THE EFFECTS OF PAPAYA LEAVES JELLY IN LIPID PROFILE AMONG OVERWEIGHT WOMEN

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ABSTRACT

Background: Insulin resistance that occurred in diabetic state could promote endothelial dysfunction which lead to metabolic disease in obese subjects. Although several studies showed papaya leaves had antidiabetic and antihyperlipidemic agent, the effect of papaya leaves jelly is rarely studied on lipid profiles among overweight women.

Objectives: We aimed to examine the effect of papaya leaves jelly on lipid profiles in women with overweight.

Methods: This study was a pre-posttest controlled group design with both of the groups were overweight. The treatment group consumed papaya leaves jelly with 24.6 grams papaya leaves jelly that contains 182.4 mg chlorophyll, while the control group consumed 24.6 grams jelly with green dye for 20 days in a row. Three-day recall in three non-consecutive days and physical activity using International Physical Activity (IPAQ) were taken three times. Fasting blood sugar was measured using Glucose Oxidase Phenol 4-Aminophenazone (GODPAP), LDL, HDL, total cholesterol, triglyceride levels were measured using Cholesterol Oxidase Para Aminophenazone (CHOD-PAP). Statistical analysis using Paired t-test was used within group, while Independent t-test and Mann-Whitney were used in between groups. Papaya leaves jelly effects on lipid profiles was analyzed using multiple linear regression after considering energy, protein, fat, and carbohydrate intakes.

Results: Triglyceride levels was reduced significantly (p=0.014) in the treatment group despite there were no differences in triglyceride (p= 0.407), LDL (p= 0.923), HDL (p= 0.749) and total cholesterol (p= 0.277) between 2 groups.

Conclusion: Papaya leaves jelly consumption could lower triglyceride levels significantly in the treatment group.

Key words: Papaya leaves; lipid profile; overweight; women

INTRODUCTION

Diabetes has become a major health problem worldwide, including in Indonesia. Data from Basic Health Research from Ministry of Health of Republic of Indonesia describes that the prevalence of diabetes in 2013 is 1.5% and increase 2% in 2018. The magnitude of the incidence, prevalence, and complication of diabetes shows the importance of early prevention and diabetic management, especially during prediabetic stage. Prediabetes is identified as a reversible circumstance which increases risk of diabetes and comorbidities. American Diabetes Association (ADA) postulated that prediabetes is defined as a condition in which glucose levels do not meet the criteria for diabetes but are too high to be considered normal. Individual with prediabetes have fasting blood glucose levels between 100 to 125 mg/dl and / 2-hr postprandial glucose level between 140 to 199 mg/dl.

Subject with prediabetes has a greater risk for the development of diabetes and cardiovascular disease (CVD). Diabetes generally occurred with increased production of reactive oxygen species (ROS) and suppression of antioxidant through glucose autoxidation, polyl pathway, and non-enzymatic glycation of proteins.

Evidence suggests that underlying disorder including metabolic syndrome is manifested during prediabetes and type 2 diabetes. Several markers such as obesity, triglycerides, high total cholesterol, high LDL cholesterol, low HDL cholesterol, and hypertension are higher in subjects with prediabetes than those without prediabetes.

Lipid abnormalities are common in diabetes since insulin deficiency causes excessive metabolism of free fatty acids and insulin resistance which reduces lipoprotein lipase (LPL) activity that causes hyperlipidemia (hypertriglyceridemia, low HDL cholesterol, elevated LDL cholesterol and elevated serum cholesterol). Moreover, the increase in lipid profile may be a result of increased lipid breakdown and mobilization of free fatty acids from peripheral deposits.

Diabetes and hyperlipidemia may be prevented during reversible condition at prediabetic state by consuming green leafy vegetables that contain chlorophyll which inhibits oxidative DNA damage and lipid peroxidation both by reducing
reactive oxygen species \(^\text{2,12}\). Another antioxidant component was superoxide dismutase (SOD) which is located in cell compartments such as chloroplasts and mitochondria that also play a role in catalyzing the dismutation of \(\text{O}_2^+\) to less reactive compound such as \(\text{O}_2\) and \(\text{H}_2\text{O}_2\).\(^\text{13-15}\) Research described that papaya leaves have the highest chlorophyll content among green leafy vegetables such as cassava leaves, pegagan, spinach, grass-jelly, water spinach and basil.\(^\text{16}\)

Papaya leaves have been shown to contain many components that can increase the total antioxidant level in blood. A study using chlorophyll in papaya leaves gives effects on superoxide dismutase and glucose level of diabetic rats.\(^\text{17}\) The component of papaya leaves such as quercetin, tannin, and alkaloid carpaine could lower both cholesterol and triglycerides levels.\(^\text{18,19}\) Another study using papaya leaves extract could significantly decrease LDL cholesterol and increase HDL cholesterol in serum significantly.\(^\text{20}\)

However, papaya leaves have a bitter taste caused by saponin compound which according to research acts both as an antidiabetic and antidiyslipid.\(^\text{21,22}\) Several food processes are made in order to increase acceptance, one of them is in jelly form. It has been shown in a preliminary study that papaya leaves jelly was satisfying. Foodstuffs were incorporated into the product to reduce bitterness and improve the taste. The product developed was composed of papaya leaves juice, jelly, stevia powder, and skim milk. This article is aimed to investigate the effect of papaya leaves jelly on lipid profile in prediabetic women.

**METHODS**

This research was conducted at Sendangmulyo, Tandang (Tembalang Sub-district) and Semarang City Government office in Pandanaran Building Semarang, Indonesia from March to June 2016 using a pretest-posttest controlled group design. The sample size was calculated using unpaired numerical analytical formulas with standard deviations based on chlorophyll study.\(^\text{23}\) The treatment group was provided with papaya leaves jelly while the control group received jelly with green dye.

Subjects were recruited from residential areas and offices in Semarang with inclusion criteria that were overweight according Asia Pacific criteria (Body Mass Index above 23 kg/m\(^2\)).\(^\text{24}\) women aged 35-50 years, waist circumference above 80 cm, not consuming alcohol, non-smoking, not taking anti-hyperglycemic or anti-hypertensive drugs, and not being pregnant or breastfeeding. Eligible subjects were those with fasting blood sugar above 90 mg/dl and willing to comply with research procedures and providing informed consent was recruited.

Food intake data were obtained using 3 times repeated of 24 hours recall consist of 2 weekdays and 1 day at weekend, while physical activity data used International Physical Activity Questionnaire (IPAQ) with 3 times data retrieval. Lipid profile (triglycerides, total cholesterol, LDL cholesterol and HDL cholesterol) was measured using fasting blood samples, collected by a qualified phlebotomist, and measured using Cholesterol Oxidase Para Aminophenazone (CHOD-PAP).

Anthropometric data of body weight was measured using digital weight scales with 0.1 precision and height was measured using a microtoise with 1 mm accuracy. Compliance data was obtained from filling out the checklist form filled by the researcher through direct observation while the subject consuming the products.

The safe dose to lower lipid profile were based on Panam Parikh study which gave daily spirulina supplementation by 8 grams containing 60.8 mg of chlorophyll for 60 days.\(^\text{25}\) According to the laboratory test, 8.1 grams of papaya leaves jelly contain 7.4% chlorophyll. The dose given to the subjects was 24.6 grams, contains of 182.4 mg of chlorophyll for 20 days.

The analysis was conducted using SPSS. A normality test using Saphiro-Wilk was conducted. Differences in triglyceride, LDL, HDL, and total cholesterol before and after intervention were compared using paired t-tests, while differences between groups were analyzed using independent t-test. Significance was tested using alpha < 0.05 two tailed. This research was approved under Ethical clearance number 149/EC/FK-RSDK/2016.

**RESULTS**

**Characteristics of The Subjects**

Total subjects of 221 women were screened with a final number of 26 women were recruited, 13 in each group. The characteristics comparison before intervention between the treatment and the control group were shown in table 1. Statistical analysis showed that the characteristics between both groups were no different (p>0.05).

**Lipid Profile**

Not all subjects were in prediabetic stage despite they were prone for this condition related to their body mass index. Among all lipid profile, triglyceride in treatment group was the only parameter that reduced significantly (table 2) with 18.23 mg/dl reduction (table 3). However, triglyceride level as well as other parameters were not different (p>0.05) when it compares with the control group (table 3).
Despite the number was insignificant, fasting blood glucose and LDL apparently increased, while HDL lowered (table 3).

**DISCUSSION**

According to the CDC, approximately 90% of subjects with pre-diabetes were not realized they have it. Furthermore, nearly 3 out of 4 subjects with this condition will develop type 2 diabetes within 5 years. However, in some cases it can be treated through diet and lifestyle modification. Green leafy vegetables not only as a part of diet with abundant source of vitamins and minerals, but also as medicinal plants that have bioactive components to be used as pharmaceuticals. Among them, carica papaya is not only cultivated for its pleasant fruit, but also its leaf for their bioactive properties. Hypoglycemic agent as well as anti-hyperlipidemic agent are shown to be the strength of this leaves.

Characteristic subjects by age, BMI, and waist circumference in both groups showed no difference (p>0.05). There was no difference in nutritional intake and physical activity of the subjects in both groups during intervention except sodium intake with mean intake in the treatment group was higher than the control one. Several subjects in the treatment group consume high-sodium food such as salted fish, instant noodles, light snacks with flavorings and artificial preservatives. Nutrition education about balanced nutrition had been conducted in both groups as an effort in controlling intake.

There was a significant decrease in triglyceride levels but not in LDL, HDL, and total

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**Table 1. Characteristics of Subjects Before Intervention, Data of Nutritional Adequacy and Physical Activity During Treatment**

<table>
<thead>
<tr>
<th>Characteristic/ Variable</th>
<th>Treatment (n=13)</th>
<th>Control (n=13)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>43.46±4.29</td>
<td>43.69±3.49</td>
<td>0.88a</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28.09±3.17</td>
<td>29.09±2.78</td>
<td>0.41a</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>89.43±5.58</td>
<td>89.41±7.23</td>
<td>0.71b</td>
</tr>
<tr>
<td>Food intake</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy intake (%)</td>
<td>75.60±22.27</td>
<td>74.41±15.94</td>
<td>0.87a</td>
</tr>
<tr>
<td>Carbohydrate intake (%)</td>
<td>47.46±31.78</td>
<td>68.31±24.10</td>
<td>0.07a</td>
</tr>
<tr>
<td>Fat intake (%)</td>
<td>71.70±62.66</td>
<td>84.48±32.60</td>
<td>0.52a</td>
</tr>
<tr>
<td>Protein intake (%)</td>
<td>52.47±38.09</td>
<td>62.77±21.40</td>
<td>0.52b</td>
</tr>
<tr>
<td>Fiber intake (%)</td>
<td>25.40±14.31</td>
<td>26.43±20.90</td>
<td>0.48b</td>
</tr>
<tr>
<td>Sodium intake (%)</td>
<td>24.35±20.26</td>
<td>12.60±16.29</td>
<td>0.02b</td>
</tr>
<tr>
<td>Potassium intake (%)</td>
<td>23.74±8.15</td>
<td>18.58±6.85</td>
<td>0.09a</td>
</tr>
<tr>
<td>Calcium intake (%)</td>
<td>23.61±12.84</td>
<td>18.15±8.51</td>
<td>0.24b</td>
</tr>
<tr>
<td>Magnesium intake (%)</td>
<td>49.59±12.82</td>
<td>55.88±25.32</td>
<td>0.70b</td>
</tr>
<tr>
<td>Vitamin C (%)</td>
<td>75.95±87.19</td>
<td>33.12±24.53</td>
<td>0.08b</td>
</tr>
<tr>
<td>Physical activity (MET-minute)</td>
<td>3822.44±2051.96</td>
<td>4278.03±5445.17</td>
<td>0.34b</td>
</tr>
</tbody>
</table>

1 Independent t-test; *significantly different; a Mann-Whitney test

**Table 2. Difference of lipid profile between the control and treatment group in diabetic women**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Treatment (n=13)</th>
<th>Control (n=13)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before (mean±SD)</td>
<td>After (mean±SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FBG (mg/dl)</td>
<td>101.62±10.03</td>
<td>98.08±9.67</td>
<td>0.427a</td>
</tr>
<tr>
<td>Triglyceride (mg/dl)</td>
<td>128.00±49.87</td>
<td>89.69±32.20</td>
<td>0.113a</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>140.92±30.95</td>
<td>147.31±16.67</td>
<td>0.462a</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>40.62±9.57</td>
<td>37.31±4.59</td>
<td>0.668a</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dl)</td>
<td>207.31±39.59</td>
<td>205.69±23.73</td>
<td>0.207a</td>
</tr>
</tbody>
</table>

1 Paired t test; b Wilcoxon; *significant

**Table 3. Difference of lipid profile change between groups**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Treatment (Mean±SD)</th>
<th>Control (Mean±SD)</th>
<th>Sig (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΔFBG (mg/dl)</td>
<td>5.53±10.76</td>
<td>-2.00±8.77</td>
<td>0.057a</td>
</tr>
<tr>
<td>ΔTriglyceride (mg/dl)</td>
<td>-18.23±30.07</td>
<td>-9.69±20.43</td>
<td>0.407a</td>
</tr>
<tr>
<td>ΔLDL (mg/dl)</td>
<td>3.00±14.90</td>
<td>3.61±17.15</td>
<td>0.923a</td>
</tr>
<tr>
<td>ΔHDL (mg/dl)</td>
<td>-0.15±7.53</td>
<td>0.69±5.67</td>
<td>0.749a</td>
</tr>
<tr>
<td>ΔTotal Cholesterol (mg/dl)</td>
<td>-1.76±16.20</td>
<td>4.46±12.04</td>
<td>0.277a</td>
</tr>
</tbody>
</table>

1 Independent t-test; a Mann-Whitney

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Cholesterol after intervention in the treatment group which may be affected by the papaya leaves content in jelly. Papaya leaves contain several antioxidant compounds that potentially balanced the state of oxidative stress. Previous studies showed that chlorophyll has high bioactivity such as antioxidant, catalyzer, which prevent lipid oxidation 28,29.

Chlorophyll has an ability to scavenge DPPH free radical that produced by lipid autooxidation process and act as a chain breaker by donating its electron to free radical and becoming stable 30. Saponin and steroid play a role as antihyperlipidemic by inhibiting intestinal lipid absorption via resin-like action and inhibition of lipase activity 10,11,31. Papaya leaves also contain flavonoid names kaemperol and quercetin. Saponin and flavonoid could enhance antioxidative system activity and increase the activity of lipoprotein lipase (LPL) that reduce free fatty acid and hence decrease triglyceride levels 32.

There was a reduction in total cholesterol in the treatment group by 1.76 mg/dl, while total cholesterol in the control group increased 4.46 mg/dl. The decrease of total cholesterol in the treatment group due to chlorophyll in papaya leaves. Chlorophyll could stimulate heart function in lowering total cholesterol by enhancing activity and amount of LDL receptor, increase bile acids excretion, decrease renin levels, and widen blood vessel 33.

The decrease of total cholesterol in the treatment group also due to papaya leaves contain active components, such as saponin, flavonoid quercetin, tannin, and alkaloid carpaine. 34 Saponin inhibits bile acid reabsorption in small intestine then excreted to feces. To compensate that mechanism, cholesterol serum converted by the heart into bile acid so there will be a decrease in cholesterol levels in the blood. 35 Flavonoid quercetin as antioxidant flavonoid protects LDL cholesterol so it is not oxidized by free radical. Besides, as antioxidant, flavonoid could potentially decrease total cholesterol by increase bile acid excretion. 36 Tannins on papaya leaves decrease cholesterol absorption in the small intestine and increase bile acid excretion by the same mechanism as saponins 37. Alkaloid carpaine on papaya leaves inhibit lipase enzyme, thus inhibiting fat breakdown into smaller molecules. This process results a decrease in the amount of fat that can be absorbed by intestine so that the total cholesterol levels lowered 38.

There was no significant reduction in LDL, HDL, and total cholesterol in the treatment group. This might due to the baseline condition of LDL cholesterol which still in borderline high, while HDL was particularly in control group is in desirable category although the difference was not significant in both groups. 39 According to the chinese guideline, the recommendation of lipid lowering target is a reduction of minimum 40% and above. 40 The overweight subjects also not likely represent a higher level of lipid profile. Furthermore, several subjects were in desirable level of total cholesterol.

CONCLUSION
The consumption of papaya leaves jelly for 20 days can reduce triglyceride, LDL, HDL, and total cholesterol levels in treatment group. Future study needs to be conducted to investigate the effectiveness of papaya leaves among prediabetes subjects on lowering LDL, HDL, and total cholesterol. A comprehensive approach is needed to promote a healthy lifestyle including physically active and diet modification include an adequate green leavy vegetables to maintain a normal nutrition status thus avoid in developing diabetes.

ACKNOWLEDGEMENTS
This research was funded by Universitas Diponegoro Research Funding year 2016.

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