



Effect of Avocado Pulp Extract on HbA1c and Fasting Blood Glucose in Diabetes Mellitus Patients

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Abstract

Diabetes mellitus is a complicated necessitates ongoing medical attention and is a serious health problem that has grown to worrisome proportions. The study aimed to assess the avocado pulp extract's glycemic control in individuals with type 2 diabetes mellitus (T2DM) in a clinical setting in 2023. From the Klinik IMAN database, patients >18 years with T2DM who had previously been treated with oral hypoglycemic medications were included. The index date—the first day that avocado pulp extract was consumed—was used to collect baseline data. A laboratory measurements analysis was used to evaluate the change in glycated hemoglobin (HbA1c) and fasting blood glucose levels after a month of consuming avocado pulp extract and placebo. At one month, the percentage of patients who achieved their goal HbA1c and fasting blood glucose levels was determined. Overall, 30 patients were included and had baseline HbA1c and fasting blood glucose levels values available. Added avocado flesh extract not associated with improved HbA1c (0.04 [95% CI: -0.22-0.30], $p>0.05$) and fasting blood glucose levels values (0.85 [95% CI: -24.7-26.4], $p>0.05$) versus baseline at a month. Added avocado flesh extract not associated with improved glycemic control during a month of follow-up in patients with T2DM.

Introduction

Diabetes mellitus is a complicated, chronic condition that necessitates ongoing medical attention as well as multifaceted risk-reduction techniques beyond glucose control. A class of metabolic diseases known as diabetes mellitus is typified by persistently high blood sugar levels brought on by deficiencies in insulin secretion, insulin action, or both. The prevention of acute complications and the mitigation of the risk of long-term problems depend on ongoing diabetes self-management education and assistance. There is substantial evidence in favor of a variety of therapies to improve diabetes outcomes. Diabetes mellitus is a serious health problem that has grown to worrisome proportions. Today, diabetes mellitus affects more than 500 million individuals globally (ElSayed et al., 2023; Lasari

et al., 2021; Magliano., 2021). In Indonesia provinces have a higher prevalence of diabetes DKI Jakarta with 3.4 percent, followed by DI Yogyakarta (3.1 percent) and East Kalimantan (3.1 percent). (Oktora & Butar., 2022).

The number of persons with diabetes worldwide is predicted to reach 537 million in 2021, 643 million in 2030, and 783 million in 2045. Additionally, it is anticipated that 541 million individuals will have reduced glucose tolerance by 2021. Over 6.7 million persons between the ages of 20 and 79 are anticipated to pass away in 2021 as a result of diabetes-related diseases. Every year, more kids and teenagers (i.e., those under the age of 19) are diagnosed with diabetes. More than 1.2 million kids and teenagers will have type 1 diabetes in 2021. Diabetes-related direct medical costs have already reached about \$1 trillion. IDF predicts

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that by 2045, there will be 152 million diabetics in the South-East Asia (SEA) region, a 68% increase from the current figure. The prevalence of diabetes will rise by 30% to 11.3% throughout the same time frame. At 51.2%, the percentage of undiagnosed diabetes is the third-highest among the IDF Regions. The highest rate of hyperglycemia-affected pregnancies (25.9%) among IDF Regions (Magliano, 2021).

After being identified as a biomarker of glycemic management in the late 1960s, glycated hemoglobin (HbA1c) has gradually increased over the past four decades. Glycated hemoglobin (HbA1c), frequently utilized in diabetes, determines the average plasma glucose concentration. Because hemoglobin and glucose in the blood combine to generate HbA1c, this explains why HbA1c is used to diagnose diabetes rather than just blood glucose levels. Historically, it was believed that HbA1c represented long-term average blood sugar levels. It is restricted to the typical red blood cell lifecycle over 120 days. Since RBCs do not lyse simultaneously, HbA1c is only used as a three-month measurement. Patients are at a higher risk of acquiring diabetes-related problems the higher their HbA1c levels are (Indranila, 2017).

Among the acknowledged risk factors for macro- and microvascular complications in type 2 diabetes are older age and higher glycated hemoglobin (HbA1c) levels (Kaneko *et al.*, 2021). A1c has several benefits over FPG and OGTT, including being more convenient (fasting is not necessary), having greater preanalytical stability, and being less susceptible to fluctuations daily due to stress, dietary changes, or sickness (ElSayed *et al.*, 2023). According to National Health and Nutrition Examination Survey (NHANES) statistics, only 30% of the diabetes patients identified using A1C, FPG, or 2-h PG are diagnosed using the A1C test, which has a diagnostic threshold of > 6.5% (48 mmol/mol). Despite these drawbacks, the International Expert Committee introduced A1c to the diagnostic standards in 2009 to boost screening (Karnchanasorn *et al.*, 2016).

The avocado tree, a member of the Lauraceae family and the genus *Persea*, is indigenous to Mexico and Central America (Talavera *et al.*, 2023; Weschenfelder *et al.*,

2015). *Persea* and *Eriodaphne* are the two subgenus that make up this genus. However, there are two major species in horticulture: *Persea drymifolia* cham, which includes Mexican race avocados and is currently thought to be a botanical variant of *Persea Americana*, and *Persea americana* Mill (Galindo *et al.*, 2008). The avocado is a fruit with 114 calories per 70 grams, 4.6 grams of fiber, 345 mg of potassium, 19.5 mg of magnesium, 1.3 mg of vitamin E, and 57 mg of phytosterols. It has a caloric density of 1.7 kcal per gram and a half (Dreher & Davenport., 2013).

Methods

This study used retrospective database technology and secondary data from Klinik IMAN. The CDMP club (Chronic Disease Management Program) participants with T2DM and hypertension who routinely attend monthly counseling and health checks are included in the Klinik IMAN database as outpatient administrative data. People having a T2DM diagnosis but no type 1 diabetes diagnosis were deemed eligible for inclusion in the study if they were older than 18 years old. Study participants were excluded if they had blood sugar levels < 50 mg/dL and > 350 mg/dL at the pre-intervention examination. Study participants were divided into two groups. The first group consumed avocado pulp extract, while the second consumed placebo. There were no limitations on taking concurrent anti-diabetic drugs. This research has received ethical approval from the Health Research Ethics Committee Faculty of Medicine University of Muhammadiyah Sumatera Utara No 1011/KEPK/FKUMSU/2023.

The avocado fruit used in this study was butter avocado obtained from Medan, Sumatera Utara. The avocado pulp is separated from the peel and seeds, and then thinly sliced for easy drying. The sliced avocado pulp is weighed and then dried for 4-5 days in a drying cabinet at $40 \pm 2^{\circ}\text{C}$, and then grinded using a grinder to produce avocado flesh *simplicia* powder. The extract was prepared by maceration of dry powder using 70% Food-grade ethanol. As much as 500 grams of *simplicia* powder was macerated with 5 liters of ethanol 70% FG (1:10) put into a closed vessel. Soak for the first

6 hours with occasional stirring, then let stand for 18 hours at room temperature, protected from sunlight and filtered. The macerate results were evaporated using a rotary evaporator and a thick extract was obtained (Kementrian Kesehatan RI., 2017). Preparation of avocado flesh extract powder by weighing 300 grams of amyllum maydis and 200 grams of avocado flesh extract, then mixing until homogeneous. Then the mixture is sieved to speed up drying. The powder or granules are dried in an oven at 60°C. The dry powder is ready to be filled in capsules using a capsule filler. A creamy, avocado-scented powder. The 500 gram capsule contains a placebo containing 500 mg of amyllum maydis. The normality test for differences in HbA1c and fasting blood glucose levels in the experimental group had a normal distribution, so the test used was the paired T-test. The normality test for the difference in HbA1c and fasting blood glucose levels in the control group had an abnormal distribution, so the test used was the Wilcoxon test.

Results and Discussion

Of the 30 patients with T2DM in the Klinik IMAN database were included in the study. 2 participants did not continue the study, so the total who took part was 28 participants, 14 participants for each group. Table 1 displays demographics and baseline characteristics. The mean age (standard deviation [SD]) was 64 (9.3) years, and the baseline T2DM duration was 10.3 (8.7) years on average. An overall history of hypertension was present in 64.3% of

the population. Other comorbidities that were noted included a history of dyslipidemia (85.7%) and a body mass index of 25.3 (3.4) kg/m². Comorbidities were evenly distributed across the treatment groups, except hypertension and body mass index, which were more prevalent and high in patients who consumed Avocado Pulp Extract (Table 1).

Of the total population, all patients had a baseline HbA1c and fasting blood glucose measurement; the mean (SD) baseline HbA1c was 8 ± 1.6% while the mean (SD) baseline fasting blood glucose was 153 ± 58.4 mg/dl. From the results of this study, there was no decrease in HbA1c levels and fasting blood glucose levels in participants who consumed avocado pulp extract compared to a placebo for one month. From the results of the study, it was found that there was an increase in HbA1c levels in study participants who consumed avocado pulp extract compared to placebo (0.04 [95% CI: -0.22-0.30], p>0.05). It also happened in examining fasting blood glucose levels, where an increase in fasting blood glucose levels was found in study participants who consumed avocado pulp extract compared to placebo (0.85 [95% CI: - 24.7-26.4], p>0.05). Using outpatient administrative data from the Klinik IMAN database, this study provides the first proof of the effects of avocado pulp extract in T2DM patients. Based on the variations between baseline and 1-month data, the study showed that adding avocado pulp extract was not associated with decreases in HbA1c and fasting blood glucose levels in patients with

Table 1. Patient Demographics and Baseline Clinical Characteristics

	Avocado Pulp Extract (n=14)	Placebo (n=14)	Total population (n=28)
Age, mean ± SD (years)	64.6 ± 9.6	63.5 ± 9.3	64.0 ± 9.3
Female, n (%)	10 (71.4)	11 (78.6)	21 (75.0)
BMI, mean ± SD (kg/m ²)	26 ± 2.9	24.7 ± 3.9	25.3 ± 3.4
Duration of T2DM, mean ± SD (years)	8.6 ± 7.7	12 ± 9.5	10.3 ± 8.7
HbA1c pre-test, mean ± SD (%)	7.9 ± 1.9	8.1 ± 1.3	8.0 ± 1.6
HbA1c post-test, mean ± SD (%)	8.0 ± 1.7	8.2 ± 1.6	8.0 ± 1.7
Fasting blood glucose pre-test, mean ± SD (mg/dl)	143.3 ± 56.8	164.2 ± 60.3	153 ± 58.4
Fasting blood glucose post-test, mean ± SD (mg/dl)	144.1 ± 59.0	157.6 ± 69.5	150.8 ± 63.6
History of hypertension, n (%)	10 (71.4)	8 (57,1)	18 (64.3)
History of dyslipidemia, n (%)	12 (85.7)	12 (85.7)	24 (85.7)

BMI body mass index, SD standard deviation

T2DM who had previously been treated for blood glucose levels.

In the current study, the mean baseline HbA1c was $8 \pm 1.6\%$ and fasting blood glucose was 153 ± 58.4 mg/dl, reflecting the fact that many of the patients in this sample received initial treatment with inadequate glycemic control. Unfortunately, the addition of avocado flesh extract did not cause a decrease in either HbA1c levels or fasting blood glucose levels in the patients participating in this study. This result is not in line with a study where a decrease in blood glucose levels was found in male white rats induced by alloxan. The ethanol extract of avocado flesh at doses of 100 mg/kg body weight and 200 mg/kg body weight had a significant difference with a significance value of 0.024 and 0.026 and a dose of 50 mg/kg body weight had no significant difference with a significance value of 0.275. Both the treat-to-target study design and the fact that the population in the prior study was an animal population, which was anticipated to attain this aim more readily, are likely to be to blame for these disparities. The hemoglobin A1c (HbA1c; also known as glycosylated or glycated hemoglobin) level, which represents the average blood glucose control over about three months, is one approach to blood glucose measuring. HbA1c readings, like any laboratory tests, are subject to fluctuation, which can be exacerbated by factors including race and ethnicity (Sacks *et al.*, 2011; Wolffenbuttel *et al.*, 2013; Bergenstal *et al.*, 2017).

Adults (average baseline age, 53 to 66 years) participating in five large, long-term randomized controlled trials were compared between intense (achieved HbA1c levels, 6.3% to 7.4%) and less intensive (achieved HbA1c levels, 7.3% to 8.4%) treatment target strategies. They discovered that tighter glycemic control mainly reduced the risk for microvascular surrogate events, such as retinopathy identified by ophthalmologic screening or nephropathy determined by the onset or progression of albuminuria, by tiny absolute amounts (Jenkins *et al.*, 2015; Hayward *et al.*, 2015). Studies have not consistently demonstrated a reduction in clinical microvascular events, such as vision loss or impairment, end-stage renal disease, or painful neuropathy, or a reduction in macrovascular events, such as death, with

stringent glycemic management to HbA1c levels below 7%. In one study, overweight persons who took metformin experienced a decline in all-cause and diabetes-related deaths for at least ten years (Taylor *et al.*, 2021; Chawla *et al.*, 2016). Several things are the weaknesses of this study, which may play a big role in not achieving the objectives of this study. First, the study participants did not consume avocado pulp extract regularly. Even though an attempt was made to contact study participants regularly to remind them about consuming avocado pulp extract regularly, at the end of the study, study participants still found that they had remaining capsule extract.

Second, the short research time. By consuming avocado extract for a month, it may not be possible to achieve changes in HbA1c as expected. As a comparison, the study conducted by Kaneko *et al.*; to find changes in HbA1c with the addition of insulin to the therapy that had been carried out previously by study participants was carried out for 12 months (Kaneko *et al.*, 2021). Lastly, the small number of study participants will also play a role in the results that are not by previous expectations. For this reason, a follow-up study should add more participants with a longer observation time so that more meaningful results are found.

Conclusions

Glycated hemoglobin (HbA1c) represents long-term average blood sugar levels and is used to diagnose diabetes rather than just blood glucose levels. In this research, an effort was made to reduce HbA1C levels by using avocado extract consumable daily, easily and cheaply. But unfortunately, the research results did not get the results as expected. The research found no decrease in both HbA1c levels and fasting blood glucose levels in participants who consumed avocado pulp extract compared to placebo for a month. We recommend to conduct further research with more samples and a longer research time.

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