EFFECT OF *SYZYGIUM CUMINI* (L.) SKEELS SEED EXTRACT ON LOWERING BLOOD GLUCOSE LEVEL IN THAI PEOPLE WITH IMPAIRED FASTING GLUCOSE

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MASTER OF SCIENCE
IN
ANTI-AGING AND REGERNATIVE MEDICINE

SCHOOL OF ANTI-AGING AND REGENERATIVE MEDICINE

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Thesis Title	Effect of *Syzygium cumini* (L.) Skeels Seed Extract on Lowering Blood Glucose Level in Thai People with Impaired Fasting Glucose
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ABSTRACT

Since the global number of diabetic patients is increased continuously, it is very important to look for ways to reduce and control blood sugar levels in order to delay full blown diabetic status in the future. Until now, several herbal extracts have been found to have an effect on reducing blood sugar, such as *Syzygium cumini* (L.) Skeels seed extract. It is possible that *Syzygium cumini* (L.) Skeels seed extract could decrease fasting blood glucose (FBG) in pre-diabetic patients. In this study, 38 subjects who have impaired fasting glucose (100-125 mg/dl) were randomly divided into 2 groups. *Syzygium cumini* (L.) Skeels seed extract and placebo were given to subjects in group 1 and group 2 respectively. The subjects' levels of FBG were compared between baseline and week 4, 8 and 12 after treatment. Levels of HbA1c were compared between baseline and week 12 after treatment. The levels of FBG in group 1 with *Syzygium cumini* (L.) Skeels seed extract treatments were significantly reduced from baseline at week 4 and week 12 ($p = 0.017$ and $p = 0.040$, respectively). Furthermore, the levels of HbA1c were significantly reduced from baseline at week 12 ($p = 0.030$). However, Group 2 subject who received placebo did not show significant difference of FBG and HbA1c levels between baseline and after treatment ($p > 0.05$). The levels of FBG and HbA1c were not different between drug and placebo groups. ($p > 0.05$).

These results suggest that *Syzygium cumini* (L.) Skeels seed extract treatment in subjects with impaired fasting glucose could reduce FBG and HbA1c within 12 weeks

Keywords: *Syzygium Cumini* (L.) Skeels Seed Extract/Impaired Fasting Glucose/Fasting Blood Glucose (FBG)/Glycated Hemoglobin (HbA1c)

TABLE OF CONTENTS

TABLE OF CONTENTS (continued)

LIST OF TABLES

LIST OF FIGURES

Figure **Page**

CHAPTER 1

INTRODUCTION

1.1 Background and Rationale of the Study

Diabetes mellitus (DM) is going to increase in many countries. Globally, 171 million diabetic patients reported by the WHO in 2000. This number was predicted to increase to 336 million in 2030. (Wild, Roglic, Green, Sicree & King, 2004) According to the Bureau of Non- Communicable Diseases of Thailand, the trend of diabetic patients is set to increase from 4.4% in 1997 to 6.9% of Thais in 2009. Furthermore, 501,299 new cases of DM were found in 2011. This number was estimated to increase to a total of 8,200,000 DM patients in 2020. (นิพา ศรีช้าง, 2553, หน้า 622-624) DM is a metabolic syndrome affecting high levels of blood glucose. Many studies have proven that both beta cell impairment and peripheral insulin resistance can cause DM and lead to multiple and complex medical complications. Major complications involve both cardiovascular disease (CVD) (heart disease, stroke, and peripheral vascular disease) and microvascular disease (i.e., retinopathy, neuropathy, and microalbuminuria). (Harvey & David, 2009) From the epidemiological evidence, the minute complication could be found in normal glucose tolerance persons and slightly progressed until they became full diabetics. If we can detect the condition of prediabetes and perform the proper treatment to these patients, the progression of the disease's onset should be delayed and we can alleviate the complications of CVD and microvascular disease.

Prediabetes is the term for people who have impaired fasting glucose (IFG) or impaired glucose tolerance (IGT). According to the International Diabetes Federation, the number of people with prediabetes globally was estimated to be 340 million and is projected to be 462 million in 2030. (Rhee & Woo, 2011) Without any medical intervention, prediabetes patients are more prone to become DM type II compared to people with normal fasting blood glucose by 3.1-3.2 times within 10 years. (Zachary, 2008) The risks and adverse consequences usually occur at higher glucose levels more than lower glucose levels in patients which are currently defined as having diabetes. However, this is not an inevitable situation, as it has been found that blood glucose can be limited within normal ranges if we can control and adapt lifestyle factors such as nutrition, exercise and weight control.

Recently, the proper treatment of prediabetes patients involves an intensive lifestyle modification program because weight loss and physical activity are much more effective than any medication for reducing diabetes risk. Although According to the American Association of Clinical Endocrinologists (AACE), it is suggested that Metformin and Acarbose are the drug that should be considered for use in diabetes prevention. (Yehuda, 2008) However, the adverse effects from these drugs, such as

lactic acidosis, is a serious concern in patients with kidney and liver disease. This lays the reasons why many physicians and researchers are investigating for the alternative treatments with endeavor for prediabetes patients.

Among 1,200 plant species with anti-diabetic activity, which have been recorded to be used empirically worldwide, (Tundis, Loizzo & Menichini, 2010) *Syzyguium cumini* (L.) Skeels or Eugenia jambolana is in Myrtaceae which is a family of large evergreen trees (15-25 m) originating in tropical Asia. *S. cumini* was found in several countries. In Thailand, *S. cumini* is found in Petchaburi province. It was found that the potential benefit of *S. cumini* came from its seed. (Ravi, Sekar & Subramanian, 2004) In animal models, it was found that FBG and HbA1c were significantly decreased after *S. cumini* (L.) Skeels seed extract administration in DM rats and rabbits. (Sridhar, Sheetal, Pai & Shastri, 2005; Sharma, Nasir, Prabhu & Murthy, 2006; Sharma, Balomajumder & Roy, 2008; Sharma, Rajpoot, Nasir, Prabhu & Murthy, 2011)

Several studies have demonstrated that *S. cumini* (L.) Skeels seed extract could decrease FBG and 2 hr postprandial blood sugar in DM patients. In this time many researches don't have side effect or adverse event after *S. cumini* (L.) Skeels seed extract administration. (Ramahandridona & Rakotondravoavy, 1985; Sahana et al., 2010; Yarnell, Abascal & Rountree, 2009)

In conclusion, the potential effects of *S. cumini* (L.) Skeels seed extract are: (1) It could inhibit carbohydrate hydrolyzing enzymes, including Alpha-Glucosidase, Alpha-amylase, and Sucrase, thus reducing blood glucose postprandial. (Menakshi, Smita, Shobha, Ameeta & Bimba, 2008) (2) It could increase glucose uptake activities by elevating the expression of GLUT4. (Rajasekar ,Kirubanandan & Lakshmi, 2009) (3) It could inhibit the uptake of glucose transport at intestinal brush border membrane. (David, Theras, Hemachandran, Elumalai & Thirumala, 2010) From the above mechanisms, it is possible that *S. cumini* (L.) Skeels seed extract could be the best treatment to decrease FBG in prediabetes patients. However, the reports of its potential effects in prediabetes treatment is still limited. The objective of this study is to determine the effects of *S. cumini* (L).Skeels seed extract on decreasing levels of FBG & HbA1c in impaired fasting glucose subjects. We expect that *S. cumini* (L).Skeels seed extract will be an alternative treatment in the new strategy to delay overt DM.

1.2 Research Objectives

To study the effects of *Syzygium cumini* (L.) Skeels seed extract on lowering blood glucose level in Thai people with impaired fasting glucose.

1.3 Research Question

Is there any effect of *Syzygium cumini* (L.) skeels seed extract on lowering blood glucose level in Thai people with impaired fasting glucose?

1.4 Research Hypothesis

Oral administration of *Syzygium cumini* (L.) skeels seed extract for 12 weeks can reduce fasting blood glucose and HbA1c in Thai people with impaired fasting glucose.

1.5 Conceptual Framework

Normally when we eat starch, the carbohydrate hydrolyzing enzymes from salivary gland and pancreas in our body will be digest into monosaccharide which can be absorb through the small intestine by glucose transporter. Then the monosaccharide will diffuse through the capillaries to the blood circulation and will cause hyperglycemia. Insulin will secrete to decrease the blood glucose by binding with the receptor at the cell membrane and will activate the GLUT4 expression to completely shift the glucose into the cells.

From the information of *Syzygium cumini* (L.) Skeels seed extract, the mechanisms are as the following: 1.It could inhibit carbohydrate hydrolyzing enzymes (Alpha-Glucosidase, Alpha-amylase,Sucrase) 2.It could inhibit the uptake of glucose transport via intestinal brush border membrane 3.It could increase glucose uptake activities by elevating the expression of GLUT4. With these three mechanisms, it reduces the glucose after meal.

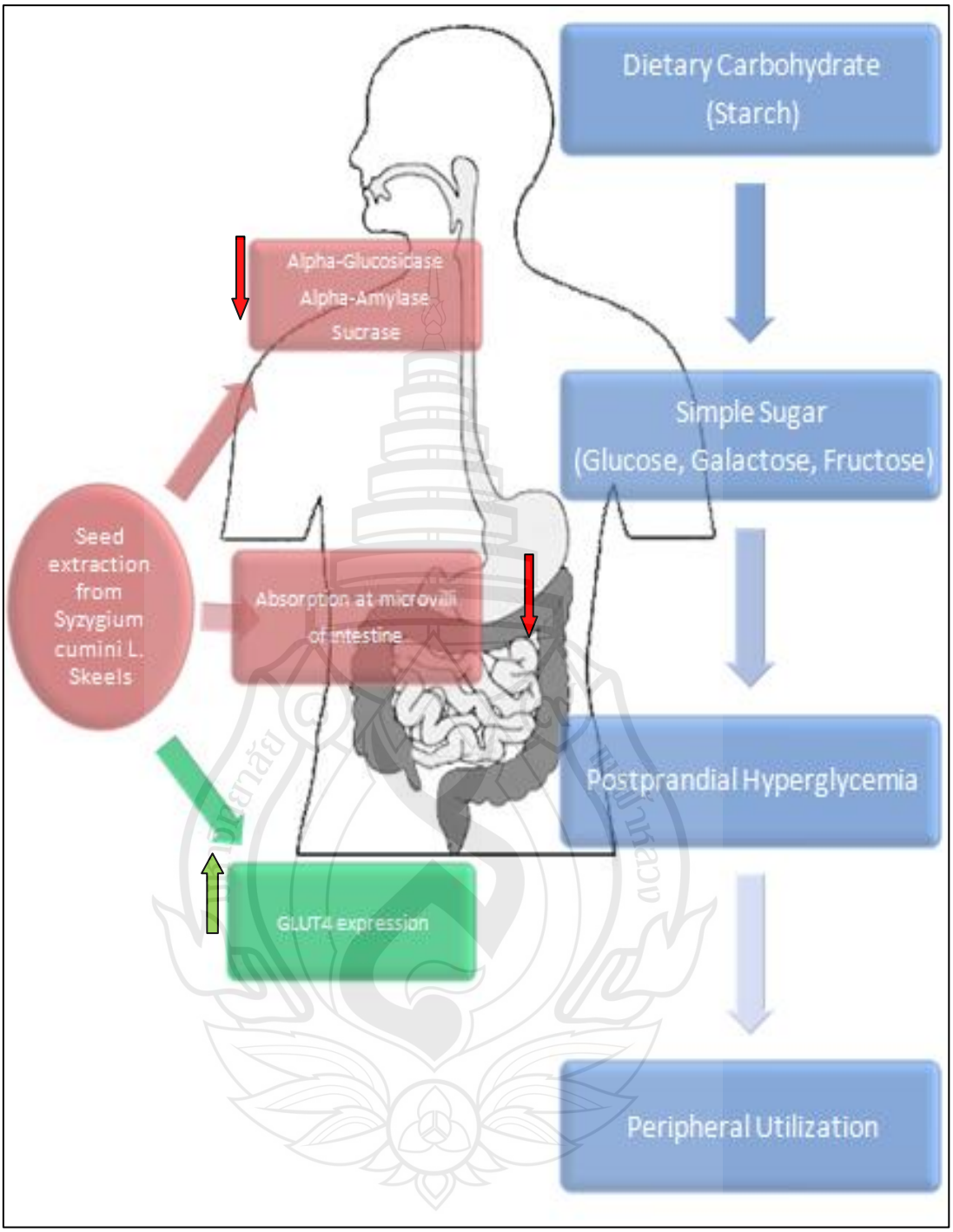


Figure 1.1 Conceptual Framework of Study

1.6 Contribution of the Study

1.6.1 The study findings may support herbal medicine promotion on reducing blood glucose in impaired fasting glucose people.

1.6.2 To reduce the incidence rate of DM type II patients.

1.6.3 To encourage using of Thai herbs in treatment.

1.6.4 To be source of relevant information for further investigation.

1.7 Scope of Research

We will include the volunteers who are circumference in Bangkok, male and female and aged between 20-60 years.Their fasting blood glucose has to be in a range of 100-125mg/dl at 9.00 am. Who come to the Srinakarin medical clinic during December 2011 to January 2012.

They will be recruited and divided into two groups, one group receiving lifestyle modification with *Syzygium cumini* (L.) Skeels seed extract, the other group receiving lifestyle modification with placebo. Subjects will be required to come back to the Srinakarin medical clinic after 4 weeks, 8 weeks and 12 weeks of supplementation. Follow up measures will include general interview, fasting blood glucose and HbA1c. Data on changes of fasting blood glucose and HbA1c will be analyzed and compared within the group, at 4 weeks, 8 weeks and 12 weeks and between groups at the same period of investigation.

1.8 Terms and Definition

1.8.1 DM Diabetes mellitus: A chronic disease, which occurs when the pancreas does not produce enough insulin, or when the body cannot effectively use the insulin it produces.

1.8.2 Pradiabetes Prediabetes: Intermediate stage between completely normal glucose levels and type II DM which includes impaired fasting glucose and impaired glucose tolerance.

1.8.3 IFG Impaired fasting glucose: Fasting blood glucose levels of 100 to 125 mg/dl.

1.8.4 IGT Impaired glucose tolerance: Blood glucose levels of 140 to 199 mg/dl 2-hour postprandial.

1.8.5 FBG Fasting blood glucose: A test to determine how much glucose (sugar) is in a blood sample after an overnight fast. The fasting blood glucose test is commonly used to detect diabetes mellitus.

1.8.6 HbA1c Glycated hemoglobin: A form of hemoglobin that is measured primarily to identify the average plasma glucose concentration over prolonged periods of time. It is formed in a non-enzymatic glycation pathway by hemoglobin's exposure to plasma glucose.

CHAPTER 2

LITERATURE REVIEW

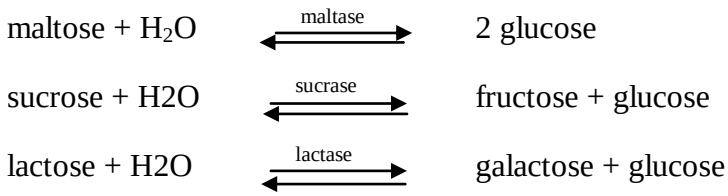
2.1 Carbohydrate Digestions and Metabolisms

2.1.1 Carbohydrate Digestions

Digestion is basically the process of food breakdown, both mechanical and chemical. Food needs to be digested into smaller components so that they can be more easily absorbed into the body.

When referring to normal food intake, the process of digestions begins since the food enters the mouth. The teeth are the first organ that is responsible for mechanical digestion, grinding the food into smaller pieces. Carbohydrate, in particular, will be digested chemically by a salivary enzyme known as alpha-amylase. Salivary alpha-amylase is specific for digesting only carbohydrate glycosidic bond of type alpha (1->4). The final products of the process are mainly dextrins, which is an oligosaccharide that comprise of an average of 8 to 10 units of monosaccharides, primarily glucose, with a slight amount of maltose and maltotriose. Branched-chain glycosidic bond of type alpha (1->6) can also be found in dextrins. All of the products then continue toward the stomach.

The stomach has a very high level of acidity, inhibiting the action of amylase enzymes which are attached with the food. Thus, carbohydrate digestions do not occur while in the stomach. The food then continues downward into the small intestine, starting with the duodenum. Duodenum provides a variety of enzymes which aid in the digestion and absorption process. Pancreatic alpha-amylase is released from this point. It is responsible for the digestion of dextrins into smaller molecules of sugar, namely maltose, maltotriose, and other oligosaccharides with 3 to 5 units of glucose (alpha-limit dextrins). These oligosaccharides contain branched-chain glycosidic bond of type alpha (1->6). They are further digested into monosaccharides by several types of enzymes, including dextrinase (paired with dextrins), maltase (paired with maltose), sucrase (paired with sucrose), and lactase (paired with lactose), respectively.



The latter process completes the process of carbohydrate digestions. Monosaccharides will then go through the process of absorption into the bloodstream. (ศุภศิษฐ์ อรุณรุ่งสวัสดิ์, 2552, หน้า 162-163)

2.1.2 Carbohydrate Absorptions

Most of the carbohydrate molecules which are orally administered are primarily absorbed at jejunum in the form of monosaccharides. D-Glucose is the commonly found monosaccharides, followed by a fewer amount of D-Fructose and D-Galactose. Other types of hexose may also be found, such as mannose. These simple sugar molecules are absorbed at a higher rate than simple diffusion. Each type of monosaccharide is absorbed at different rates. This depends on the transport molecules which are type-specific. The absorption mechanism requires these transporters, which are specific protein molecules located at intestinal cell membrane.

D-Glucose absorption mechanism is an active transport, requiring energy to function. Sodium atoms are required to be uptake together with the glucose molecule. Sodium atoms will bind with the cell membrane proteins, allowing D-Glucose molecules and the sodium atoms to be let through. Sodium atoms then return out of the cells for further use, exchanging themselves with potassium atoms. These processes require a system of enzymes known as the Sodium-Potassium ATPase which require energy from the catabolism of ATP molecules. D-Galactose absorption process happens similarly to the previous mentioned mechanism.

The absorption mechanisms of D-Fructose and D-Mannose also require transporters which are cell membrane proteins. The difference is that they do not require sodium atoms. This mechanism is called facilitated diffusion. Absorption of this type happens at a faster rate than simple diffusion.

Other types of monosaccharides that can be absorbed by the human body include pentose, L-Glucose, L-Galactose, and L-Fructose. They are absorbed through simple diffusion.

After the absorption process at the small intestine, monosachharides are released from the intestinal wall into the bloodstream, feeding the liver and other cells throughout the body.

The rate in which each tissue absorbs the glucose into its cells is different. This depends on the Glucose Transporter (GLUT), which is a type of protein embedded in the cell membranes of different tissues. Several types of GLUT are different in properties, and different tissues have different number of each GLUT type. For instance, the skeletal muscles' and adipose tissues' cell membranes contain a certain type of GLUT (GLUT4) which is uniquely stimulated by the hormone insulin. Stimulation of GLUT4 by insulin molecules accelerates the glucose uptake of the latter tissues. However, GLUT proteins at hepatic cells are different and are not as much sensitive to insulin stimulation. (พัชรี บุญศิริ, เปรมใจ อารีจิตรานุสรณ์, อุบล ชาอ่อน และปีติ ธุวจิตต์, 2551, หน้า 210-213)

2.1.3 Cellular Glucose Uptake

Cells all over the body have insulin receptors embedded in their membranes. Glucose uptake from the bloodstream is triggered when insulin molecules bind to these sites. The insulin receptors are categorized as a member of the tyrosine kinase protein receptor group.

The primary mechanism of these insulin receptors is known as Phosphorylation. It is the process of addition of a phosphate group to tyrosine molecules. The precursor of this process is called the IRS1, standing for insulin receptor substrate 1. It is essential for the regular function of GLUT4. GLUT4 is sequestered in intracellular vesicles in skeletal muscles and adipose tissues during the absence of insulin. The binding of insulin molecules to their specific receptors trigger the phosphorylation of GLUT4 in several cells all over the body. The active GLUT4 then allows glucose molecules in the bloodstream to be uptake into the cell, completing the process of glucose transportation. (Bowen, 2009)

2.2 Diabetes Mellitus

2.2.1 Definition of DM

The World Health Organization (2011) defined DM as, 'A chronic disease, which occurs when the pancreas does not produce enough insulin, or when the body cannot effectively use the insulin it produces. This leads to an increased concentration of glucose in the blood (hyperglycemia).

2.2.2 Incidence of DM

According to the statistics from all 191 WHO member states and the predictions of DM in 2004, the incidence of DM for all age-groups was expected to be 2.8% in 2000 and tended to reach almost double (4.4%) in 30 years later. In other word, the amount of DM patients will tremendously increase from 171 million in 2000 to 336 million patients in 2030 especially in those aging population (age >65 years old). (Wild at al., 2004) Center for Disease Control and Prevention (2011) reported the incidence of DM in the United States (U.S.) up to 26 million patients with 79 million of prediabetes in 2011. Of all DM patients, according to the report by National diabetes fact sheet, 27 percent (7 million) of DM patients do not realize that they have diabetes.

Regarding incidence in Thailand, the amount of DM patients gradually increased from 4.4% in 1997 to 6.9% in 2009. The ratio of new cases of DM in 2020 versus cases in 2011 is about 16 times (estimations of 8,200,000 new DM patients in 2020 and 501,229 new DM cases in 2011, respectively). (นิพา ศรีช้าง, 2553, หน้า 622-624)

2.2.3 Importance of DM

DM is a very important illness as it is a prime cause of morbidity and mortality in the U.S. In 2002, the medical expenses of DM patients were about $13,243 per year whereas non-DM patients spent only $2,560 per year. In addition, it is the cause of blindness in U.S. population with the age range of 20-74 years. Moreover, the diabetic retinopathy accounts for 12,000 – 24,000 newly blind persons every year. It is, also, a

prime cause of end stage renal disease (ESRD) in the U.S. where 44% of these new cases acquired DM prior to ESRD. Furthermore, the high incidences of lower limb amputations of DM patients are 15-40 times higher than those DM-free healthy controls. (Hogan, Dall & Nikolov, 2003)

DM patients are at risk of developing the cardiovascular disease, it is also the main cause of death in type II diabetes as shown by two thirds die of heart disease or stroke. The risk of developing the CVD is 2-4 times higher than normal. According to the statistics, the emergency department utilization of DM patients was twice as much as those non-DM patients. (Romesh et al, 2011)

According to the information, it is necessary to study and design the appropriate healthy care for DM patients.

2.2.4 Classifications of DM

2.2.4.1 Type I diabetes (β-cell destruction, usually leading to absolute insulin deficiency) Immune-mediated diabetes

Type I DM can be found 5-10% among all DM patients. In the past, this type of DM was so called; 'insulin-dependent diabetes', 'type I diabetes', or 'juvenile-onset diabetes.' At present, the main reason for this type of DM is cellular-mediated autoimmune destruction of the β-cells of the pancreas. Moreover, one and usually more of these autoantibodies are present in 85-90% of individuals detected with fasting hyperglycemia.

The crucial complication of DM is ketoacidosis as a matter of fact that it can be found as the first manifestation of the disease. Moreover, under sepsis condition or stress, hyperglycemia can increase dramatically which may cause the comorbidity with ketoacidosis. Adults with adequate β-cell function can prevent ketoacidosis for many years. However, as the condition progresses forward, insulin supplementation becomes necessary since the blood insulin level becomes low and later runs out.

2.2.4.2 Type II diabetes (ranging from predominantly insulin resistance with relative insulin deficiency to predominantly an insulin secretory defect with insulin resistance)

This type of DM can be found in 90-95% among DM patients. It was called in the past as; 'non-insulin-dependent diabetes', 'type II diabetes', or 'adult-onset diabetes.' This type of DM is also regarded to those with insulin resistance and insulin deficiency. Type II DM differs from Type I DM as it is not necessary to supplement insulin to survive at the development of the disease. (American Diabetes Association, 2004)

Though this kind of DM is multi-factorial, obesity is one of the most observable factors since it can cause insulin resistance. However, sometimes DM can be found in pear-shaped obesity or even in non-obese patients with hyperlipidemia. Generally, type II DM patient received quite late diagnosis with observable macrovascular and microvascular complications since the symptoms are not predominant at the initiation of the illness. Moreover, the insulin level of this group will be normal or moderate hyperinsulinemia because the insulin homeostasis will try to compensate the insulin resistance condition. (Romesh et al, 2011)

Ketoacidosis can also be found with this type of DM with high stress or infection.

Table 2.1 Criteria for Diagnosis of Diabetes

	Test	Results
1.	HbA1C	≥ 6.5%
2.	FBG	≥126 mg/dl (7.0 mmol/l) Fasting is defined as no caloric intake for at least 8 hours.
3.	2-h blood glucose	≥200 mg/dl (11.1 mmol/l) during and OGTT. The test should be performed according to WHO, using glucose load containing equivalent of 75g anhydrous glucose solution.
4.	Random blood glucose	≥200 mg/dl (11.1 mmol/l) Verified test should be conducted if result shows normal value or close to normal value in hyperglycemic patient.

Notice: Since this study aimed at Type II diabetes and Prediabetes condition, other details of DM will be limited. (Romesh et al, 2011)

2.2.5 Pathophysiology of Type II Diabetes

The pathophysiology of type II DM can be characterized by both peripheral insulin resistance and relative insulin deficiency as follows: (Paul & Kenneth, 2009)

2.2.5.1 Loss of first-phase insulin release which leads to postprandial hyperglycemia,

2.2.5.2 Peripheral insulin resistance which refers to body tissues (muscle, lipid, liver) inefficiently response to insulin,

2.2.5.3 Insulin deficiency which is caused by β-cell of pancreas works deficiently

At initial, the pancreas will continue secreting insulin to compensate the insulin resistance condition which maintains blood sugar level. However, when prolonged with the condition, β-cells will be decreased and later caused impaired various conditions such as: glucose tolerance condition, postprandial hyperglycemia, impaired fasting glucose and finally Type II DM.

As Type II DM is multifactorial disease, the factors which are associated with disease progressions include genetic predisposition, environmental factors (obesity, physical inactivity, aging) and acquired defect. However, the factor which is proven associated with peripheral and hepatic insulin resistance in men and women with type II diabetes is abdominal adiposity. Regardless of controversy about its relation with disease, the theory of the releases of free fatty acids, tumor necrosis factor-α, interleukin-1 and -6, and resistin, as well as the decreased release of adiponectin from adipose tissue may cause insulin resistance.

Though primary pathophysiology defect of type II DM are insulin resistance and β-cell dysfunction, sometimes it can be caused by excessive hepatic glucose production and increase glucagon secretion from alpha cell of pancreas. In fact, it may be caused by decreased glucose homeostatic hormones such as Amylin and the incretin hormones glucagon-like-peptide-1 (GLP-1) and glucose-dependent insulintropic polypeptide (GIP). The result of decreased hormones is that it may cause the hyperglycemia. The prolonged hyperglycemia will lead to insulin resistance and decrease the insulin secretion which causes DM.

2.2.6 Risk Factors for Type II DM

2.2.6.1 Age greater than 45 years

2.2.6.2 Weight greater than 120% of desirable body weight

2.2.6.3 Family history of type II DM in a first-degree relative

2.2.6.4 Hispanic, Native American, African American, Asian American, or Pacific Islander descent

2.2.6.5 History of previous impaired glucose tolerance (IGT) or impaired fasting glucose

2.2.6.6 Hypertension (>140/90mmHg) or dyslipidemia (high-density lipoprotein [HDL] cholesterol level <40 mg/dl or triglyceride level >150 mg/dl)

2.2.6.7 History of gestational DM or delivery a baby with a birth weight of >9 lb

2.2.6.8 Polycistic ovarian syndrome (which results in insulin resistance) (Romesh et al, 2011)

2.2.7 Symptoms of type II diabetes

Early symptoms: (Ari, 2011)

2.2.7.1 Polyuria and frequent urination

2.2.7.2 Nocturia

2.2.7.3 Polydipsia

2.2.7.4 Fatigue and weakening

2.2.7.5 Weight loss (especially for overweight people)

2.2.7.6 Frequent sepsis, e.g. dermal infection

2.2.7.7 Unhealed wound

First symptom of type II DM: (symptoms may not show in some patients)

2.2.7.8 Blurred vision

2.2.7.9 Erectile dysfunction

2.2.7.10 Pain or numbness in the feet or hands

2.2.8 Complications of type II DM

2.2.8.1 Diabetic retinopathy

This complication is caused by the invasion of glucose into endothelium of retina arterioles and later caused the glycoprotein production for the basement membrane layer and leads to thickening of arterioles. When the fragile thickened arterioles are torn, the blood and plasma will leak and cause macula to swell which. This causes the blurred vision. The torn arterioles will be regenerated and will cause the retina impairment. The worst complication for this is blindness after the chronic retina impairment.

2.2.8.2 Diabetic nephropathy

Kidneys of the DM patients are always prone to renal impairment and failure which are due to the pathological disorders of the glomeruli basement membrane. It will allow albumin to pass the membrane of at the nephron to the filtrate. Proximal tubule will be responsible for chemical reabsorption. The prolonged overwork of proximal tubule leads to renal failure. The life duration after being diagnosed renal failure in general is 3 years.

2.2.8.3 Diabetic neuropathy

DM causes the pathology at arterioles which support the extremities and later causes the nerve numbness or pain. This neuropathy will prevent the patient from acknowledgement of the diabetic wounds which may cause gangrene and amputation. Erectile dysfunction or impotence can also be found in male patient.

2.2.8.4 Coronary vascular disease

DM causes the stimulation of body blood vessels degeneration. Together with the degeneration of the coronary vascular, DM, and hyperlipidemia, myocardia infarction can happen through the blockade of coronary artery. In some DM patients, myocardiac muscles work inefficiently due to the blockade and the fragile arteries. The best medical treatment so far is to perform the cardiac transplantation. In DM patients, they will not realize if they have cardiac problem until major symptoms are shown such as acute myocardial infarction.

2.2.8.5 Cerebrovascular disease

DM patients are at risk of paralysis due to stiffed blood vessels. If the stiffed blood vessels exist in brain, paralysis may happen. In general, DM patients acquire 2-4 times higher to become paralysis which can be observed from acute fatigue, extremities immobilization, visual loss, and severe headache.

2.2.8.6 Diabetic ulcer

This can be found on foot which may further cause gangrene and amputation.

2.2.8.7 Peripheral vascular disease

As for the insufficient blood supply at the extremities, DM patients may experience cramps, gangrene, etc. (Harvey & David, 2009)

2.2.9 Treatment for Type II DM

Blood glucose should be maintained at near-normal levels (preprandial of 90-130 mg/dl)

Hemoglobin A1C should be less than7 %.

DM Patients should do as follows:

2.2.9.1 Lifestyle Modification

1. Weight loss Reduce weight 5-10%
2. Exercise moderate-intensity aerobic activity, 30-90 min/day or 150 min/week and weight training 3 times/week
3. Diet control Consider portion control, carbohydrate intake, glycemic index and glycemic load and should consider the total fat and saturated fat, cholesterol, carbohydrate, fiber, and protein intake.

2.2.9.2 Drug

Lifestyle modification treatment should be used with all patients, however; drug treatment should be considered seriously due to that 80% of type II DM patients are depending on insulin control medicine. (Paul & Kenneth, 2009) Medicine can be arranged into groups as follows:

Table 2.2 Medicine for Diabetes

Class	Examples	Primary mode of action	Route of glycemic control	Adverse event
Alpha-glucosidase Inhibitors	Acarbose, Miglitol	Inhibit enzyme central to digestion of carbohydrates	Postprandial glucose	Diarrhea, abdominal pain, flatulence, ↑ transaminases
Biguanides	Metformin	↓Hepatic glucose production,↑muscle sensitivity to insulin	Fasting glucose, insulin sensitivity	Diarrhea, nausea, lactic acidosis
DPP-4 inhibitors	Sitagliptin	Inhibition of DPP-4 results in ↑GLP-1	Postprandial glucose	Upper respiratory infection, nasopharyngitis, headache
Meglitinides	Nateglinide, Repaglinide	Beta-cell secretagogue	Fasting and postprandial glucose	Hypoglycemia
Sulfonylureas	Glimepiride, Glipizide, Glyburide	Beta-cell secretagogue	Insulin sensitivity, postprandial and fasting glucose	Hypoglycemia, weight gain
Thiazolidinediones	Pioglitazone, Rosiglitazone	Enhanced peripheral insulin sensitivity, improved hepatic insulin sensitivity	Postprandial glucose	Fluid retention, weight gain, heart failure
Amylin analogues	Pramlintide	↓Glucagon secretion, gastric emptying, and food intake	Postprandial glucose	Nausea, hypoglycemia
Incretin mimetics	Exenatide	↓Glucagon secretion, gastric emptying, and food intake; ↑insulin secretion	Fasting and postprandial glucose	Nausea, diarrhea, hypoglycemia, pancreatitis
Insulin	-	-	Fasting and postprandial glucose	Hypoglycemia, weight gain

From Mark, W. S., Byron, J. H., Patrick, J. B., Stephen, M. G. & Dirk, O. W. (2008). Managing type 2 diabetes: Going beyond glycemic control. **Journal of managed care pharmacy, 14**(5), 1-19.

2.2.9.3 Monitor complication

1. HT: BP goal be below 130/80 mm Hg.

In patients with greater than 1 g/d proteinuria and renal insufficiency, goal should be considered (ie, 125/75 mm Hg)

2. Lipid: age >40 years with a total cholesterol >= 135 mgl/dl should received statin therapy to achieve an LDL <100mg/dl. However, if CVD available, patient should use statin LDL <70 mg/dl.

3. Cardiovascular events, due to the cause of DM, all patients should be prevented by using low-dose enteric-coated aspirin. For patients with aspirin hypersensitivity or intolerance, clopidogrel is recommended.

4. Eye see ophthalmologist every 6-12 months. Three-year retinal screening may be feasible for patients with mild diabetes and no retinopathy.

5. Peripheral neuropathy is the frequently found condition which the patients come with paresthesias, numbness, or pain. Moreover, blood sugar control will help decrease the symptoms.

6. Infection, DM patients have higher chance to become sepsis especially; Malignant otitis externa, Rhinocerebral mucormycosis, Bacteriuria, Pyuria, Cystitis, Upper urinary tract infection, Intrarenal bacterial infection, Skin and soft tissue infections, Osteomyelitis

7. Parkinson disease is 36% higher in those with diabetes mellitus and Type II DM patient usually found higher rate of pancreatic neoplasm than normal especially aged 45-65 years.

8. Considerations during surgery, Bariatric surgery can be used in morbidly obese patients; bariatric surgery has been shown to improve diabetes control and, in some situations, normalize glucose tolerance. It is certainly a reasonable alternative in carefully selected patients if an experienced team (providing appropriate preoperative evaluation as well as technical surgical expertise) is available**.** (Romesh et al, 2011)

As a matter of fact that DM has high chance of complication and mortality, it is possible to prevent or protect from complications. Prior to the insulin resistance, and insulin deficiency, type II DM patients generally acquire prediabetes condition.

2.3 Prediabetes

2.3.1 Definition of Prediabetes

Prediabetes means intermediate stage between completely normal glucose levels and type II DM which includes impaired fasting glucose and impaired glucose tolerance. (Vanita & Robert, 2008)

2.3.2 Incidences

The estimation of those with IGT condition worldwide is around 340 million and the amount will increase at the rate of 8.4% (462 million) by the year 2030. (Rhee & Woo,2011) Regarding to geographic distribution, North America (10.4%) holds the higher percentage of geographic distribution than Europe and Middle East. In U.S., 57 million people were found to have the prediabetes conditions. In Thailand, the incidences of prediabetes were 13.6/1000 persons in male and 6.4/1000 persons in female, respectively. The age range with the highest incidence of prediabetes was at 35-60 years (6.2/1000 persons). (นิพา ศรีช้าง, 2010)

2.3.3 Importance of Prediabetes Condition

Prediabetes patients are more prone to become DM type II compared to people with normal fasting blood glucose by 3.1-3.2 times within 10 years. (Zachary, 2008) Furthermore, the death rate increases linearly when the blood sugar increases from 95 to 200 mg/dl. Not only the mortality changes in prediabetic, those with IGT condition acquire high risk (13%) to become diabetic retinopathy almost the same rate as those with DM. Other studies suggested the high possibility to become hypertensive within 3 years as well as increase the rate of CVD (5%) within 4 years. In addition, hyperglycemia may cause an increase in sudden death as shown in 23-year-follow-up study. (Laurie, 2009)

2.3.4 Criteria for Diagnosis Prediabetes

Prediabetes condition is defined as followings :

2.3.4.1 Impaired fasting glucose (IFG): fasting blood glucose levels of 100 to 125 mg/dl.

2.3.4.2 Impaired glucose tolerance (IGT) with blood glucose levels of 140 to 199 mg/dl 2-hour postprandial.

2.3.4.3 HbA1c of 5.7 to 6.4% (Rhee & Woo, 2011)

However, in 2010, Lorenzo et al. reported the comparison of HbA1c versus fasting blood glucose and 2-hour blood glucose in prediabetes as HbA1c at the range of 5.7 – 6.4% was more selectivity in detecting at-risk individuals than IFG and IGT. On the other hand, IFG had the high sensitivity in broad screening. (Carlos, 2010)

2.3.5 Pathophysiology of Prediabetic Condition

The pathophysiology of type II DM are increased insulin resistance and decreased insulin secretion. The recent study found the distinguishable characteristics between subtypes of IFG and IGT patients.

2.3.5.1 Perspective on insulin resistance

IFG tended to have hepatic insulin resistance comorbidity whereas IGT tended to have predominant peripheral insulin resistance. However, when compared both groups with normal control, both hepatic and peripheral insulin resistance conditions are significantly recognized.

2.3.5.2 Perspective on insulin secretion

Basically, progressive β-cell failure is the cause of type II DM development. The secretion of pancreatic insulin occurs biphasically; the sharp increase at the early phase secretion and late phase secretion can be divided by post-continuous glucose stimulation during initial glucose loading. This is well-regarded that a reduction in insulin secretion due to β-cell failure is an early step in NGT and prediabetic stages. However, there are different insulin secretions in each subtype of prediabetes. The study based on oral glucose tolerance found the decrease of early-phase insulin secretion in IFG whereas the IGT patient acquired the decreased late-phase insulin secretion.

2.3.5.3 Racial difference in the pathophysiological characteristics of prediabetes

From abovementioned information, it is obvious that there are differences in both insulin resistance and insulin secretion in both IFG and IGT subgroups. However, the different study showed increased insulin resistance in IFG and reduced insulin secretion in IGT which may be related to the unknown pathway regarding the prediabetic control. (Rhee & Woo, 2011)

2.3.6 Prediabetes risks factors

According to the report from American Diabetes Association, the recommendation for prediabetes check-up should be done in men and women age of 45 years and older especially those with a body mass index (BMI) at or above 25 (for the age below 45 years, the BMI will be the decision criteria). (Francine, 2010) The risk factors of prediabetes generally resemble to those of DM.

2.3.6.1 Overweight or obese

2.3.6.2 First-degree family history of diabetes

2.3.6.3 Being age 45 or older

2.3.6.4 Sedentary lifestyle

2.3.6.5 Low HDL cholesterol (35 mg/dl; 0.90 mmol/l) and high triglycerides (250 mg/dl; 2.82 mmol/l)

2.3.6.6 High blood pressure (consistent reading of 140/90 mmHg or higher)

2.3.6.7 History of gestational diabetes or gave birth to a baby weighing more than 9 pounds

2.3.6.8 Belonging to one of the following ethnic populations: African Americans, Native American Indians, Latinos, Asian Americans, Pacific Islanders

2.3.6.9 Having polycystic ovary syndrome (PCOS)

2.3.6.10 Having a history of vascular disease

2.3.7 Treatment for Prediabetes

Table 2.3 Treatment for Prediabetes

Treatment	The results of treatment
1. Lifestyle modification	Reduce weight 5-10%
1) weight loss	Moderate intensity, 30-60 mins/day at least 5 days/week
2) exercise	Low in total fat, saturated fat, trans-fatty acid, adequate fiber, low sodium intake, and cease alcohol consumption.
3) diet control	
2. Drug	FDA does not approve any medication for prediabetes. However, in addition to life style modification in high risk group, metformin and acarbose may be prescribed.
3. Lipid level control	Same as DM group. Statin may be prescribed in order to achieve the goal of LDL 100 mg/dL, non-HDL lipoprotein of 130 mg/dL, and apolipoportein at 90 mg/dL. Possibly prescribe fibrates, bile acid sequestrants, and ezetimibe in some patients.
4. Blood pressure control	Systolic < 130 mmHg and diastolic at 80mmHg. Angiotensin-converting enzyme inhibitors or angiotensin receptor blockers are recommended for prescription.
5. Aspirin	If patient has no underlying conditions, it is possible to describe. (increased risk for gastrointestinal tract, intracranial, or other bleeding)

From Laurie, B. (2009, July). New AACE Guidelines for Prediabetes Management. **Medscape**. Retrieved August 20, 2011, from http://www.medscape.org/viewarticle/578048.html

Diabetes Prevention Program Research Group (2002) reported the lifestyle modification in IGT patients that it helped decrease DM incidence. The result of liftstyle modification is better than Metformin. However, it was very difficult to implement and maintain.

Up to this point, it is necessary to start the healthcare process from prediabetic condition prior to type II DM development. According to the data, lifestyle modification is a problem-free treatment but difficult to implement and takes time to accomplish. In contrast, medication is effective and fast but contained side effects. Therefore, the author would like to seek for another treatment scheme especially herb extract which can be an alternative for prediabetic group.

2.4 Alternative Treatment for Diabetes & Prediabetes

Other than pharmaceutical products, there are many nutritional supplements and herbs to control diabetes and prediabete, as listed in table 4 below:

Nutritons for diabetes & prediabetes

Table 2.4 Lists of nutritional supplements and herbs use in controlling diabetes and prediabetes

Supplement	Dosage	Comments
1. *Essential*		
Alpha-lipoic acid	As directed on label	For treatment peripheral nerve damage in DM patients
Chromium picolinate	400-600 mcg daily	Improve insulin efficiency
Garlic	As directed on label	Decrease and stabilizes blood sugar level
L-carnitine	500 mg twice daily	Mobilizes fat
plus L-glutamine	500 mg twice daily	Reduces the craving for sugars
plus taurine	500 mg twice daily	Aids in release of insulin
Quercetin	100 mg 3 times daily	Protect the membrane of the lens of the eye
Raw adrenal glandular	As directed on label	Aids in rebuilding and
Raw pancreas glandular	As directed on label	nourishing these organs
Thyroid glandular	As directed on label	
Vanadium	As directed on label	Aids insulin's ability to move glucose into the cells
Vitamin B complex	50 mg of each major B vitamin 3 times daily	The B vitamin work best when taken together
plus extra biotin	50 mg daily	Improves the metabolism of
And inositol	50 mg daily	glucose
		Important for circulation and for prevention of atherosclerosis

Table 2.4 (Continue)

Supplement	Dosage	Comments
Vitamin B 12 plus folic acid	As prescribed by physician	Need to prevent diabetic neuropathy
zinc	50-80 mg/day	Deficiency has been associated with diabetes
2. Very inportant		
Coenzyme Q_{10}	80 mg daily	Improves circulation and
Plus Coenzyme A	As directed on label	stabilizes blood sugar
Magnesium	750 mg daily	Important for enzyme systems and pH balance Protects against coronary artery spasm in arteriosclerosis
Manganese	5-0 mg daily	Needed for repair of the pancreas
Psyllium husks or Aerobic Bulk Cleanse	As directed on label	Good fiber source and fat mobilizer
3. Important		
Vitamin A with carotenoids	15,000 IU daily ,If you are pregnant ,do not exceed 10,000	An important antioxidant needed to maintain the health of the eyes
Vitamin c with bioflavonoids	3000-6000 mgdaily	Deficiency may lead to vascular problem
Vitamin E	200 IU daily	Improves circulation and
Helpful		prevents complications
calcium	1500 mg daily	Important for pH balance
Copper complex	As directed on label	Aids in protein metabolism and in many enzyme systems
Maitake extract	1-4 gm daily	May help to normalize blood sugar levels
Multienzyme complex	As directed on label	To aids digestion
Plus proteolytic enzymes	As directed on label	
Pantethine	As directed on label	A form of pantothenic acid
Pycnogenol or grape seed extraction	As directed on label	Contains powerful antioxidants

From Phyllis, A. B. (2006). **Prescription for Nutritional Healing**. N.P.: n.p.

2.5 Plants for Diabetes & Prediabetes

In the past time ,we use plants and plant extracts to treatment the disease as early 1550 B.C. The World Health Organization that there are people who use herbal medicine for primary health about 4 billion or 80 % of the world population . Herbal medicine usually uses in Ayurvedic, homeopathic, naturopathic, traditional oriental and indigenous peoples' traditional medicine.

There are 119 plant-derived pharmaceutical medicines. About one hundred plants are reported that have ant diabetic activity, by many mechanisms.

We can summary the mechanisms to 7 group.

2.5.1 Alkaloids

Action by inhibit alpha glucosidase and glucose transport via the intestinal epithelium.

2.5.2 Imidazoline Compounds

Action by induce insulin secretion

2.5.3 Polysaccharides

Action by increase the levels of serum insulin, reduce the blood glucose levels.

2.5.4 Flavonoids

Action by reduce blood glucose level and blood lipid, increase insulin release from pancreatic islets.

2.5.5 Dietary Fibers

Action by decrease blood glucose and blood lipid by many mechanisms, It may alter gastric emptying time and intestinal transit rates, so the absorption of carbohydrates are decreased.

2.5.6 Saponin

Action by increase the release insulin and blocks the formation of glucose in the bloodstream.

2.5.7 Ferulic Acid

Action by stimulate of insulin secretion. (Misha, Rao, Ojha,Vijayakumar & Verma, 2010)

Table 2.5 Lists of Plants with Anti-Diabetic Activity

Botanical name	Family	Parts used	Mechanism of action	Chemical constituents
Abies pindrow Royle	Pinaceae	Entire plant	Insulin secretagogue activity	Volatile oil
Abroma augusta Linn	Sterculiaceae	Roots & Leaves	Lowering blood sugar	Fixed oil, Alkaloid
Acacia arabica Wild	Leguminosae	Seed	Initiates release of insulin	Arabin
Achyranthus aspera L		Entire plant	Decreases blood sugar	-
Agrimony eupatoria L.	Rosaceae	Leaves	Insulin releasing & insulin like activity	
Ajauga iva Wall. ex. Benth	Labiatae	Entire plant	Decreases plasma glucose level	
Allium sativum Linn.	Liliaceae	Roots	Antihyperglycemic and antinociceptive effect	Volatile oil, Allin, Allicin
Allium cepa Linn.	Liliaceae	Bulb	Stimulating effects on glucose utilization and antioxidant enzyme	Protein, carbohydrate, vitamin A, B, C, Allyl propyldisulphide
Aloe vera Tourn. ex. Linn.	Liliaceae	Entire plant		Aloin glycoside
Aloe barbadensis Miller	Liliaceae	Leaves	Stimulating synthesis and/or release of insulin	Barbaloin, isobarbaloin, resin
Amaranthus spinosus Linn.	Amaranthaceae	Stem		
Anacardium occidentale Linn	Anacardiaceae	Entire plant		Flavonols, terpenoid, caumarin, phenolic compound,essential oil
Andrographis paniculata Nees	Acanthaceae	Entire plant	Increases glucose metabolism	Diterpenoid lactone andrographoloid
Annona squamosa	Annonaceae	Leaves	Hypoglycemic and anti-hyperglycemic activities	Acetogenins-squamosin B, squamosamide, reticulatain-2,isosquamosin
Artemisia pallens Wall	Compositae	Aerial parts	Leaf-extract, increased plasma insulin level, hypoglycemic, increases peripheral glucose utilization or inhibits glucose reabsorption	Essential oil, davanone
Averrhoa bilimbi	Oxalidaceae	Leaves	Increases serum insulin level	
Azadirachta indica A.juss.	Meliaceae	Leaves	Glycogenolytic effect due to epinephrine action was blocked	Nimbidin, nimbin, nimbidol, nimbosterol

Table 2.5 (Continue)

Botanical name	Family	Parts used	Mechanism of action	Chemical constituents
Beta vulgaris Linn	Chenopodiaceae		Reduces blood glucose level by regeneration of beta cells	
Bidens pilosa	compositae	Aerial parts		Polyacetylenic glucoside
Bixa orellana L.	Bixaceae	Entire plant	Increases plasma insulin concentration & increases insulin binding on insulin receptor	Oleo-resin
Boerhaavia diffusa L.	Nyctaginaceae	Leaves & Entire plant	Increases in hexokinase activity, decreases in glucose-6-phosphatase	Alkaloid punarnavaine, punarnavoside
Brassica juncea L.	Cruciferae		Food adjuvants for diabetic patients	Isothiocyanate glycoside singrin, protein, fixed oil
Caesalpinia bonducella Flem.	Leguminose	Seed kernels	Free radical scavenging	Fatty oil
Camellia sinensis	Theaceae	Leaves	Increases insulin secretion	Polyphenolic constituents (EGCG)
Capparis deciduas Edgew	Capparidaceae	Powder	Hypoglycemic, antioxidant, hypolipidaemic	
Capsicum frutescens Linn.	Solanaceae		Increases insulin secretion & reduction of insulin binding on insulin receptor	
Carum carvi Linn.	Umbelliferae	Fruits		V.oil, resin, carvone, fixed oil
Cassia alata	Caesalpiniaceae	Leaves		
Cassia auriculata	Caesalpiniaceae	Flower	Increases utilization of glucose through increase glycolysis	
Catharanthus roseus G.Don	Apocynaceae	Leaves, twig & flower	Increases metabolisation of glucose	Indole alkaloid, vincristine vinblastin
Cinnamomum zeylanicum Nees	Lauraceae	Bark	Elevation in plasma insulin	Volatile oil, tannin, mannitol, calcium oxalate
Clausena anisata Burm.f.	Rutaceae	Roots	Stimulates secretion of insulin	
Coriandrum sativum Linn.	Umbelliferae	Seed		Volatile oil, fixed oil, protein
Coscinium fenestratum Calebr	Menispermaceae	Stem	Increases enzymatic antioxidants	Barberine , glycoside, saponin

Table 2.5 (Continue)

Botanical name	Family	Parts used	Mechanism of action	Chemical constituents
Croton cajucara Benth	Euphorbiaceae	Bark		Fixed oil
Cryptolepis sanguinolenta R.	Asclepidaceae	Entire plant	Increases glucose uptake by 3T3-L1 cells	Cryptolepine
Eclipta alba Linn.	Compositae	Leaves	Decreases activity of glucose-6-phosphatase & fructose-1-6,bisphasphatase	Ecliptin alkaloid
Embellica officinalis Gaertn.	Euphorbiaceae	Fruits	Reduces 5-hydroxymethylfurfural, creatinine albumin level	Vitamin C, tannin
Enicostemma littorale Blume	Gentianaceae	Entire plant	Decreases glycosylated Hb & glucose 6 phosphatase	Swertiamarine glycoside
Eugenia jambolana Lam.	Myrtaceae	Seed, fruit , leaves, kernel	Lowers plasma glucose level	
Eucalyptus globulus Labill.	Myrtaceae	Leaves	Increases insulin secretion from clonal pancreatic beta line (BRIN-BD 11)	Essential oil , cineol
Euphrasia officinale	Scrophulariaceae	Leaves		
Ficus religiosa Linn.	Moraceae	Entire plant	Initiating release of insulin	Tannin
Ficus bengalensis Linn.	Moraceae	Bark	Rising serum insulin	Tannin
Ficus carica	Moraceae	Leaves		
Gymnema montanum Hook f.	Asclepiadaceae	Leaves	Antioxidant & antiperoxidative	
Gymnema sylvestre R.	Asclepiadaceae	Leaves	Lowers plasma glucose level	Gymnemic acid, quercital
Gentiana olivier Griseb.	Gentianaceae	Flowers	Lowers plasma glucose level	Iso-orientin C-glycoside
Glycerrhiza glabra Linn.	Leguminosae	Root	Lowers plasma glucose level	Triterpenoid,saponin , glycerrhizin
Gynura procumbens	Compositae	Leaves	Lowers plasma glucose level	
Hibiscus rosa sinensis Linn.	Malvaceae	Entire plant	Stimulates insulin secretion from beta cells	Vitamin B, C, fat
Helicteres isora Linn.	Sterculiaceae	Root	Decreases plasma triglyceride level & insulin sensitizing activity	Saponin, tannin, lignin

Table 2.5 (Continue)

Botanical name	Family	Parts used	Mechanism of action	Chemical constituents
Hordeum vulgare	Graminaeae			
Hovenia dulcis Thunb	Rhamnaceae	Entire plant		Flavonoids
Ipomoea aquatica Forsk.	Convolvulaceae	Leaves	Reduces fasting blood sugar level & serum glucose level	Carotene
Ipomoea batata Linn.	Convolvulaceae	Tubers	Reduces insulin resistance & blood glucose level	
Juniperus communis Linn.	Pinaceae	Fruits	Increases peripheral glucose consumption & induce insulin secretion	
Lupinus albus Linn.	Fabaceae	Seed	Lowering serum glucose level	Alkaloid, fatty oil, asparagines
Luffa aegyptiaca Mill.	Cucurbitaceae	Seed	Lactigogue activity	Fatty oil
Leucas lavandulaefolia Rees	Labiatae	Entire plant	Reduces blood glucose level	
Lagerstronemia speciosa	Lythraceae	Leaves		
Lepidium sativum	Cruciferae	Seeds		
Mangifera indica Linn.	Anacardiaceae	Leaves	Reduction of intestinal absorption of glucose	Mangiferin
Myrtus communis L.	Myrtaceae	Leaves	Lowering blood glucose level	Volatile oil, mirtii oleum
Memecylon umbellatum Burm	Melastomataceae	Leaves	Lowering serum glucose	
Momordica cymbalania Fenzl ex naud	Cucurbitaceae	Fruit powder	Reduces blood glucose level	
Mucuna pruriens L.	Leguminosae	Seed	Reduces blood glucose level	
Musa sapientum Linn.	Musaceae	Flower	Reduces blood glucose & glycosylated Hb	
Momordica charantia Linn.	Cucurbitaceae	Fruit	Reduces blood glucose level	Momordicine alkaloid, ascorbic acid
Morus indica L.	Moraceae	Leaves	Increases glucose uptake	
Murraya koeingii (L) spreng.	Rutaceae	Leaves	Increases glycogenesis , decrease glycogenolysis & gluconeogenesis	
Nelumbo nucifera Gaertn.	Nymphaeaceae	Rhizome	Reduces blood sugar level	Nuciferin, nornuciferin

Table 2.5 (Continue)

Botanical name	Family	Parts used	Mechanism of action	Chemical constituents
Ocimum sanctum Linn.	Labiatae	Leaves	Lowering blood sugar level	Volatile oil, phenol, aldehyde, fixed oil, alkaloid, tannin, ascorbic acid
Olea europia Linn.	Oleaceae	Leaves	Potentiation of glucose , induced insulin released , & increase peripheral uptake of glucose	Oleuropeoside
Opuntia ficus-indica Mill	Cactaceae	Stem		
Pandanus odorus Linn.	Pandanaceae	Root	Decreases plasma glucose level	Essential oil
Panax ginseng Mey.	Araliaceae	Root & entire plant	Lowering blood sugar level	Glycans, panaxans I,J,K & L
Punica granatum Linn	Punicaceae	Seed	Reduces blood sugar level	Vitamin C, protein, tannin, gallic acid, pelletierine
Picrorrhiza kurroa Royle ex. Benth	Scrophulariaceae	Entire plant	Decreases serum glucose	Picrorrhizin, kutkin
Phyllanthus amarus	Euphorbiaceae	Entire plant	Decreases blood glucose level	Alkaloids
Phaseolus vulgaris	Papilionaceae	Pod, seed, whole plant	Hypoglycemic, hypolipidemic, inhibit alpha amylase activity, antioxidant.	
Salacia oblonga	Celastraceae	Root	Inhibition of alpha glucosidase activity	
Salacia reticulata Wight.	Celastraceae	Stem & root	Inhibition of alpha glucosidase activity	
Swertia chirayata Roxb.ex.Flem	Gentianaceae	Entire plant	Stimulates insulin release from islets	Zanthone mangiferin, gentianine, swerchirin
Syzygium cumini Linn	Myrtaceae	Seed	Decreases blood glucose level	
Scoparia dulcis Linn.	Scrophulariaceae	Leaves	Decreases glycosylated Hb & Increases total Hb, Insulin-secretagogue activity	
Trigonella foenum graceum	Leguminosae	Seed	Decreases blood glucose concentration	Protein, fat, volatile oil, fixed oil, carbohydrate
Tribulus terrestris Linn.	Zygophyllaceae	Saponin	Decreases serum glucose	Harmine
Tinospora crispa Linn.	Menispermaceae	Stem	Anti-hyperglycemic, stimulates insulin release from islets	

Table 2.5 (Continue)

Botanical name	Family	Parts used	Mechanism of action	Chemical constituents
Tinospora cardifolia Wild.	Menispermaceae	Root	Decreases blood glucose & brain lipid	Berberine, starch
Tamarindus indica Linn.	Caesalpimiaceae	Seed		
Teramnus labialis (Roxb) Benth	Fabaceae	Aerial parts		Caumarin -fraxidin
Urtifca dioica Linn.	Urticaceae	Leaves	Increases insulin secretion	Fatty oil
Viscum album Linn.	Loranthaceae	Entire plant	Alpha glucosidase inhibitor	
Vinca rosea	Apocynaceae	Leaves	Beta cell rejuvenation, regeneration, & stimulation	Vincristine , vinblastine
Withania somnifera Dunal	Solanaceae	Root	Decrease blood sugar level	Withanine, somnine, withaferine, withanolides
Xanthium strumarium	Compositae	Fruits	Increases glucose utilization	Phenolic compound , caffeic acid
Zingiber officinale Roscoe	Zingiberaceae	Rhizome	Increases insulin level & decrease fasting glucose level	Sesquiterpene
Zizyphus sativa Gaertn	Rhamnaceae	Leaves	Dose dependent reduction in blood glucose level	Tannin

The study of Thai natural blood glucose regulator herbs compared with the efficacy of Acarbose by Rungprom et al. (2010) showed the inhibit efficacy on alpha glucosidase enzyme. The study used *Momordica charantia, Gynura divaricata DC, Pseuderatherum platiferum, Lagerstroemia speciosa* (L.), *Pers Aegel marmelos* (Linn.), *and Corr. and Wedelia trilobata* (L.) *Hitchc.Z.* as herbal medicines. Since the study supported the hypoglycemic effect of Thai herb, it is necessary to conduct further study in order to use with diabetic patient.

2.6 Syzygium cumini (L.) Skeels

Synonymy: *Calyptranthes caryophyllifolia* (Lam.) Willd., *Calyptranthes oneillii* Lundell, *Eugenia cumini* (L.) Druce, *Eugenia jambolana* Lam., *Eugenia caryophyllifolia* Lam., *Eugenia cumini* (L.) Druce, *Eugenia jambolana* Lam., *Myrtus cumini* L., *Syzygium jambolana* (Lam.) DC., *Syzygium jambolanum* DC., *Syzygium caryophyllifolium* (Lam.) DC., *Syzygium jambolanum* (Lam.) DC.

Common names: black plum (English), damson plum (Jamaica), djoowet (Java), doowet (Java), druif (Surinam), duhat (Guam), duhat (Philippines), faux-pistachier (French), guayabo pesjua (Venezuela), indian blackberry (Jamaica), jalao (Brazil), jaman (India/Malaya), jambhool (India/Malaya), jamblang (India/Malaya), jambol (Brazil), jambolan plum (English), jambolanier (French), jambool (India/Malaya), jambu (India/Malaya), jambul (India/Malaya), jambulao (Brazil), jamelao (Brazil), jamelong (India/Malaya), jamelongue (India/Malaya), jam longue (French), jamelonguier (New Caledonia), jamelon-guier (French), jammun (Fiji), jamoen (Surinam), Java plum (English), jiwat (India/Malaya), Ka'ika (Cook Islands), kavika ni India (Fiji), koeli (Surinam), koriang (India/Malaya), lomboy (Philippines), lunaboy (Philippines), ma-ha (Thailand), Malabar plum (English), mesegerak (Palau), mesekerrak (Palau), mesekerrk (Palau), mesigerak (Palau), paramu (Cook Islands (Aitutaki)), pesjua extranjera (Venezuela), pistati (Cook Islands), Portuguese plum (English), pring bai (Cambodia), pring das krebey (Cambodia), purple plum (English), salam (India/Malaya), va (Laos), voi rung (Vietnam), wa (Thailand) (Pierre, 2006)

Organism type: tree

Description: The jambolan is fast-growing, reaching full size in 40 years. It ranges up to 100 feet (30m) in India and Oceania; up to 40 or 50 feet (12-15m) in Florida; and it may attain a spread of 36 feet (11m) with a trunk diameter of 2 or 3 feet (0.6-0.9m). It usually forks into multiple trunks, a short distance from the ground. The bark on the lower part of the tree is rough, cracked, flaking and discoloured; further up the trunk it is smooth and light-grey. The turpentine-scented evergreen leaves are opposite, 2 to 10 inches (5-25cm) long, 1 to 4 inches (2.5-10cm) wide; oblong-oval or elliptic, blunt or tapering to a point at the apex; pinkish when young; when mature, leathery, glossy, dark-green above, lighter beneath, with conspicuous, yellowish midrib. The fragrant flowers, in 1to 4 inches (2.5-10cm) clusters, are 1/2 inch (1.25cm) wide, 1 inch (2.5cm) or more in length; have a funnel-shaped calyx and 4 to 5 united petals, white at first, then rose-pink, which quickly shed leaving only the numerous stamens.

The fruit, in clusters, is round or oblong, often curved; 1/2 to 2 inches. (1.25 - 5cm) long, and usually turns from green to light-magenta, then dark-purple or nearly black as it ripens. A white-fruited form has been reported in Indonesia. The skin is thin, smooth, glossy, and adherent. The pulp is purple or white, very juicy and normally encloses a single, oblong, green or brown seed, up to 1 1/2 inches. (4cm) in length, though some fruits have 2 to 5 seeds tightly compressed within a leathery coat and some are seedless. The fruit is usually astringent, sometimes unpalatably so, and the flavour varies from acid to fairly sweet. (Morton, 1987)

Origin and Distribution: The jambolan is native in India, Burma, Ceylon and the Andaman Islands. It was long ago introduced into and became naturalized in Malaya. In southern Asia, the tree is venerated by Buddhists, and it is commonly planted near Hindu temples because it is considered sacred to Krishna. The leaves and fruits are employed in worshipping the elephant-headed god, Ganesha or Vinaijaka, the personification of “Pravana” or “Om”, the apex of Hindu religion and philosophy.

The tree is thought to be of prehistoric introduction into the Philippines where it is widely planted and naturalized, as it is in Java and elsewhere in the East Indies, and in Queensland and New South Wales, also on the islands of Zanzibar and Pemba and Mombasa and adjacent coast of Kenya. In Ghana, it is found only in gardens. Introduced into Israel perhaps about 1940, it grows vigorously there but bears scantily, the fruit is considered valueless but the tree is valued as an ornamental and for forestry in humid zones. It is grown to some extent in Algiers

By 1870, it had become established in Hawaii and, because of seed dispersal by mynah birds, it occurs in a semiwild state on all the Hawaiian islands in moist areas below 2,000 ft (600 in). There are vigorous efforts to exterminate it with herbicides because it shades out desirable forage plants. It is planted in most of the inhabited valleys in the Marquesas. It was in cultivation in Bermuda, Cuba, Haiti, Jamaica, the French Islands of the Lesser Antilles and Trinidad in the early 20th Century; was introduced into Puerto Rico in 1920; but still has remained little-known in the Caribbean region. At the Lancetilla Experimental Garden at Tela, Honduras, it grows and fruits well. It is seldom planted elsewhere in tropical America but is occasionally seen in Guatemala, Belize, Surinam, Venezuela and Brazil.

The Bureau of Plant Industry of the United States Department of Agriculture received jambolan seeds from the Philippines in 1911, from Java in 1912, from Zanzibar and again from the Philippines in 1920. The tree flourishes in California, especially in the vicinity of Santa Barbara, though the climate is not congenial for production or ripening of fruit. In southern Florida, the tree was rather commonly planted in the past. Here, as in Hawaii, fruiting is heavy, only a small amount of the crop has been utilized in home preserving. The jambolan has lost popularity, as it has in Malaya where it used to be frequently grown in gardens. Heavy crops litter streets, sidewalks and lawns, attracting insects, rapidly fermenting and creating a foul atmosphere. People are eager to have the trees cut down. Where conditions favor spontaneous growth, the seedlings become a nuisance, as well. (Morton , 1987, p.375-378)

2.6.1 Pharmocognostic standards for the seeds of Syzygium cumini

In 2010, Modi, Patel, Shah & Nayak (2010) conducted the pharmacognostic study regarding the efficacy of *Syzygium cumini* (L.) Skeels seed extract through macroscopy, microscopy, preliminary phytochemical screening and physiochemical evaluation from flavonoids, phenols, tannins, alkaloids, glycosides, saponins, steroids, triterpenoids, protein, and amino acids. The predominant substances in the seeds of *S.cumini* were flavonoids, alkaloids, and glycosides which well-verified the hypoglycemic effectiveness of *Syzygium cumini* .

2.6.2 Research of *Syzygium cumini*

2.6.2.1 In Vitro studies

Various studies have been conducted in order to proof hypoglycemic effect of *Syzygium cumini*. The studies can be concluded as follows:

1. Inhibition of Carbohydrate hydrolyzing enzymes.

In 2008, Menakshi, Smita, Shobha, Ameeta & Bimba (2008) studied the seed extraction of *Syzygium cumini* on the carbohydrate hydrolyzing enzymes (porcine pancreatic α-amylase, rat intestinal α-glucosidase and sucrase) inhibition activity with both untreated and heat-treated aqueous extracts. They found the dose-dependent

manner activity of the extract in pancreatic amylase and intestinal glucosidase in untreated extract. However, the inhibition activity did not increase with dosage of untreated extract in sucrase. Heat-treated extract showed significant inhibition activity in the pancreatic α-amylase whereas others showed slight increase but not statistically accepted. Hence, heat restricted the inhibition efficacy of the seed extract. Other study by Menakshi et al.(2008) reported 6 herbal extract with amylase inhibitory power on type of solvent extraction. Chloroform, methanol and aqueous solvents were used as a solvent of *Syzygium cumini* seed extract in the study to examine the inhibitory effect on glycosidases. Inhibitory activity of chloroform extract (IC_{50} values of 4.28, 3.72, and 5.60 μg/ml against procine-α-amylase, murine pancreatic and murine intestinal glucosidases, respectively) was observed in all glucosidase enzymes. However, the mathanolic extract of *Syzygium cumini* showed inhibitory effect only with murine liver glucosidases (IC_{50}=2.68 μg/ml). Therefore, the solvent used for extraction was vital for the efficacy of the seed extract inhibitory power.

2. Uptake Inhibition of glucose transport at intestinal membrane

In 2010, The study by David (2010), Theras, Hemachandran, Elumalai and Thirumala showed inhibition of glucose uptake using incubation of rat intestinal sacs compared with control group.

3. Increased intracellular uptake activities of glucose

Study of *Syzygium cumini* (L.) Skeels seed extract on key glucose transport mediators such as IRTK, GLUT4, P13K and PPAR showed that the methanol extract of *Syzygium cumini* increased the glucose uptake by 2 fold when compared with insulin and Rosiglitazone. The PPARy expression was comparable with Rosgilitazone treated cells. Moreover, Rajasekar ,Kirubanandan & Lakshmi, (2009) suggested that the mechanism may be caused by methanol crude extracts of *Syzygium cumini* which showed elevated GLUT4 mRNA expression comparable with insulin and Rosiglitazone. This extract functioned as insulin sensitizer.

In Vivo studies

1. Study to find appropriate dosage

Comparative study of *Syzygium cumini* (L.) Skeels seed extract administration at various dosages (250, 500, 1000 mg/kg rat) compared with Gilbenclamide administration in streptozotocin-diabetic rats showed that the extract administration (15 days) at 500mg/kg and 1000 mg/kg somewhat decreased fasting and peak blood glucose levels but not as effective as Gilbenclamide. However, when evaluate the overall factors including an increase in mean body weight, a post-treatment difference between fasting and peak blood glucose levels, the percent reduction in pre-treatment versus post-treatment fasting and peak blood glucose levels, and elevation in liver glycogen values, the rats with extract administration of 500 and 1000 mg/kg showed comparable effective results. Therefore the 500 mg/kg concentration should be the optimum dosage regarding the lesser adverse effects. (Sridhar et al., 2005)

Sharma, Nasir, Prabhu & Murthy (2006)suggested that the aqueous seed extract of *Syzygium cumini* also possess the higher efficacy in decreasing the fasting blood glucose and peak blood glucose after 90 minutes glucose tolerance test in both normal, diabetic, and severe alloxan-induced diabetic rabbits compared with ethanolic seed extract. The optimum dosage is at 25 mg/kg since this could decrease 21% and 24% of fasting blood glucose in diabetic, and severe diabetic groups, respectively. When continued administrating the aqueous seed extract, fasting blood glucose

decreased by 38% and 48% in diabetic and severe diabetic groups respectively. In vitro study of pancreatic islets also showed 2.5 folds increase in insulin level compared with those untreated rabbits.

2. Pharmaceutical composition analyses

The study by Ravi, Sekar & Subramanian (2004) conducted the efficacy evaluation of whole seed, kernel, and seed coat of *Syzygium cumini* on strepotzotocin-induced diabetic rats and found that the 100 mg/kg extracted kernel possessed the maximum efficacy which decreased the level of blood glucose, blood urea, and cholesterol while increased glucose tolerance and level of total proteins and liver glycogen. Moreover, it decreased the activities of glutamate oxaloacetate transaminase and glutamate pyruvate transaminase, whereas; seed coat found no hypoglycemic activity. Hypoglycemic activity of inorganic part of *Syzygium cumini* in Streptozotocin-diabetic rats found that rats which received the inorganic part were able to control their blood sugar level. From this study, Ravi et al. suggested that the pharmacodynamic substance which was related to the hypoglycemic activity may be from this inorganic portion.

The study in Brazil also reported the study of *Syzygium cumini*'s leaves extract with streptozotocin-diabetic rats with various study parameters such as body weight, food and fluid intake, urinary volume, glycemia, urinary glucose and urea, serum cholesterol, HDL-cholesterol Triglycerides, and angiotensin-converting enzyme. However, no hypoglycemic effects were detected in the study. (Pepato, Folgado, Kettelhut & Brunetti, 2001)

3. The study in mild and severe diabetics

In 2008, Study of Sharma, Balomajumder & Roy used the flavonoid rich extract with both mild and severe streptozotocin-diabetic rats. After intervention, fasting blood glucose and glucose level after 60 minutes glucose tolerance test decreased while other parameters such as glycogen biosynthesis, glucose homeostatic enzyme (glucose-6-phosphatase, hexokinase) activity significantly increased ($p<0.05$). Moreover, they found decreased levels of LDL (27%), triglycerides (35%), and increased HDL (21%). Therefore, it can be concluded that the flavonoid extract of *Syzygium cumini* was promising for treatment of DM. Further study in diabetic and severe diabetic rabbits also suggested that the seed extract of *Syzygium cumini* was efficient to decrease FBG after 90 minutes(21%), 7 days (35.6%) of extract administration in mild diabetic group and 15 days (59.6%) in severe diabetic group. Glycosylated hemoglobin decreased significantly after 15 days of treatment and plasma insulin increased significantly ($p<0.01$). (Sharma, Rajpoot, Nasir, Prabhu & Murthy , 2011)

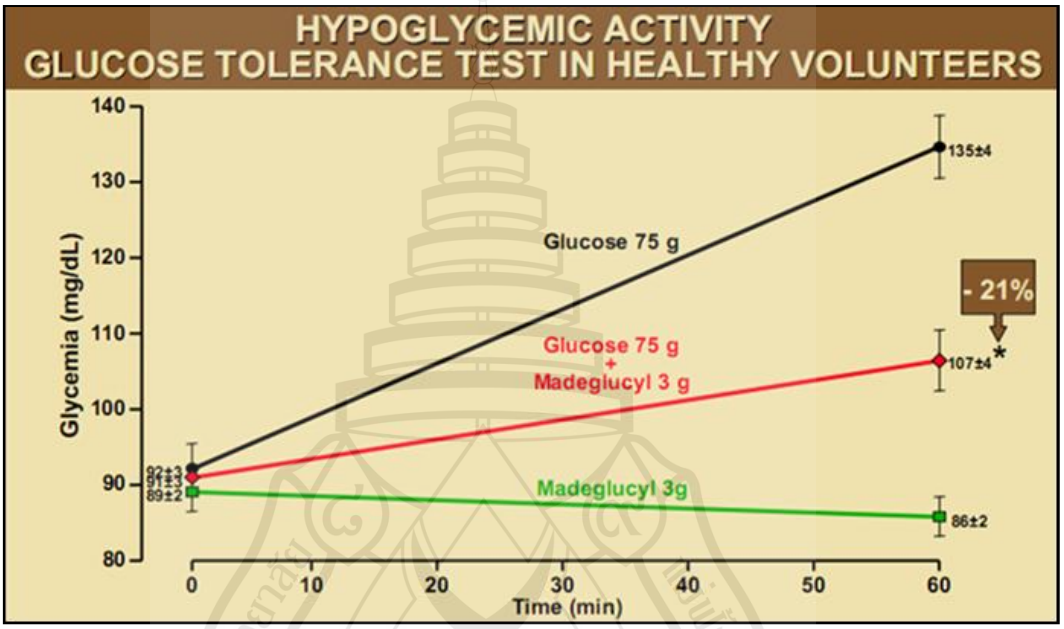
4. Controversial research

Pepato re-perfomed the experiment by using the Brazilian *Syzygium cumini* seed extracts administration in streptozotocin-induced diabetic rats using 50mg/day for 41 days. The results showed no significant changes found in the study. Therefore, geographical difference may relate to the contents of seed extract. (Pepato et al., 2005)

2.6.2.2 Study in human

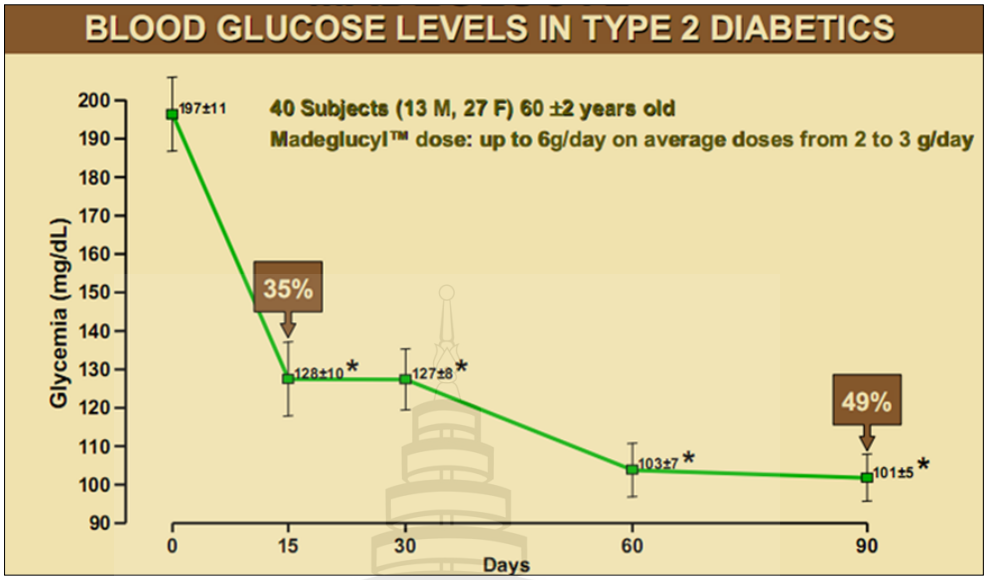
Study in human was conducted since 1985 by Ramahandridona and Rakotondravoavy. They found that subjects within the same group had 20% decreased blood glucose level (after 60 minutes of GTT) whenever subjects consume seed extract (Figure 2.1). Study in 40 type II DM patients found that subjects who consumed 2-3

g/day of seed extract for 90 days showed 35% and 49% decreased blood glucose level on day 15 and day 90 respectively (Figure 2.2). Schleicher (1991a,b) intervented 3g/day of seed extract with type II DM patients for 6 weeks and reported the successful hypoglycemic efficacy up to 73%. Sohn, Berzono, Shonkman & Young (1992), Ten-weeks study were performed using 1.5-6g/day with type II DM patient found that it can decrease 33% blood sugar level as well as 35% decrease in 2 hr postprandial blood level.



From Ramahandridona, G. A. & Rakotondravoavy, L. E. (1985). Our Experiency of Professor Rakoto Ratsimamanga on Eugenia Jambolana Lamarck Seeds Extract, as Additive or Exclusive Treatment of Various Types of Diabetes Mellitus. **Indena internal report.**

Figure 2.1 Hypoglycemic Activity Glucose Tolerance Test in Healthy Volunteers



From Ramahandridona, G. A. & Rakotondravoavy, L. E. (1985). Our Experiency of Professor Rakoto Ratsimamanga on Eugenia Jambolana Lamarck Seeds Extract, as Additive or Exclusive Treatment of Various Types of Diabetes Mellitus. **Indena internal report.**

Figure 2.2 Blood glucose levels in type II DM

Recently Sahana et al.(2010) conduct a case-control study in type II DM. Divided into 3 groups, patients were asked to received 5 gram bid *Syzygium cumini* seed extract (Group I), 500 mg Metfomin (Group II) or Lifestyle modification (Group III). The result showed that group I had the significant decrease in fasting blood glucose in month 3 and 6 (152±22.5 to 140.7±26.6 mg/dl, $P<0.05$ in 3 months; 152±22.5 to 134±21.3 mg/dl, $P<0.05$ in 6 months respectively). The homeostatic model assessment for insulin resistance also decreased significantly while the HDL-Cholesterol increased significantly.

2.6.2.3 Toxicity of Syzygium cumini

The adequate dose of *Syzygium cumini* seed extract is 1-3 gm /day but the optimal dosage is not know. In this time many researches don't have side effect or adverse event but if patients use this herb overdose , they may have gastrointestinal upset. (Yarnell, Abascal & Rountree, 2009)

Study of Yele & Veeranjaneyulu (2010) is about acute oral and repeated-dose toxicity of the stem bark in albino mice and Wistar rats. Result of this study safety of acute and repeated oral administration of the aqueous extract of this herb, because of the result, this herb may be continuously used safely.

In 2010, Jayanta (2010) study in Swiss albino mice. Their study for evaluate the safety of ethanolic seed extract of *Syzygium cumini* by using acute and sub-chronic toxicity assays. The result show administration seed extract of *Syzygium*

cumini is safety, Although use 10 fold of normal dosage. This result of study is same like Sridhar et al. (2005), study Their study found the streptozotocin-diabetic rats, that received seed extraction from herb for 14 days, with no evidence of mortality or abnormalities.

All the studies up to now lead the interest of administrating the seed extract of *Syzygium cumini* with prediabetic patients since the extract itself is well-accepted both in vivo and in vitro. Though, it is still controversial about the pharmacokinetic efficacy in human study due to the research limitation, the extract has no severe side effects which is good for medical practice. Possible usage of the study proposed is the new alternative for prediabetes treatment as well as support for local herbal market support.

CHAPTER 3

RESEARCH METHODOLOGY

3.1 Population and Sample

Study population

We include the volunteers who are circumference in Bangkok, male and female and age between 20-60 years. Their fasting blood glucose have to be in range 100-125mg/dl at 9.00 am. Who come to the Srinakarin medical clinic during December 2011 to January 2012.

3.2 Sample Size Determination

Sample size is defined by the following formula

$$n_0 = \frac{Z_\alpha^2 PQ}{d^2}$$

Set confident interval at 95 % $\alpha = 0.05$

(P = 0.49 Q = 0.51: PQ = 0.25)

P defines from the study of Ramahandridona & Rakotondravoavy (1985) Decreasing rate of FBS 49% (P =0.49)

d = 20%

n = 17 subjects per group

Set allowance for 15% drop out rate: Sample size will be 20 subjects per group. Hence, total sample size is 40 subjects.

3.3 Research Design

Experimental research: double blinded, clinical, randomized, controlled-trial.
12 weeks follow up for result
Study variables
Independent variables are the treatment given. (*Syzygium cumini* (L.) Skeels seed extract and Placebo)
Dependent variable are the change in fasting blood glucose and HbA1c.

3.4 Selection of Sample

Populated sample will be randomly selected from the volunteer, who come to the Srinakarin medical clinic. The Cases have clearly been described on the purpose of the study, cases will be given a preliminary test using Fasting blood glucose Analyzer to discriminate if inclusion criteria are met. After enrolled, the cases will be subjects into 2 groups allocated, one basing on lifestyle modification with *Syzyguim cumini* (L.) Skeels seed extract, other one basing on lifestyle modification with Placebo.

3.4.1 Inclusion Criteria

3.4.1.1 Male or female at the age of 20-60 years.
3.4.1.2 Each Subjects' agreement depends on its volunteer to join in the research and signed Informed consent form at the beginning of the study.
3.4.1.3 Subject has impaired fasting glucose (FBG 100-125 mg/dl).
3.4.1.4 Subject can attend incoming visit that will be on the end of 12th week.
3.4.1.5 Subject doesn't have previous history about hyperglycemic treatment.

3.4.2 Exclusion Criteria

3.4.2.1 Subject who have a history of allergic to Syzyguim cumini (L.) Skeels.
3.4.2.2 Subject who using medicine acting on glucose and carbohydrate metabolism. e.g. Patients with Polycystic Ovarian Syndrome who is giving Metformin.
3.4.2.3 Subject with known abnormality of renal and liver function.
3.4.2.4 Women in pregnancy and breast feeding will be excluded from this study.
3.4.2.5 Subject who loss follow up.

3.5 Research Tools

3.5.1 *Syzygium cumini* (L.) Skeels seed extract 3 g/day
3.5.2 Placebo: Sodium carboxymethyl cellulose 3 g/day
3.5.3 Fasting blood glucose and HbA1c examination : Blood collecting test

3.5.4 Research protocol declaration
3.5.5 Informed consent form
3.5.6 Investigator record form
3.5.7 Volunteer's Self-assessment form

3.6 Research Procedure

3.6.1 Subject will be selected according to inclusion and exclusion criteria.

3.6.2 Each subject will be described objectives, methods and benefit from our research study.

3.6.3 Each subject will sign inform consent to reveal their personal history of drug allergy and disease.

3.6.4 Each subject will be examine and measure fasting blood glucose and HbA1c.

3.6.5 Interviews subjects on general information, lifestyles, medical history. Investigator keeps records of all data obtained in research record form.

3.6.6 The investigator of the experiment randomly assigns each subject into either the group of study protocol or the control group. Subjects are provided with oral supplements according to their allocated group. The assignment is randomized using quota sampling technique. This is implemented using a randomization web-based program from the website http://www.randomizer.org/form.htm. A sequence of number ranging from 1 to 40 will be randomly assigned to each participating subject. The subject receiving any number less than or equal to 20 will receive the *Syzygium cumini* (L.) Skeels seed extract, whereas the subject receiving any number more than 20 will receive the placebo.

3.6.7 Investigator explains the proper use of the supplement.

Drug administration;

3.6.7.1 Experimental group will intake *Syzygium cumini* (L.) Skeels seed extract 1.5 gram (3 capsule) before breakfast and dinner 15 minutes. (Total 3 g/day)

3.6.7.2 Control group will intake a placebo 1.5 gram (3 capsule) before breakfast and dinner 15 minutes. (Total 3 g/day)

The benefit and possible side effect will be explained to each subject. The supplement given will be enough for the period of 4 weeks, when subject are required to come back for follow up.

3.6.8 Subjects will be follow up FBG on the end of 4 and 8 week .Their nutritional lifestyle and behavior during an experiment will be interviewed.

3.6.9 Subject comes back at the end of the 12 week for follow up. FBG and HbA1c will be determined again.

3.6.10 Subjects are also required to fill up a self-assessment questionnaire.

3.7 Result Evaluation

3.7.1 Result Evaluation

3.7.1.1 Measuring blood glucose levels after fasting and HbA1c.
3.7.1.2 General evaluation by the researcher.
3.7.1.3 Query Self-assessment is made by volunteers.

3.7.2 Criteria to withdraw from the study

3.7.2.1 Subjects have their own reason to leave the study.
3.7.2.2 Subjects with severe side effects of supplement.
3.7.2.3 Subjects turn to have disease affecting our study .
3.7.2.4 Subject fails to follow up.

3.7.3 Data Collection

Investigator will perform data collection upon each follow-up visit by measuring the value of Fasting blood glucose and HbA1c. Investigator record form and Volunteer's Self-assessment form.

3.8 Statistics Used for Data Analysis

3.8.1 Use descriptive statistics to demonstrate demographic data of volunteers.
3.8.2 Compare the mean of change Fasting blood glucose between control and treatment groups by using T-test. (95% level of confidence, P value=0.05)
3.8.3 Compare the mean of change HbA1c between control and treatment groups by using T-test. (95% level of confidence, P value=0.05)
3.8.4 Compare the mean of Fasting blood glucose at basal, 4th week, 8th week and 12th week in each groups by using Two way ANOVA Repeated Measurement. (95% level of confidence, P value=0.05)
3.8.5 Compare the mean of HbA1c at basal and 12th week in each groups by using Paired T-test. (95% level of confidence, P value=0.05) 3.9 Administration and time schedule. The total process of this research take 12 months from June 2011.

CHAPTER 4

RESULTS

4.1 Basic Parameters

The 38 patients were divided into 2 groups. (n=20 in experimental; 10 males and 10 females, n=18; 6 males and 12 females in placebo groups) In placebo group, woman was excluded from the study because of personal reason.

Table 4.1 The Basic Parameters in Experimental and Control Groups

Parameter	Mean ± SD						t	p-value
	Experimental group (N=20)			Control group (N=17)				
AGE	45.800	±	7.764	44.820	±	10.984	.316	.754
BMI	26.333	±	4.545	24.941	±	5.015	.885	.382
Systolic BP	121.850	±	16.658	125.060	±	12.725	.649	.521
Diastolic BP	72.250	±	8.914	74.470	±	10.375	.700	.488

Note. The mean of difference significant at the .05 level.

The basic parameter including age, body mass index (BMI), Systolic blood pressure (SBP) and diastolic blood pressure (DBP) in all experimental groups are shown as mean and standard deviation (SD) in Table 4.1. BMI in both groups has shown to be overweight. All basic parameters in table 4.1 were not different between experimental and placebo groups. ($p>0.05$)

4.2 FBG and HbA1c

Table 4.2 The Blood Glucose Parameters in Experimental and Control Groups at Basal and Serial Times after Treatment.

Time	Mean ± SD					
	Experimental group (N=20)			Control group (N=17)		
FBG Basal	111.250	±	8.136	113.060	±	8.242
FBG Week4	104.150	±	11.690	110.240	±	24.466
FBG Week8	104.900	±	14. 618	108.530	±	20.338
FBG Week12	102.200	±	18.895	104.290	±	18.278
HbA1c basal	6.125	±	.627	6.135	±	.819
HbA1c Week12	5.875	±	.561	5.965	±	1.000

The serial blood sugar parameters were demonstrated in table 4.2. Fasting blood glucose (FBG) was recorded 4 times at first date (basal), week 4^{th}, week 8^{th} and week 12^{th}**.** In the experimental group, FBG of patients who were received *S. cumini* (L). Skeels seed extract were 111.25$\pm$8.136, 104.150$\pm$11.69, 104.9$\pm$14.186 and 102.2$\pm$18.895 at basal, week 4^{th}, week 8^{th} and week 12^{th}, respectively. In control group, FBG of patients who were received placebo were 113.06$\pm$8.242, 110.24$\pm$24.466, 108.530$\pm$20.338 and 104.29$\pm$18.278, respectively. Furthermore, the HbA1c was measured 2 times at basal and week 12^{th}. In experimental group, the HbA1c of patients who were received *S. cumini* (L). Skeels seed extract were 6.125$\pm$0.627 and 5.875$\pm$0.561at basal and week 12^{th}, respectively. In control group, the HbA1c of patients who were received placebo were 6.135$\pm$0.819 and 5.965$\pm$1 at basal and week 12^{th}, respectively.

4.3 The Comparisons of FBG and HbA1c in Each Groups

Table 4.3 The Comparison of Fasting Blood glucose (FBG) at Serial Times after Treatment in Experimental Group. (By Two Way ANOVA)

Time	Mean ± SD			p-value
FBG Basal	111.250	±	8.136	0.047*
FBG Week4	104.150	±	11.690	
FBG Week8	104.900	±	14.186	
FBG Week12	102.200	±	18.895	

Note. The mean of difference, significant at the .05 level.

The Two Way ANOVA analysis has shown that at least one FBG parameter were significantly different within experimental group. (p=0.047)

Table 4.4 The Comparison of Fasting Blood Glucose (FBG) at Serial Times after Treatment in Experimental Group. (By Pairwise Comparison)

Time	Mean ± SD			Time	Mean ± SD			p-value
FBG Basal	111.250	±	8.136	FBG Week4	104.150	±	11.690	.017*
				FBG Week8	104.900	±	14.618	.082
				FBG Week12	102.200	±	18.895	.040*
FBG Week4	104.150	±	11.690	FBG Basal	111.250	±	8.136	.017*
				FBG Week8	104.900	±	14.618	.781
				FBG Week12	102.200	±	18.895	.548
FBG Week8	104.900	±	14.618	FBG Basal	111.250	±	8.136	.082
				FBG Week4	104.150	±	11.690	.781
				FBG Week12	102.200	±	18.895	.447
FBG Week12	102.200	±	18.895	FBG Basal	111.250	±	8.136	.040*
				FBG Week4	104.150	±	11.690	.548
				FBG Week8	104.900	±	14.618	.447

Note. The mean of difference, significant at the .05 level.

There are statistically significant differences in reduction of FBG in the experiment group at week 4^{th} and 12^{th} when compare to basal (p = 0.017 and p = 0.040, respectly).

Table 4.5 The Comparison of Fasting Blood Glucose (FBG) at Serial Times after Treatment in Control Group. (By Two Way ANOVA)

Time	Mean ± SD			p-value
FBG Basal	113.060	±	8.242	1.880
FBG Week4	110.240	±	24.466	
FBG Week8	108.530	±	20.338	
FBG Week12	104.290	±	18.278	

Note. The mean of difference, significant at the .05 level.

In control group (table 4.5), we have found that FBG was not different at any time after receiving placebo. (p>0.05)

Table 4.6 The Comparison of HbA1c between Basal and week 12th after Treatment in Experimental Group. (By Paired T-test)

Time	Mean ± SD			t	df	P-value
HbA1c Basal	6.125	±	.627	2.005	19	0.030*
HbA1c Week12	5.875	±	.561			

Note. The mean of difference, significant at the .05 level.

The HbA1c at week 12th was significantly decreased from basal in the experimental group. (p=0.030)

Table 4.7 The Comparison of HbA1c between Basal and Week 12th after Treatment in Control Group. (By Paired T-test)

Time	Mean ± SD			t	df	P-value
HbA1c Basal	6.135	±	.819	1.484	16	0.079
HbA1c Week12	5.965	±	1.000			

Note. The mean of difference, significant at the .05 level.

In control group, the HbA1c in patient receiving placebo at week 12th was not different from basal. (p>0.05)

4.4 The Comparisons of FBG and HbA1c between Experimental and Control Groups

Table 4.8 The Comparison of Fasting Blood Glucose (FBG) at Serial Times between Experimental and Control Groups. (By T-test)

Time	Mean ± SD						t	df	p-value
	Experimental group (N=20)			Control group (N=17)					
FBG Basal	111.250	±	8.136	113.060	±	8.242	.670	35	.253
FBG Week4	104.150	±	11.690	110.240	±	24.466	.939	22.111	.179

Table 4.8 (Continue)

Time	Mean ± SD						t	df	p-value
	Experimental group (N=20)			Control group (N=17)					
FBG Week8	104.900	±	14.186	108.530	±	20.338	.637	35	.264
FBG Week12	102.200	±	18.895	104.290	±	18.278	.341	35	.367

Note. The mean of difference, significant at the .05 level.

The FBG was not different between experimental and control groups at every time after treatment including basal, week 4^{th} , week 8^{th} and week 12^{th} ($p>0.05$)

Table 4.9 The Comparison of HbA1c at Basal and Week 12^{th} between Experimental and Control Groups. (By T-test)

Time	Mean ± SD						t	df	p-value
	Experimental group (N=20)			Control group (N=17)					
HbA1c Basal	6.125	±	.627	6.135	±	.8193	.042	29.709	.484
HbA1c Week12	5.875	±	.561	5.965	±	1.000	.343	35	.367

Note. The mean of difference, significant at the .05 level.

The HbA1c was not different between experimental and control groups at every time after treatment including basal and week 12^{th}. ($p>0.05$)

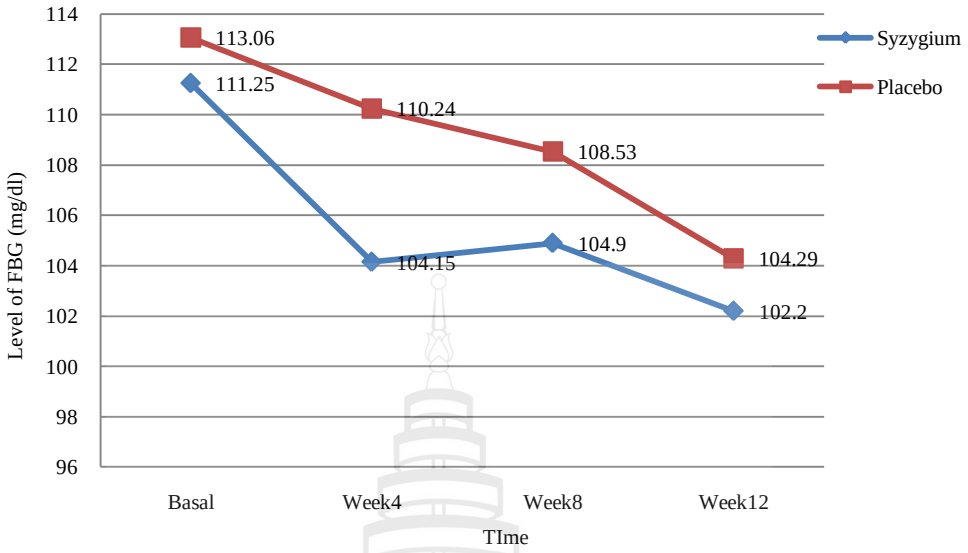


Figure 4.1 The level of fasting blood glucose (FBG) after treatment *(Syzygium cumini* (L). Skeels seed extract vs. Placebo) at basal, week 4th, week 8th and week 12th

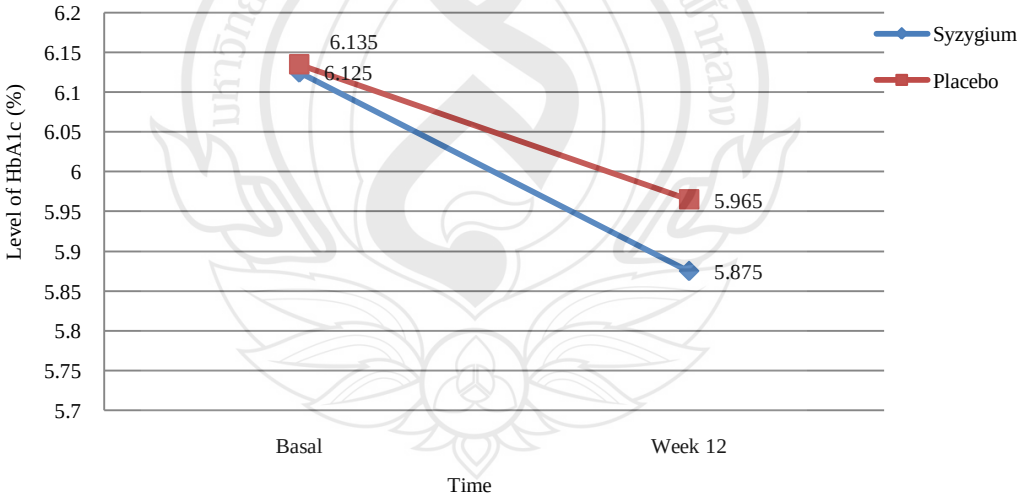


Figure 4.2 The level of HbA1c after treatment *(Syzygium cumini* (L). Skeels seed extract vs. Placebo) at basal and week 12th.

4.5 Abnormal Symptoms

Table 4.10 Abnormal Symptoms after Taking Drug Administration

Symptoms	The number of patients	
	Experimental group (20)	Control group(17)
Stomach irritation/ Distention	2	2
Nausea/Vomiting	-	1
Constipation	2	1
Palpitation/ Tachycardia	1	1
Dizziness/Headache	-	3
Fatigue	1	1
Hypothermia	2	1

Although some patients who were received *S. cumini* (L). Skeels seed extract have symptoms of stomach irritation, constipation, nausea and hypoglycemic symptoms but dose symptoms were found in both experimental and control group.

CHAPTER 5

CONCLUSION, DISCUSSION, AND SUGGESTION

5.1 Discussion

Intensive lifestyle modification program has been recommended according to the New AACE guideline for the deceleration and prevention of diabetes progression in pre-diabetes group nowadays. This program includes: 1)Diet control: low in total fat, saturated fat, trans-fatty acid, adequate fiber, low sodium intake, and cease alcohol consumption; 2) Exercise: moderate intensity 30-60 min/day at least 5 days a week; 3) Weight loss: reducing weight 5-10%. However, the implication of intensive lifestyle modification program in early stage prediabetes may be troublesome. Hence, the medication was also introduced to people with prediabetes. According to the American Association of Clinical Endocrinologists (AACE), it suggested that Metformin and Acarbose are the drug that should be considered for use in diabetes prevention. (Yehuda, 2008) However, the adverse effects from these drugs, such as lactic acidosis, should be a serious concern in patients with kidney and liver disease, this lays the reason why many physicians and researchers investigate the alternative treatment with endeavor for people with prediabetes.

Among 1,200 plant species with anti-diabetic activity, which have been recorded to be used empirically worldwide, (Tundis et al., 2010), *Syzygium cumini* (L.) Skeels or Eugenia jambolana interested our attention since the plant is commonly available in Thailand and has been proven by research studies on their anti-diabetic activity from its seed extract. In 1985, Ramahandridona & Rakotondravoavy (1985) reported that 2-3 g/day of *S. cumini* (L.) Skeels seed extract administration in type II diabetes patients could decrease up to 49% of blood glucose level within 90 days. In 1990, the group reported the combination therapy with extract, sulfonylurea, and insulin in type I diabetic patients. Forty seven percent of glucose was decreased within 6 months. Moreover, Schleicher (1991) suggested that the administration of this extract at level of 3g/day in type II diabetes patients for 6 weeks, could lessened 73% blood glucose level. Sahana et al. (2010) conducted the comparative type II diabetes studies recently. In brief, the patients were divided into 3 groups and were treated with: 10 g/day *S. cumini*(L.) Skeels seed extract (A); 1 g/day Metformin (B); and lifestyle modification(C). The result found the significant decrease in blood glucose level in group A (152±22.5 to 140.7±26.6 mg/dl, $P<0.05$ in 3 months; 152±22.5 to 134±21.3 mg/dl, $P<0.05$ in 6 months, respectively) whereas group C showed the decrease in glucose level but not significant. Sahana et al. reported the HbA1c level decreased after consumption of the *S. cumini*(L.) Skeels seed extract within six months (8±1.3% to 8±1.43%, $P=0.95$ in 3 months; 8±1.3% to 7.6±0.7%, $P=0.233$ in 6 months, respectively). (Sahana et al., 2010) The study in pre-diabetic population has not been

clearly defined. Therefore, we decided to study the blood lowering activity in people with prediabetes. Our study showed as followings:

5.1.1 Fasting Blood Glucose (FBG) Level Reduction Activity

Our results showed that after introduction of diet control, exercise and intake of *S. cumini* (L.) Skeels seed extract or placebo to subjects, both group showed lessened blood glucose level. However, only the group with *S. cumini* (L.) Skeels seed extract showed significant decrease in blood glucose level.

Our finding correlates with the results of Ramahandridona & Rakotondravoavy (1985) and Schleicher (1991) which used the same dosage of extract. Although our results showed weaker effect on blood glucose level, this may be due to the population difference in both previous studies. They reported the studies in type 2 diabetes; however, our study focused on the impaired fasting glucose (pre-diabetic population).

Fasting blood glucose level in placebo group slightly decreased though it is not significant. Our finding correlates with the study by Sahana et al (2010). This may be due to the lifestyle modification and diet control education. The placebo group tended to change their behaviors which resulted in the decrease FBG. However, only *S. cumini* group showed significant decrease in FBG level.

5.1.2 Glycated Hemoglobin (HbA1c) Level Reduction Activity

Basal HbA1c level and 3 month level showed the decrease. However, only group with *S. cumini* (L.) Skeels seed extract lessened the HbA1c significantly. The adverse result was reported by Sahana et al. (2010) which found the slight decrease of HbA1c after 6 months without significance. This may be due to high basal HbA1c level at 8±1.3% from the initial stage. Our basal HbA1c in impaired fasting glucose group was at 6.125±0.627%. Therefore, it may be implied that the HbA1c lowering mechanism of *S. cumini* (L.) Skeels seed extract may react potentially with acute phase than chronic or progressive diabetes.

5.1.3 Limitations of the Study

5.1.3.1 The distribution of gender in placebo group was uneven (6 males and 11 females). This is due to the randomization process which cannot customize the population.

5.1.3.2 Due to the long-term research, it is difficult to stabilize the diet control and exercise of subjects which later caused the fluctuation of blood glucose level.

5.1.3.3 Geographic distribution of this study is limited to Bangkok metropolitan and suburban areas. The results of this study may not reflect the blood glucose lowering capability nationwide since each region has unique dietary culture.

5.1.3.4 Due to the big size of tablet/capsule, it was too difficult for consumption.

5.2 Conclusion

The supplementation of *S. cumini* (L.) Skeels seed extract in impaired fasting glucose population can decrease both FBG and HbA1C level which also correlates with the previous studies in type II diabetes. The efficacy to decrease HbA1c in the people with prediabetes will be higher when compares with diabetic patients. Therefore, the early treatment may prevent the progression to diabetes or delay the existed condition. *S. cumini* (L.) Skeels seed extract should be one of the alternatives for people with impaired fasting glucose level.

5.3 Suggestion

5.3.1 Although the plant can be found nationwide in Thailand, *S. cumini* (L.) Skeels seed extract used in this study was originated in India. Therefore, the efficacy test on both Indian extract and Thai extract should be conducted in the future. If Thai extract acquires the compatible activity, it will result in economic benefit for Thailand and will benefit the diabetic and pre-diabetic population.

5.3.2 The results might show significant data if we could include more subjects to our study.

5.3.3 The measurement of HbA1c could interfere by some factor such as hemoglobinopathy or any condition with an increased red-cell turnover. Therefore these error inducing factors will give an artificially low HbA1c. To limit these confounding factors, we should take blood exam for hemoglobin and HbA1c at the same time to make reliable results.

5.3.4 According to the findings, the administration of extract in people with early stage impaired fasting glucose will cause the short duration of glucose lessening. Interestingly, the normalization of FBG and HbA1c in some people was reported within short time. This supports that the treatment indeed prevents and prolongs the progression to type II diabetes which is a type that predominates in Thai population. Moreover, diabetes causes severe complications which devastate quality of life of patients. In conclusion, it is the most advantageous to prevent people with prediabetes condition and/or people with early stage impaired fasting glucose level from progression to diabetes.

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APPENDICES

APPENDIX A

INFORMED CONSENT FORM

หนังสือยินยอมเข้าร่วมโครงการวิจัย (Informed Consent Form)

วันที่.....เดือน..... พ.ศ.....

ข้าพเจ้า (นาย/นาง/นางสาว)..... อายุ.....ปี อยู่บ้านเลขที่..... หมู่ที่..... ถนน.....ตำบล.....อำเภอ.....จังหวัด.....รหัสไปรษณีย์..... ขอทำหนังสือแสดงความยินยอมเข้าร่วมโครงการวิจัยเพื่อเป็นหลักฐานแสดงว่า

1. ข้าพเจ้ายินยอมเข้าร่วมโครงการวิจัยของ (หัวหน้าโครงการ)น.ส.วรรณพร พัวประเสริฐเรื่อง.....ผลของสารสกัดจากเมล็ดหว้าต่อการลดระดับน้ำตาลในเลือดในคนไทยที่มีภาวะน้ำตาลในเลือดหลังอดอาหารผิดปกติ..... ด้วยความสมัครใจ โดยมิได้มีการบังคับ หลอกลวงแต่ประการใด และพร้อมจะให้ความร่วมมือในการวิจัย

2. ข้าพเจ้าได้รับการอธิบายและตอบข้อสงสัยจากผู้วิจัยเกี่ยวกับวัตถุประสงค์การวิจัย วิธีการวิจัย ความปลอดภัย อาการ หรืออันตรายที่อาจเกิดขึ้น รวมทั้งประโยชน์ที่จะได้รับจากการวิจัย โดยละเอียดแล้วตามเอกสารชี้แจงผู้เข้าร่วมการวิจัยแนบท้าย

3. ข้าพเจ้าได้รับการรับรองจากผู้วิจัยว่าจะเก็บข้อมูลส่วนตัวของข้าพเจ้าเป็นความลับ จะเปิดเผยได้เฉพาะในรูปแบบของการสรุปผลการวิจัยเท่านั้น

4. ข้าพเจ้าได้รับทราบจากผู้วิจัยแล้วว่า หากเกิดอันตรายใดๆ จากการวิจัย ผู้วิจัยจะรับผิดชอบค่ารักษาพยาบาลที่เป็นผลสืบเนื่องจากการวิจัยนี้

5. ข้าพเจ้าได้รับทราบว่า ข้าพเจ้ามีสิทธิที่จะถอนตัวออกจากการวิจัยครั้งนี้เมื่อใดก็ได้ โดยไม่มีผลกระทบใดๆ ต่อการรักษาพยาบาลตามสิทธิ์ที่ข้าพเจ้าควรได้รับ

ข้าพเจ้าได้อ่านและเข้าใจข้อความตามหนังสือนี้แล้ว จึงได้ลงลายมือชื่อไว้เป็นสำคัญ พร้อมกับหัวหน้าโครงการวิจัยและพยาน

ลงชื่อ..... ผู้ยินยอมผู้ปกครอง
(.....)

ลงชื่อ..... หัวหน้าโครงการ
(....น.ส.วรรณพร พัวประเสริฐ.....)

ลงชื่อ..... พยาน
(.....)

ลงชื่อ..... พยาน
(.....)

APPENDIX B

INFORMATION SHEET

เอกสารคำอธิบาย/คำชี้แจง โครงการวิจัยแก่ผู้เข้าร่วมโครงการ (Information Sheet)

1. ชื่อโครงการวิจัย

ผลของสารสกัดจากเมล็ดหว้าต่อการลดระดับน้ำตาลในเลือดในคนไทยที่มีภาวะน้ำตาลในเลือดหลังอดอาหารผิดปกติ

2. วัตถุประสงค์และวิธีการวิจัย

1) วัตถุประสงค์

แพทย์หญิงวรรณพร พัวประเสริฐ ได้ทำการศึกษาวิจัยครั้งนี้ โดยมีจุดประสงค์เพื่อประเมินผลของสารสกัดจากเมล็ดหว้าต่อการลดระดับน้ำตาลในเลือด ในคนไทยที่มีภาวะน้ำตาลในหลังอดอาหารผิดปกติ และเพื่อหาทางเลือกใหม่ในการรักษาสำหรับผู้ที่มีภาวะผิดปกติกลุ่มนี้

ข้าพเจ้าถูกถามให้เข้าร่วมในการศึกษาวิจัยนี้เพราะข้าพเจ้ามีภาวะน้ำตาลในเลือดหลังอดอาหารผิดปกติ โดยไม่อาจทราบได้ว่า สารสกัดจากเมล็ดหว้า จะสามารถทำให้ภาวะนี้ของข้าพเจ้าหายได้หรือไม่

จะมีผู้เข้าร่วมทดลองในการศึกษานี้ประมาณ 40 คน

2) วิธีการวิจัย

หากข้าพเจ้าตกลงเข้าร่วมการศึกษานี้ สิ่งดังต่อไปนี้จะเกิดขึ้น:

ก. ข้าพเจ้าจะได้รับคัดเลือกเพื่อดูว่าข้าพเจ้ามีคุณสมบัติเหมาะสมสำหรับการศึกษาหรือไม่

ข. ก่อนทำการรักษาข้าพเจ้าได้รับการตรวจระดับน้ำตาลกลูโคสหลังอดอาหาร (FBG), และการตรวจค่าระดับน้ำตาลสะสมที่ผิวเม็ดเลือดแดง (HbA1c)

ค. ข้าพเจ้าจะได้รับยาแคปซูล โดยทานครั้งละ 3 แคปซูล ก่อนอาหารเช้าและอาหารเย็น 15 นาที ทุกวัน

ง. ข้าพเจ้าจะได้รับการประเมินผลระดับน้ำตาลกลูโคสหลังอดอาหาร (FBG) ที่สิ้นสัปดาห์ที่ 4, 8, และ 12

จ. ข้าพเจ้าจะได้รับการประเมินผลค่า HbA1c เมื่อสิ้นสุดสัปดาห์ที่ 12

ฉ. ข้าพเจ้าจะถูกขอให้กรอกแบบสอบถามเพื่อประเมินความพึงพอใจด้วยตัวเอง หลังทำการรักษาครบ 12 สัปดาห์

ช. ข้าพเจ้าจะถูกขอให้ไม่ให้ใช้วิธีการรักษาอื่น ๆ หรือสารที่มีผลต่อระดับน้ำตาลระหว่าง 12 สัปดาห์ที่ทำการวิจัย

ซ. ข้าพเจ้าจะแจ้งให้แพทย์ของข้าพเจ้าทราบทันทีว่าข้าพเจ้าได้ใช้วิธีการรักษาอื่น ๆ ที่มีผลต่อระดับน้ำตาลนอกเหนือจากยาที่ได้รับ และข้าพเจ้าอาจถูกเพิกถอนออกจากการวิจัย

ฌ. แพทย์มีสิทธิที่จะเพิกถอนข้าพเจ้าออกจากการวิจัยได้ทุกเมื่อแล้วแต่แพทย์เห็นสมควร

ญ. การศึกษาเป็นการแจกจ่ายแบบสุ่ม โดยวิธีการสุ่มตัวอย่างแบบโควต้า (Quota Sampling)

โดยใช้โปรแกรมสุ่มตัวเลข (การทำแบบสุ่มหมายความว่าทั้งแพทย์ของข้าพเจ้าและข้าพเจ้าไม่ได้เป็นผู้กำหนดการรักษา ที่ข้าพเจ้าจะได้รับ โอกาสที่จะได้รับการรักษาอันใดอันหนึ่งเกือบเท่ากัน)

3. ความเป็นมาของโครงการ ที่ทำให้ต้องศึกษาเรื่องนี้

ความเป็นมาและความสำคัญของโครงการ

ปัจจุบันพบว่าจำนวนผู้ป่วยเบาหวานเพิ่มสูงขึ้นทุกปีทั้งในประเทศไทยและทั่วโลก ทั้งนี้พบว่าเบาหวานยังทำให้เกิดภาวะแทรกซ้อนที่อันตรายต่าง ๆ และทำให้มีโอกาสเสียชีวิตได้มากกว่าคนปกติ ในขณะเดียวกันเราพบว่าก่อนที่จะพัฒนาจากคนปกติไปเป็นคนที่เป็นเบาหวานนั้น จะมีภาวะที่สำคัญเกิดขึ้น คือ ภาวะก่อนเบาหวาน ซึ่งถ้าเราไม่ทำการดูแลรักษาคนไข้กลุ่มนี้อย่างจริงจัง คนไข้กลุ่มนี้จะกลายไปเป็นโรคเบาหวานได้มากกว่าคนปกติ 3.2 เท่า แต่ขณะเดียวกันก็พบว่าหากเราให้การดูแลรักษาคนกลุ่มนี้ก็จะทำให้โอกาสการเกิดเบาหวานในคนกลุ่มนี้ลดลงอย่างชัดเจน การรักษาหลักที่แนะนำให้ผู้ที่มีภาวะก่อนเบาหวานก็คือ การคุมอาหาร ออกกำลังกาย ซึ่งการดูแลวิธีนี้เป็นวิธีที่มีประสิทธิภาพมากที่สุด แต่ผู้ป่วยส่วนใหญ่ไม่สามารถปฏิบัติได้ในระยะยาว ส่วนการใช้ยามีที่พิจารณาให้ใช้ได้ แต่ก็พบผลข้างเคียงหลายอย่างรวมถึงผลข้างเคียงที่อันตราย ปัจจุบันจึงเริ่มมองหาทางเลือกอื่น ๆ ในการรักษาคนที่ภาวะผิดปกตินี้

ข้อมูลในปัจจุบันพบว่า มีพืชจำนวนมากกว่า 1200 ชนิดที่สามารถนำมาใช้รักษาโรคเบาหวานได้ โดยพบว่ามีฤทธิ์ลดระดับน้ำตาลในจริงในห้องปฏิบัติการ หนึ่งในพืชที่น่าสนใจและสามารถหา

ได้ในประเทศไทย คือ หว้า โดยพบข้อมูลการวิจัยทั้งในห้องปฏิบัติการ สัตว์ทดลอง และในคนที่เป็นโรคเบาหวาน พบว่าสามารถใช้ลดระดับน้ำตาลได้อย่างชัดเจน และไม่พบผลข้างเคียงอันตราย

จึงเป็นที่มาที่ทำให้ผู้วิจัยมีความสนใจที่จะทำการวิจัยโดยเลือกใช้สารสกัดจากเมล็ดหว้ามาใช้ในการลดระดับน้ำตาลในผู้ที่มีภาวะก่อนเบาหวาน แบบมีน้ำตาลในเลือดหลังอาหารผิดปกติ ซึ่งถ้าผลการวิจัยสามารถลดระดับน้ำตาลได้ในคนกลุ่มนี้จริง จะเป็นทางเลือกใหม่ในการรักษาของผู้ที่มีภาวะก่อนเบาหวาน

4. สถานที่และระยะเวลาที่ต้องทำการวิจัยกับอาสาสมัคร

1) สถานที่ทำการวิจัย

คลินิกเวชกรรมแพทย์ศรีนครินทร์ 1/77 หมู่บ้าน บ้าน ณ นครินทร์ ซ.สุภาพงษ์ 3 แยก 8 ถ.ศรีนครินทร์ 40 แขวงหนองบอน เขตประเวศ กทม. 10250

2) ระยะเวลาการทำวิจัย

ใช้เวลาทั้งหมด 3 เดือน ภายในเดือน ธันวาคม 2554 – กุมภาพันธ์ 2555

5. รายละเอียดที่จะปฏิบัติต่ออาสาสมัคร

ข้าพเจ้าจะได้รับการรักษาดังต่อไปนี้

1) ข้าพเจ้าจะได้รับการรักษาด้วยสารสกัดจากเมล็ดหว้า หรือยาหลอก จะทานครั้งละ 3 แคปซูล ก่อนอาหารเช้าและอาหารเย็น 15 นาที นาน 12 สัปดาห์

2) แพทย์ที่ประเมินจะไม่ทราบว่าข้าพเจ้าได้รับการรักษาด้วยวิธีใด

3) ข้าพเจ้าจะมาพบแพทย์หลังการรักษาที่ 4,8 และ 12 สัปดาห์ รวมทั้งสิ้น 3 ครั้ง

4) ข้าพเจ้าจะถูกประเมินผลการลดระดับน้ำตาลโดยการเจาะเลือด เพื่อดูค่า ระดับกลูโคสในเลือดหลังอดอาหาร (FBG) และค่า HbA1c

ข้าพเจ้าจะได้รับการบอกกล่าวถึงการค้นพบใหม่ ๆ ในระหว่างการศึกษาวิจัยนี้ ที่มีผลเกี่ยวพันกับความสมัครใจในการร่วมการศึกษาวิจัยต่อไป

6. ประโยชน์ที่คาดว่าจะเกิดขึ้นกับอาสาสมัครและผู้อื่น

ประโยชน์ที่คาดว่าจะเกิดขึ้นกับอาสาสมัคร

แนวโน้มในการรักษาที่ข้าพเจ้าได้รับอาจพิสูจน์ว่ามีประสิทธิภาพในการรักษาภาวะก่อนเบาหวานได้ โดยมีผลข้างเคียงน้อย แม้ว่าจะเป็นสิ่งที่ไม่สามารถรับประกันได้ แต่หลังจากสิ้นสุดการวิจัยหากข้าพเจ้ายังมีภาวะก่อนเบาหวาน ข้าพเจ้าจะได้รับการดูแลรักษาภาวะนี้ต่อไป

7. ความเสี่ยงหรือผลข้างเคียงที่จะเกิดขึ้นต่ออาสาสมัคร พร้อมทั้งระบุมาตรการหรือวิธีแก้ไขที่ผู้วิจัยเตรียมไว้

จากการวิจัยต่าง ๆ พบว่าสารสกัดจากเมล็ดหว้ามีผลข้างเคียงน้อยมาก แต่ก็อาจจะเกิดอาการไม่พึงประสงค์ได้บ้าง หากมีการรับประทานไม่ถูกวิธี โดยภาวะที่อาจเกิดขึ้นได้ คือ ภาวะน้ำตาลในเลือดต่ำ

1) ภาวะน้ำตาลในเลือดต่ำ

ก. อาการและอาการแสดงของน้ำตาลในเลือดต่ำแบ่งออกเป็นสองประเภท

ก) อาการทางออโตโนมิค ได้อาการใจสั่น หัวใจเต้นเร็ว ความดันโลหิตสูง มือสั่น กระสับกระส่าย คลื่นไส้ เหงื่อออก ชา รู้สึกหิว

ข) อาการสมองขาดกลูโคส เมื่อสมองขาดน้ำตาลจะมีอาการอ่อนเพลีย ผิวหนังจะเย็นและชื้น อุณหภูมิร่างกายต่ำ มึนงง ปวดศีรษะ ความจำลดลง สับสน ปฏิกิริยาตอบสนองลดลง ตาพร่า พูดช้า ง่วงซึม หลงลืม พฤติกรรมเปลี่ยน บางคนมีอาการอ่อนแรงครึ่งซีกคล้ายหลอดเลือดสมอง หากอาการเป็นมากจะชักและหมดสติได้

ข. การประเมินความรุนแรงของภาวะน้ำตาลในเลือดต่ำ

ความรุนแรงของภาวะน้ำตาลในเลือดต่ำแบ่งออกได้เป็น 3 ระดับตามอาการและอาการแสดงที่ปรากฏและความสามารถในการช่วยเหลือตนเอง ได้แก่

ก) ภาวะน้ำตาลในเลือดต่ำระดับไม่รุนแรง Mild hypoglycemia หมายถึงผู้ป่วยที่มีระดับน้ำตาลในเลือดต่ำแต่ไม่มีอาการออโตโนมิค เช่นอาการใจสั่น ผู้ป่วยสามารถแก้ปัญหาได้ด้วยตนเอง

ข) ภาวะน้ำตาลในเลือดต่ำระดับปานกลาง Moderate hypoglycemia หมายถึงภาวะที่มีน้ำตาลในเลือดต่ำ และมีอาการออโตโนมิค และอาการสมองขาดกลูโคสเกิดขึ้นเล็กน้อยหรือปานกลาง ผู้ป่วยสามารถแก้ไขด้วยตนเอง

ค) ภาวะน้ำตาลในเลือดต่ำระดับรุนแรง Severe hypoglycemia ผู้ป่วยจะมีอาการรุนแรงจนไม่สามารถช่วยเหลือตัวเองต้องอาศัยผู้อื่นช่วยเหลือ หรือรุนแรงมากจนหมดสติหรือชัก

2) การป้องกันและการแก้ไขภาวะน้ำตาลในเลือดต่ำ

ก. การป้องกันภาวะน้ำตาลในเลือดต่ำ

ง) การรับประทานอาหาร ควรจะต้องทำตามคำแนะนำของแพทย์อย่างเคร่งครัด รับประทาน อาหารให้ตรงเวลา และจำกัดอาหารแต่ละมื้อให้พอเหมาะไม่มากหรือน้อยเกินไป ห้ามอดอาหารหรือทานอาหารไม่ตรงเวลา เพราะอาจเกิดภาวะน้ำตาลในเลือดต่ำได้

จ) รับประทานสารสกัดตามที่แพทย์สั่ง ข้อสำคัญอย่าใช้เกินขนาดที่แพทย์สั่ง หากต้องรับยาอื่นต้องปรึกษาแพทย์

ฉ) แนะนำคนใกล้ชิดให้ทราบอาการของน้ำตาลในเลือดต่ำ และวิธีการแก้ไขเบื้องต้น

ช) หากออกกำลังกายมากกว่าครึ่งชั่วโมงต้องได้รับอาหารว่างเสริม เช่น นมหนึ่งแก้ว หรือขนมแครกเกอร์ 1 แผ่นก่อนออกกำลัง

3) การแก้ไขภาวะน้ำตาลในเลือดต่ำ

ก) ภาวะน้ำตาลในเลือดต่ำระดับไม่รุนแรงและระดับปานกลาง

ให้รับประทานอาหารที่มีแป้ง 15 กรัม เช่นน้ำส้มคั้นหนึ่งแก้ว น้ำอัดลม 180 ซีซี น้ำผึ้งสามช้อนชา ขนมปังหนึ่งแผ่น นมสดหนึ่งกล่อง กล้วยหนึ่งผล โจ๊กหรือข้าวต้มครึ่งถ้วย อาการมักจะดีขึ้นหลังได้รับอาหารดังกล่าว หลังจากรับประทานอาหารดังกล่าวไปแล้ว 15 นาทีหากอาการไม่ดีขึ้นให้รีบพบแพทย์

ข) ภาวะน้ำตาลในเลือดต่ำชนิดรุนแรง

สำหรับผู้ป่วยที่พอจะรู้สึกตัวก็ให้ดื่มน้ำหวานก่อนนำส่งโรงพยาบาล หากผู้ป่วยไม่รู้สึกตัวก็แนะนำว่าไม่ควรที่จะให้ดื่มหรือรับประทานอาหารเพราะจะทำให้ผู้ป่วยสำลักและเกิดปอดบวมได้และให้รีบนำส่งโรงพยาบาล

นอกเหนือจากอาการที่ได้แสดงนี้อาจเป็นอาการที่ไม่เคยพบมาก่อน แพทย์ของข้าพเจ้าจะตรวจข้าพเจ้าอย่างใกล้ชิดเพื่อดูว่าอาการข้างเคียงเหล่านี้เกิดขึ้นไหม ข้าพเจ้าจะแจ้งแพทย์ผู้วิจัยให้ทราบทันทีหากมีอาการข้างเคียงเกิดขึ้นกับข้าพเจ้า และจะรีบมาพบแพทย์ทันทีแม้ว่าจะอยู่นอกตารางนัดหมาย ข้าพเจ้าจะได้รับการรักษาที่เหมาะสมโดยไม่เสียค่าใช้จ่ายและข้าพเจ้ามีสิทธิ์ที่จะถอนตัวจากการศึกษา ณ เวลาใดก็ได้ โดยแพทย์ผู้วิจัยหลักจะให้เบอร์โทรศัพท์ติดต่อโดยตรงแก่ข้าพเจ้าเพื่อที่จะสามารถติดต่อได้ตลอดเวลาหากมีข้อซักถามหรือเกิดปัญหาใด ๆ ขึ้นระหว่างการรักษา

การเข้าร่วมในโครงการวิจัยนี้อาจจะทำให้การรักษาภาวะก่อนเบาหวานได้ผลหรืออาจไม่ได้ผลในการรักษาเลยก็ได้

8. ขอบเขตการดูแลรักษาความลับของข้อมูลต่าง ๆ ของอาสาสมัคร

การเข้าร่วมงานวิจัยทำให้สูญเสียความเป็นส่วนตัว แต่ข้อมูลเกี่ยวกับข้าพเจ้าจะถูกปกปิดไว้เป็นความลับ ความเป็นส่วนบุคคลจะไม่ถูกเปิดเผยแก่สาธารณะชน ในกรณีที่ผลงานวิจัยได้รับการตีพิมพ์ ชื่อและที่อยู่ของข้าพเจ้าจะได้รับการปกปิดอยู่เสมอ ผู้กำกับดูแลการวิจัยจะได้รับอนุญาตให้ตรวจสอบเวชระเบียนต้นฉบับของข้าพเจ้าโดยตรง เพื่อตรวจสอบ ความถูกต้องของวิธีการดำเนินวิจัย

ทางคลินิก และ/หรือข้อมูลอื่นๆโดยไม่ละเมิดสิทธิของข้าพเจ้าในการรักษาความลับเกินขอบเขตที่กฎหมายอนุญาตไว้ โดยข้าพเจ้าได้ลงนามในเอกสารใบยินยอมอนุญาตให้บุคคลต่างๆ ข้างต้นมีสิทธิตรวจสอบเวชระเบียนของข้าพเจ้าโดยตรง

9. การดูแลรักษาที่ผู้วิจัยจัดให้

ข้าพเจ้าไม่ต้องเสียค่าใช้จ่ายในส่วนที่เป็นยา หรือค่าการตรวจทางห้องปฏิบัติการใดๆทั้งสิ้นตลอดระยะเวลาการวิจัย

10. ค่าตอบแทนอาสาสมัคร และค่ารักษาพยาบาล ค่าชดเชย กรณีเกิดอันตรายหรือผลที่ไม่พึงประสงค์จากการวิจัยแก่อาสาสมัคร

1) ผู้เข้าร่วมวิจัยทุกคน ได้รับค่าตอบแทนการวิจัย รายละ 400 บาทและไม่ต้องเสียค่าใช้จ่ายใดๆในการรักษาตลอดระยะเวลาการศึกษาวิจัย

2) ในกรณีเกิดผลข้างเคียงจากการรักษา ผู้เข้าร่วมวิจัยจะได้รับการดูแลรักษาทันทีโดยไม่ต้องเสียค่าใช้จ่ายและได้รับเงินค่าชดเชยเป็นจำนวนเงิน 1000 บาท ในกรณีที่ต้องเข้ารับการรักษาในโรงพยาบาล

11. สิทธิของอาสาสมัครที่สามารถถอนตัวจากโครงการวิจัยได้ทุกเมื่อโดยไม่กระทบต่อการดูแลรักษาที่พึงได้รับตามปกติ

การเข้าร่วมในงานวิจัยเป็นไปตามความสมัครใจของข้าพเจ้า ข้าพเจ้ามีสิทธิ์ที่จะถอนตัวจากการศึกษา ณ เวลาใดเวลาหนึ่ง และการเพิกถอนดังกล่าวจะไม่มีผลต่อการดูแลรักษาทางการแพทย์ของข้าพเจ้าในอนาคต การเข้าร่วมของข้าพเจ้าอาจสิ้นสุดเวลาใดก็ได้ ด้วยหรือไม่ด้วยความสมัครใจของข้าพเจ้ารวมถึง แพทย์มีสิทธิที่จะเพิกถอนข้าพเจ้าออกจากการวิจัยได้ทุกเมื่อแล้วแต่แพทย์เห็นสมควร

12. ข้อพิจารณาด้านจริยธรรม

ในการศึกษาวิจัยนี้ดำเนินการตามหลักของการปฏิบัติการวิจัยทางคลินิกที่ดี (Good Clinical Practice: GCP) ซึ่งเป็นมาตราฐานสากลด้านจริยธรรมและด้านวิชาการสำหรับใช้ในการวางรูปแบบการดำเนินงาน การบันทึกข้อมูลและการเขียนรายงานการศึกษาวิจัยในมนุษย์ การปฏิบัติตามเกณฑ์มาตราฐานนี้เป็นการรับประกันต่อสาธารณชนว่า สิทธิ ความปลอดภัยและความเป็นอยู่ที่ดีของ

อาสาสมัครได้รับการคุ้มครองตามหลักการแห่งคำประกาศเฮลซิงกิ (Declaration of Helsinki) และผลการวิจัยทางคลินิกที่เชื่อถือได้

13. ชื่อ ที่อยู่ เบอร์โทรศัพท์ ของหัวหน้าโครงการวิจัย หรือแพทย์ที่ผู้วิจัยกำหนด โดยสามารถติดต่อได้ทุกเวลา กรณีมีเหตุจำเป็นหรือฉุกเฉินหัวหน้าโครงการวิจัย

แพทย์หญิงวรรณพร พัวประเสริฐ

คลินิกเวชกรรมแพทย์ศรีนครินทร์ 1/77 หมู่บ้าน บ้าน ณ นครินทร์ ซ.สุภาพงษ์ 3 แยก 8 ถ.ศรีนครินทร์ 40 แขวงหนองบอน เขตประเวศ กทม. 10250

โทรศัพท์ 084-3399832, Email : drgubgib@hotmail.com

****หมายเหตุ : เอกสารคำอธิบายโครงการนี้ จะต้องจัดทำขึ้นโดยภาษาที่เข้าใจง่าย โดยควรหลีกเลี่ยงศัพท์ทางวิชาการที่เข้าใจยาก หรือภาษาต่างประเทศ ****

APPENDIX C

PATIENT RECORD FORM

เรื่อง: ผลของสารสกัดจากเมล็ดหว้าต่อการลดระดับน้ำตาลในเลือดในคนไทยที่มีภาวะน้ำตาลในเลือดหลังอดอาหารผิดปกติ

Effect of *Syzygium cumini* (L.) Skeels seed extract on lowering blood glucose level in Thai people with impaired fasting glucose

เลขที่แบบบันทึกข้อมูล…….. วันที่.....

ข้อมูลส่วนตัว HN.....

ชื่อ..... นามสกุล.....อายุ.....ปี

เพศ ☐ 1.ชาย ☐ 2. หญิง อาชีพ.....

ที่อยู่.....

.....

เบอร์ติดต่อ.....

สถานภาพ ☐ โสด ☐ คู่ ☐ หม้าย ☐ หย่า

การศึกษา ☐ มัธยม ☐ ปวช/ปวส ☐ ปริญญาตรี ☐ สูงกว่าปริญญาตรี

☐ อื่น ๆ .....

ประวัติแพ้ยา/อาหาร

1) ไม่มี 2) มี ชื่อยา/อาหาร.....อาการ.....

ประวัติโรคประจำตัว

1) ไม่มี 2) มี โรค.....

ได้รับการวินิจฉัยเมื่อ.....

การรักษาโดย.....

ประวัติการใช้ยาเป็นประจำ

1) ไม่มี 2) มี ชื่อยา.....ระยะเวลาการใช้.....

วิธีการใช้.....ใช้ครั้งสุดท้ายเมื่อ.....

ประวัติครอบครัวที่ป่วยเป็นโรคเบาหวาน

1) ไม่มี 2) มี .....

ประวัติโรคเบาหวานขณะตั้งครรภ์หรือมีประวัติคลอดลูกตัวโต (น้ำหนักตั้งแต่4กิโลกรัมขึ้นไป)

1) ไม่มี 2) มี .....

มีประวัติหรือเคยมีประวัติน้ำตาลในเลือดสูง (FPG = 100-125 mg%หรือOGTT ≥ 140mg%)

1) ไม่มี 2) มี .....

ลักษณะการใช้ชีวิต และพฤติกรรมส่วนตัว

1. การรับประทานอาหาร

1) จำนวนมื้อ / เวลา / ความตรงเวลา / ปริมาณ / มื้อพิเศษ

.....

.....

.....

2) ลักษณะใดที่ตรงกับพฤติกรรมการรับประทานอาหารของท่านมากที่สุด (คำนึงถึงสุขภาพเป็นหลัก / คำนึงถึงสุขภาพพอสมควร / ไม่คำนึงถึงสุขภาพเลย) :

.....

3) ประเภทของอาหารที่รับประทานบ่อย :

.....

2. การดื่มน้ำและเครื่องดื่มแอลกอฮอล์

1) น้ำเปล่า : ……..……
2) น้ำอัดลม : ……
3) เครื่องดื่มแอลกอฮอล์ ……..…..

? *กรุณาระบุปริมาณต่อวัน หากเป็นน้ำอัดลมและเครื่องดื่มแอลกอฮอล์ให้ระบุความถี่ด้วย เช่น ดื่มน้ำอัดลม 1 ขวดต่อวัน ความถี่ประมาณ 4 วันต่อสัปดาห์*

3. กิจกรรมทางกาย

1) การใช้ชีวิตทั่ว ๆ ไปของท่านที่ไม่รวมถึงการออกกำลังกายอย่างจริงจังนั้นตรงกับลักษณะใดมากที่สุด (ออกแรงมาก / ออกแรงปานกลาง / แทบจะไม่ออกแรง)

……

2) การออกกำลังกาย

…….....

……..

? *กรุณาระบุ ความถี่ ระยะเวลา ในการออกกำลังกายด้วย เช่น วิ่ง (30 นาที 1 วันต่อสัปดาห์) และเล่นฟุตบอล (1 ชั่วโมง 1 วันต่อสัปดาห์) เป็นต้น*

4. การสูบบุหรี่

1) ท่านสูบบุหรี่หรือไม่

…….....

2) ท่านได้รับควันบุหรี่จากคนอื่นบ้างหรือไม่

…….....

? *หากสูบบุหรี่ กรุณาระบุจำนวนมวนต่อวันด้วย*

ตรวจร่างกาย

BW (kg)		Ht (cm)		BMI		W/H ratio	
T (°c)		PR (BpM)		RR (/min)		BP (mmHg)	

Systemic Examination			
General Appearance	☐ Normal	☐ Abnormal	
Skin	☐ Normal	☐ Abnormal	
HEENT	☐ Normal	☐ Abnormal	
Heart	☐ Normal	☐ Abnormal	
Chest	☐ Normal	☐ Abnormal	
Breasts	☐ Normal	☐ Abnormal	
Abdomen	☐ Normal	☐ Abnormal	
Extremities	☐ Normal	☐ Abnormal	
Neurology	☐ Normal	☐ Abnormal	
Others (Specify)			

ผลตรวจเลือดทางห้องปฏิบัติการ

1.Fasting BloodGlucose .....

2.HbA1c .....

APPENDIX D

RECORD FORM

แบบบันทึกข้อมูลการตรวจติดตามผล

HN.....

ชื่อ..... นามสกุล.....ยาหมายเลข.....

T1 (วันที่.....)

General assessment	....
จำนวนยาที่เหลือ จำนวนยารับเพิ่ม	....
Safety & Telorance	☐ ปรกติดี ไม่อาการแพ้ ☐ พบอาการแพ้ คือ .....
Side effect	☐ ไม่พบอาการข้างเคียง ☐ อาการข้างเคียง คือ.....

T2 (วันที่.....)

General assessment	....
จำนวนยาที่เหลือ จำนวนยารับเพิ่ม	....
Safety & Telorance	☐ ปรกติดี ไม่อาการแพ้ ☐ พบอาการแพ้ คือ .....
Side effect	☐ ไม่พบอาการข้างเคียง ☐ อาการข้างเคียง คือ.....

T3 (วันที่.....)

General assessment	....
จำนวนยาที่เหลือ จำนวนยารับเพิ่ม	....
Safety & Tolerance	☐ ปรกติดี ไม่อาการแพ้ ☐ พบอาการแพ้ คือ .....
Side effect	☐ ไม่พบอาการข้างเคียง ☐ อาการข้างเคียง คือ.....

แบบบันทึกผลการทดลอง

HN.....

ชื่อ..... นามสกุล.....ยาหมายเลข.....

week	record					
	FBG	HbA1c	BW	BMI	BP	PR
0						
4		⊗				
8		⊗				
12						

APPENDIX E

SATISFACTION QUESTIONNAIRE

สำหรับผู้เข้าร่วมวิจัย (ศึกษาผลการใช้ที่สิ้นสุดสัปดาห์ที่ 12)

HN.....

ชื่อ..... นามสกุล.....ยาหมายเลข.....

ความเห็นเกี่ยวกับลักษณะผลิตภัณฑ์

ท่านเห็นด้วยหรือไม่ กับคุณลักษณะ ต่อไปนี้	**ไม่เห็นด้วย**	**ไม่ค่อย เห็นด้วย**	**เห็นด้วย เล็กน้อย**	**เห็นด้วย**
1.ยารับประทานง่าย				
2.ยาพกพาง่าย				
หลังรับประทานข้าพเจ้ามีอาการต่อไปนี้	**ไม่เป็นเลย**	**เล็กน้อย**	**ปานกลาง**	**มาก**
3.ใจสั่น, หัวใจเต้นเร็ว, มือสั่นกระสับกระส่าย				
4.คลื่นไส้				
5.เหงื่อออก ชา				
6.อ่อนเพลีย				
7.ผิวหนังจะเย็นและชื้น อุณหภูมิร่างกายต่ำ				
8.มึนงง ปวดศีรษะ				

อาการไม่พึงประสงค์นอกจากนี้

.....

.....

.....

ความเห็นทั่วไปเกี่ยวกับการรักษา

1. ความพึงพอใจในการรักษาโดยวิธีนี้	☐ ไม่พอใจอย่างยิ่ง	☐ ไม่พอใจเล็กน้อย	☐ เฉย ๆ	☐ พอใจเล็กน้อย	☐ พอใจอย่างยิ่ง
2. คะแนนการรักษา	☐ กรุณาให้คะแนนการรักษาจาก 1-10 (คะแนนเต็ม 10)				
3. จะใช้ยาที่ได้รับต่อไปหรือ ไม่	☐ ไม่ใช้	☐ ไม่น่าจะใช้	☐ เฉย ๆ	☐ คิดว่าจะใช้	☐ ใช้แน่นอน

<u>ข้อแนะนำเพิ่มเติมสำหรับผลิตภัณฑ์นี้</u>

.....

.....

.....

.....

CURRICULUM VITAE

CURRICULUM VITAE

NAME	Miss Wannaphorn Pourprasert
DATE OF BIRTH	28 July 1982
ADDRESS	39 Moo 2, Khoktum Subdistrict, Meuang Lopburi District, Lopburi, Thailand 15210

EDUCATIONAL BACKGROUND

2001-2006	Bachelor Doctor of Medicine Srinakharinwirot University, Bangkok, Thailand

WORK EXPERIENCE

2010-Present	Part time Physician Srinakarin Medical Clinic, Bangkok, Thailand
2008-2010	Full time Physician Pattananikom Hospital, Lopburi, Thailand
2006-2007	Full time Physician Banmi Hospital, Lopburi, Thailand