induced hyperlipidemic rats.

Another study of Qureshi et al. in 2002 demonstrated the two fractions of stabilized rice bran, rice bran water soluble and rice bran fiber concentrates, significantly reduced serum glucose, cholesterol and LDL-C in both types of diabetic patients. The need of insulin and oral hypoglycemic agents were reduced among there patients. Serum insulin was also increased (4%) when rice bran water soluble was ingested by in both types of diabetes. In addition, soluble rice bran fraction was able to reduce serum fasting glucose and glycosylated hemoglobin in both types diabetic patients (Qureshi et al., 2002).

2.3 Insulin resistance

Insulin resistance is defined as the decreased ability of cells or tissues to respond to the action of insulin in transporting glucose from the bloodstream into muscle and other tissues. Tissues such as muscle, liver and fat are resistant to insulin which results in abnormal glucose metabolism. With insulin resistance, there is reduced glucose entry into the cell leading to excess glucose builds up in bloodstream. This causes the pancreatic beta-cells to release extra insulin leading to high blood insulin level and pancreatic exhaustion. Then, the diabetic state was soon or later established.

Insulin resistance is one of cluster of metabolic syndrome. It is sometimes called pre-diabetes or IFG or IGT (WHO, 1999). IGT or IFG and the other metabolic disorders increase the risk of diabetes (Gabir et al., 1997; Lorenzo et al., 2007)

The term IGT and IFG refer to a metabolic stage intermediate between normal glucose homeostasis and diabetes (ADA, 2004). It can be detected with one of the following tests: a fasting glucose; test which measures blood glucose after without eating. The condition where fasting glucose levels ≥110 but <126 mg/dl is called IFG, which reflects a tendency to develop diabetes. Glucose tolerance test is the measurement of blood glucose after overnight fast and using a glucose load containing the equivalent of 75-g anhydrous glucose dissolved in water. If blood glucose levels ≥ 140 but < 200 mg/dl this condition is called IGT (Grundy et al., 2004). IGT is characterized by impaired insulin secretion which is closer to the end point diabetes than IFG (Tripathy et al., 2000). Insulin resistance is directly involved in the pathogenesis of type 2 diabetes. IFG and IGT appear to be risk factors for type 2 diabetes, at least in part because of their correlation with insulin resistance (ADA, 2002). There are many causes of insulin resistance such as obesity, especially central obesity, lack of exercise and advancing age.

IFG and IGT correlate independently with the secretion and sensitivity of insulin. IFG indicates insulin insensitivity and other symptoms of metabolic syndrome. IGT indicates poor insulin secretion which accurately predict the chance to become diabetes mellitus and/or heart disease (Lorenzo et al., 2007). Glucose homeostasis can be assessed using several models of assessment. The popular indices of this assessment are the homeostasis model assessment insulin resistance (HOMA-IR), homeostasis model assessment of beta-cell function (HOMA-β) and quantitative insulin sensitivity check index (QUICKI). HOMA-IR index is derived from oral glucose tolerance test and calculated using the formula [fasting plasma glucose (mmol/L) x fasting insulin concentration (mU/L)]/22.5 (Matthews et al., 1985; Tripathy et al.,2000). QUICKI is defined by the following formula: $1/[\log I_0 + \log G_0]$, where I_0 is the fasting insulin (μU/ml), and G_0 is the fasting glucose (mg/dl) (Katz et al., 2000). While insulin secretion used in homeostasis model assessment of beta-cell function HOMA-β was proposed by Matthews et al. in 1985 and the formula is 20 x fasting insulin (μU/ml)/(fasting glucose (mmol/L)-3.5). The major advantage of both the QUICKI and HOMA-IR model is that both of them require only one blood draw from a fasting patient.

2.4 Metformin

Hyperinsulinemia and insulin resistance are common features of obesity in both humans and experimental animals (Kay et al., 2001). There are data on the role of metformin in insulin resistance associated with obesity before the development of type 2 diabetes in children by improvement in body composition and fasting insulin (Srinivasan et al., 2006) and shown improvement in body mass index (BMI), fasting serum glucose, and insulin and improved lipid profile in patients on metformin therapy for exogenous obesity with insulin resistance (Abbasi et al., 1998; Freemark M & Bursey D, 2001)

2.5 Diet induced obesity

Diet is an important factor in the promotion and maintenance of good health. Energy expenditure through physical activity is an important part of the energy balance equation that determines body weight. A decrease in energy expenditure through decreased physical activity is likely to be one of the major factors contributing to the global epidemic of overweight and obesity. Although obesity is caused by several factors, for example, genetic, hormonal and environmental factors but consumer behaviors is the most important role in its etiology. The increase in the quantity and quality of fats consumed in the diet is an important factor contributing to obesity.

Fast food is one of the major causes of obesity, since it tends to contain high fat, energy-dense, poor in micronutrients, and low in fiber. Nutritional analysis showed that fast food has high fat, high fructose, and low fiber. Hence, ones who eat fast foods have more chance to develop insulin resistance and obesity (Isganaitis & Lustig, 2005). Bowman and Vinyard (2004) showed that adults who reported frequent fast food consumed had higher mean body mass index values than those who did not eat fast food. In addition, amount of saturated fat intake about 40-75% of total kilocalories was able to reduce insulin stimulated glucose uptake (Rocchini et al., 1997; Wilkes et al., 1998)

The evidence from epidemiological studies in both rodent and human suggested that dietary intake of high amounts of fat has been shown to have adverse effects on insulin sensitivity and contribute to the development of glucose intolerance (Storlein et al., 1996; Lichtenstein et al., 2000; Hu et al., 2001). There is a direct relationship between a number and type of dietary fat and the development of human obesity and diabetes (Golay & Bobbiuni,1997). The prevalence of type 2 diabetes is generally high in countries with a fat-rich diet (Williams & Pickup, 1999)**.**

However, Bray and Popkin (1998) studied in 28 clinical trials found that reduction of 10% in the proportion of energy from fat was associated with a reduction in weight of 16 g/d (Bray & Popkin, 1998).

Abdominal obesity is the earliest symptom in composition of metabolic cardiovascular syndrome. Prevention or early treatment of this obesity can prevent or delay onset of diseases associated with this syndrome.

Several studies have examined the genetic modification in mouse fed with high-fat diet. Whereas the study of metabolism influenced by high-fat diet was mainly conducted in rats (Buettner et al., 2006). Diet-induced obese rats represents a fairly good model in human, since one may see lipid accumulating in tissue such as the endocrine pancreas as was seen in human (Bergman et al., 2006). Rats consuming diets with a fat content more than 50 percent of total calories exhibited a reduction in insulin sensitivity (Buettner et al., 2006; Storlien et al., 1993). In this study, Sprague-Dawley rat was used as a model representing the normal individual whose metabolic disorders can be induced by high-fat diet.