

ผลของสารสกัดจากเมล็ดหว่าต่อการลดระดับน้ำตาลในเลือดในคนไทยที่มีภาวะน้ำตาลในเลือด  
หลังอดอาหารผิดปกติ

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

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นิสิตระดับปริญญาโท สาขาวิชาเวชศาสตร์ชะลอวัยและฟื้นฟูสุขภาพ มหาวิทยาลัยแม่ฟ้าหลวง

**บทคัดย่อ**

เนื่องจากผู้ที่มีภาวะก่อนเบาหวานมีจำนวนเพิ่มขึ้นอย่างต่อเนื่อง การลดและควบคุมระดับน้ำตาลให้มีค่าปกติจึงมีความสำคัญอย่างยิ่งทั้งนี้เพื่อชะลอการเกิดโรคเบาหวานในอนาคต และในปัจจุบันเราพบว่ามีการสกัดจากพืชหลายชนิดมีฤทธิ์ในการลดระดับน้ำตาลในเลือดตั้งเช่นสารสกัดจากเมล็ดหว่า ดังนั้นหากเราให้สารสกัดจากเมล็ดหว่าในผู้ที่มีภาวะก่อนเบาหวานจึงน่าจะช่วยลดระดับน้ำตาลในเลือดในผู้ป่วยกลุ่มนี้ได้

**วัตถุประสงค์** เพื่อศึกษาประสิทธิภาพของสารสกัดจากเมล็ดหว่าในการลดระดับน้ำตาลในเลือดในผู้ที่มีภาวะน้ำตาลในเลือดหลังอดอาหารผิดปกติ

**วิธีการศึกษา** มีผู้เข้าร่วมโครงการวิจัยจำนวน 38 คนโดยคัดเลือกจากอาสาสมัครที่มีภาวะน้ำตาลในเลือดหลังอดอาหารผิดปกติ(ระดับน้ำตาลในเลือดหลังอดอาหารอยู่ระหว่าง 100-125 mg/dl) หลังจากนั้นแบ่งผู้เข้าร่วมวิจัยเป็น 2 กลุ่มโดยวิธีสุ่ม ให้ผู้เข้าร่วมวิจัยกลุ่มแรกรับประทานสารสกัดจากเมล็ดหว่าและกลุ่มที่ 2 รับประทานยาหลอก เปรียบเทียบผลการรักษาโดยวัดระดับน้ำตาลในเลือดหลังอดอาหารที่ก่อนและหลังการรักษาที่ 4,8 และ 12 สัปดาห์ และวัดระดับน้ำตาลสะสมที่ผิวเม็ดเลือดแดงที่ก่อนและหลังการรักษาที่ 12 สัปดาห์

**ผลการทดลอง** กลุ่มที่ได้รับสารสกัดจากเมล็ดหว่าที่มีค่าระดับน้ำตาลในเลือดหลังอดอาหารที่ 4 และ 12 สัปดาห์ เทียบกับก่อนการรักษามีค่าลดลงอย่างมีนัยยะสำคัญทางสถิติ ( $p = 0.017$  และ  $p = 0.040$ , ตามลำดับ) เช่นเดียวกับค่าระดับน้ำตาลสะสมที่ผิวเม็ดเลือดแดงมีระดับลดลงอย่างมีนัยยะสำคัญเช่นเดียวกันเมื่อเปรียบเทียบที่ 12 สัปดาห์และก่อนการรักษา ( $p = 0.030$ ) ส่วนกลุ่มควบคุมที่ได้รับยาหลอกค่าระดับน้ำตาลในเลือดหลังอดอาหาร และระดับน้ำตาลสะสมที่ผิวเม็ดเลือดแดงไม่เปลี่ยนแปลง ( $p > 0.05$ ) อย่างไรก็ตามเมื่อเปรียบเทียบประสิทธิภาพของการรักษาทั้งสองวิธี ไม่พบความแตกต่าง ทั้งค่าระดับน้ำตาลในเลือดหลังอดอาหารและค่าระดับน้ำตาลสะสมที่ผิวเม็ดเลือดแดง ( $p > 0.05$ )

**สรุปผล** การให้สารสกัดจากเมล็ดหว่าแก่ผู้ที่มีภาวะน้ำตาลในเลือดหลังอดอาหารผิดปกติ สามารถทำให้ระดับน้ำตาลในเลือดลดลงได้จริงทั้งค่าระดับน้ำตาลในเลือดหลังอดอาหารและค่าระดับน้ำตาลสะสมที่ผิวเม็ดเลือดแดงภายในระยะเวลา 12 สัปดาห์

**คำสำคัญ** สารสกัดจากเมล็ดหว่า, ระดับน้ำตาลในเลือดหลังอดอาหารผิดปกติ, น้ำตาลในเลือดหลังอดอาหาร, น้ำตาลสะสมที่ผิวเม็ดเลือดแดง

## 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.

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

**Materials and Methods:** 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.

**Results:** 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 ( $p > 0.05$ ).

**Conclusion:** *Syzygium cumini* treatment in subjects with impaired fasting glucose could reduce FBG and HbA1c within 12 weeks

**Key words:** *Syzygium cumini* (L.) Skeels seed extract, Impaired fasting glucose, Fasting blood glucose (FBG), Glycated hemoglobin (HbA1c)

## Introduction

Diabetes mellitus (DM) tends to increase in many countries. Globally, 171 million cases of diabetic patients were reported by the WHO in 2000. This number was predicted to increase to 336 million in 2030. (Wild, Roglic, Green, Sicree & King, 2004) Several studies have demonstrated that 100-125 mg% of fasting blood glucose could be described as a state of prediabetes. (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) 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. However, the implication of intensive lifestyle modification program in early stage patients may be troublesome. Hence, the medication was also introduced to this patient group. 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 effect 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) *Syzygium cumini* (L.) Skeels or *Eugenia jambolana* interests the author's attention, since the plant is commonly available in Thailand and has been proven by research studies on their anti-diabetic activity from its extract. Several studies demonstrated the effects of *Syzygium cumini* (L.) Skeels seed extract extensively in DM patients. (Modi, Patel & Shah, 2010) However, the report of its potential effects in prediabetes treatment is still limited. The objective of this study is to determine the effects of *Syzygium cumini* (L.) Skeels seed extract in decreasing levels of FBG & HbA1c in impaired fasting glucose subjects. We expect that *Syzygium cumini* (L.) Skeels seed extract will be an alternative treatment in the new strategy to delay overt DM.

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

**Study design and research methodology**

38 Volunteers with impaired fasting glucose (100 – 125 mg/dl) were randomized into two groups; the experiment group received *Syzygium cumini* (L) Skeels seed extract 3 g/d (1.5 g bid), and the placebo group received methylcellulose 3 g/d (1.5 g bid). Fasting blood glucose levels were tested at week 0, 4, 8, and 12 while the HbA1c were tested at week 0 and 12. There was one subject from the placebo group who dropped off from the study.

**Statistical analysis**

The means of fasting blood glucose levels at basal, 4<sup>th</sup> week, 8<sup>th</sup> week, and 12<sup>th</sup> week in each groups are compared by using Two way ANOVA Repeated Measurement. The mean of HbA1c levels at basal and 12<sup>th</sup> week in each group are by using Paired T-test. The means of change in Fasting blood glucose & HbA1c levels between control and treatment groups are compared by using T-test. (95% level of confidence, P value=0.05)

**Results**

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, one female subject was excluded from the study because of personal reason. 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 1. BMI in both groups has been shown to be overweight. All basic parameters in table 1 are not different between experimental and placebo groups. (p>0.05)

**Table 1: The basic parameters in experimental and control groups.**

Parameter	Experimental group (N=20)			Control group (N=17)			T	p-value
	Mean	±	SD	Mean	±	SD		
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

\*. The mean of difference significant at the .05 level.

The FBG levels of subjects who received *Syzygium cumini* (L) Skeels seed extract at basal, week 4, 8 and 12 are 111.25±8.136, 104.150±11.69, 104.9±14.186 and 102.2±18.895, respectively (as shown in Table 2). There are statistically significant differences in reduction of FBG in the experiment group at week 4 and 12 when compare to basal (p = 0.017 and p = 0.040) (as shown in Table 3).The FBG levels of subjects in the control group are 113.06±8.242, 110.24±24.466, 108.530±20.338 and 104.29±18.278, respectively (as shown in Table 2). We found that the FBG levels are not different at any time after receiving placebo (p > 0.05).

**Table 2: Fasting blood glucose at each visit of experimental and control groups.**

Time	Mean ± SD					
	Experimental group			Control group		
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

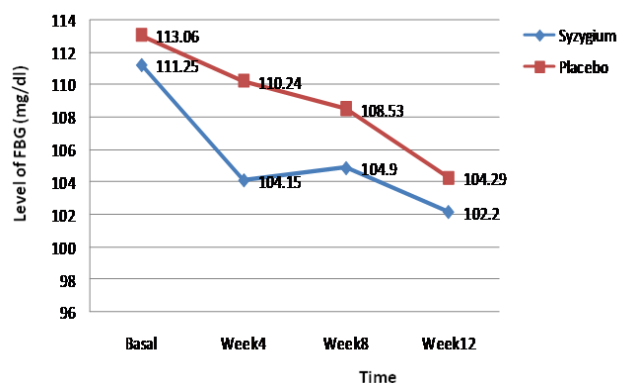
\*. The mean of difference, significant at the .05 level.

**Table 3: The comparison of fasting blood glucose (FBG) at serial times after treatment in experimental group.**

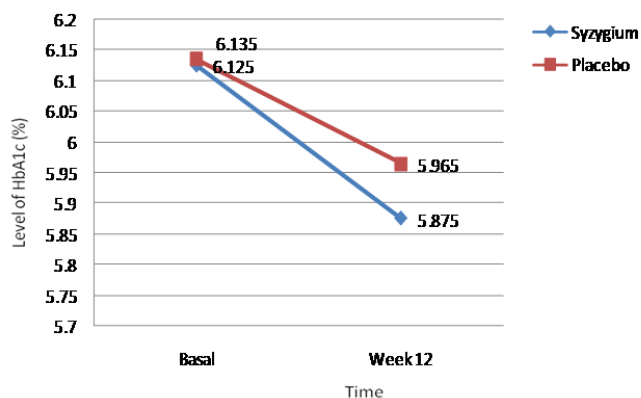
Time	Mean ± SD	Time	Mean ± SD	p-value
FBG Basal	111.250 ± 8.136	FBG Week4	104.150 ± 11.690	.017*
		FBG Week8	104.900 ± 14.618	.082
		FBG Week12	102.200 ± 18.895	.040*
FBG Week4	104.150 ± 11.690	FBG Basal	111.250 ± 8.136	.017*
		FBG Week8	104.900 ± 14.618	.781
		FBG Week12	102.200 ± 18.895	.548
FBG Week8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

\*. The mean of difference, significant at the .05 level.

**Figure 1: Fasting blood glucose at each time point after treatment (*Syzygium cumini* & Placebo).**



**Figure 2: Glycated hemoglobin (HbA1c) at each time point after treatment (*Syzygium cumini* & Placebo).**



The levels of HbA1c of subjects who received *Syzygium cumini* (L).Skeels seed extract are  $6.125 \pm 0.627$  and  $5.875 \pm 0.561$ ; and  $6.135 \pm 0.819$  and  $5.965 \pm 1.000$  in control group at basal and week 12, respectively (as shown in Table 4). There was a reduction in HbA1c levels between basal and week 12, statistically significant in the experimental group ( $p = 0.030$ ) but was not statistically significant in the control group ( $p > 0.05$ ).

**Table 4: The comparison of HbA1c between basal and week 12 in experimental and control groups.**

Experimental group							Control group						
Time	Mean	±	SD	t	df	p-value	Time	Mean	±	SD	t	df	p-value
HbA1c Basal	6.125	±	.627				HbA1c Basal	6.135	±	.819			
				2.005	19	0.030*					1.484	16	0.079
HbA1c Week12	5.875	±	.561				HbA1c Week12	5.965	±	1.00			

\*. The mean of difference significant at the .05 level.

## Discussion

### 1. Fasting blood glucose (FBG) level reduction activity

The result of this study shows that after the introduction of diet control, exercise and intake of *Syzygium cumini* (L).Skeels seed extract or placebo, both group shows lessened blood glucose level. However, only the group with *Syzygium cumini* (L).Skeels seed extract shows significant decrease in fasting blood glucose level. Our finding correlates with the result of Ramahandridona & Rakotondravoavy (1985), which used the same dosage of extract. Fasting blood glucose levels in placebo group slightly decreased, though they are not significant. Our finding correlates with the previous 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 in FBG levels. However, only *Syzygium cumini* (L).Skeels seed extract group shows significant decrease in FBG levels.

### 2. Glycated hemoglobin (HbA1c) level reduction activity

There were reductions in HbA1c levels in both groups. However, only group with *Syzygium cumini* (L). Skeels seed extract lessened the HbA1c significantly. The adverse result was reported by Sahana *et al.* (2010), which found a slight decrease of HbA1c after 6 months without significance. This may be due to high basal HbA1c level at  $8\pm 1.3\%$  from the initial stage. This study's mean basal level of HbA1c in impaired fasting glucose group was  $6.125\pm 0.627\%$ . Therefore, it may be implied that the HbA1c lowering mechanism of *Syzygium cumini* (L.) Skeels seed extract may react more effectively during the acute phase than chronic or progressive diabetes.

### 3. Limitations of the study

-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.

-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.

-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.

## Conclusion

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

## Suggestion

-Although the plant can be found nationwide in Thailand, *Syzygium 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.

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

-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.

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