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Metabolic effects of aloe vera gel complex in obese prediabetes and early non-treated diabetic patients: Randomized controlled trial

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ABSTRACT

Objective: The metabolic effects of an aloe vera gel complex (Aloe QDM complex) on people with prediabetes or early diabetes mellitus (DM) are unknown. The goal of this study was to determine the effects of Aloe QDM complex on body weight, body fat mass (BFM), fasting blood glucose (FBG), fasting serum insulin, and Homeostasis Model of Assessment - Insulin Resistance (HOMA-IR) in obese individuals with prediabetes or early DM who were not on diabetes medications.
Methods: Participants (n = 136) were randomly assigned to an intervention or a control group and evaluated at baseline and at 4 and 8 wk.
Results: The study lost six participants in the control group and eight in the intervention group. At 8 wk, body weight ($P = 0.02$) and BFM ($P = 0.03$) were significantly lower in the intervention group. At 4 wk, serum insulin level ($P = 0.04$) and HOMA-IR ($P = 0.047$) were lower in the intervention group; they also were lower at 8 wk but with borderline significance ($P = 0.09$; $P = 0.08$, respectively). At 8 wk, FBG tended to decrease in the intervention group ($P = 0.02$), but the between-group difference was not significant ($P = 0.16$).
Conclusion: In obese individuals with prediabetes or early untreated DM, Aloe QDM complex reduced body weight, BFM, and insulin resistance.

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Introduction

Prediabetes, which includes impaired fasting glucose and impaired glucose tolerance, is an important risk factor for type 2 diabetes mellitus (DM). Interventions, such as lifestyle modification or medication for prediabetes, can reduce progression to overt DM [1–5]. Moreover, especially in early DM, interventions can preserve pancreas β cells and improve prognosis [4,6–8]. In contrast, poor weight control leads to obesity, which induces insulin resistance and β-cell dysfunction [9]. Maintaining healthy weight with the aid of dietary intervention and exercise is therefore recommended.

Metabolic derangements of diabetes, obesity, metabolic syndrome, or chronic diseases are strongly affected by lifestyle such as dietary patterns and physical activity. However, some studies reported the association between some ingredients and the metabolic derangements [10,11], and recent studies have reported that Aloe vera may have some metabolic benefits for patients with DM [12]. Reportedly, aloe vera can reduce fasting blood glucose (FBG) and hemoglobin A_{1c} (HbA_{1c}) [13] and have an anti-inflammatory effect [14]. Most studies, however, were done on animals, varied in design, and showed inconsistent results. Few well-designed trials have investigated the effects of aloe on humans, and none has investigated the effects of aloe on weight and DM-related biomarkers.

Here, in a randomized controlled trial (RCT) conducted in Korea, we evaluated the effect of Aloe vera gel complex (Aloe QDM complex provided by Univera, Inc., Seoul, South Korea) on obesity- and DM-related biomarkers (body weight, body fat, FBG, fasting serum insulin, and Homeostasis Model of Assessment - Insulin Resistance [HOMA-IR] in patients with prediabetes or early DM who did not use diabetes medications.

Ho-Chun Choi and Seok-Joong Kim equally contributed to this work as first author.

H-C Choi and B-L Cho designed the research. H-C Choi, S-J Kim, B-L Cho, K-Y Son, and B-J Oh conducted the research. H-C Choi, S-J Kim, B-L Cho, and K-Y Son analyzed the data. H-C Choi and S-J Kim wrote the paper and B-L Cho had primary responsibility for final content.

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Materials and Methods

Participants

We recruited patients with prediabetes or early DM aged ≥20 y who showed the following traits:

1. Obesity (body mass index [BMI] ≥25 kg/m^2) or abdominal obesity (waist circumference ≥90 cm for men or ≥85 cm for women),
2. Impaired FBG (≥100 mg/dL) or impaired glucose tolerance (2-h oral glucose tolerance test ≥140 mg/dL), and
3. Potentially able by lifestyle modification to control blood sugar levels (FBG <180 mg/dL and HbA_{1c} <8.0%) [15].

We used Asian criteria to define obesity and abdominal obesity [16,17].

We excluded individuals who had a history of hypoglycemic medication or herb use, gestational DM, or polycystic ovarian disease. Additionally, we excluded individuals who were pregnant, in need of insulin treatment, or allergic to aloe vera or chromones. Written informed consent was obtained from all participants, and procedures were approved by the Institutional Review Board of Seoul National University Hospital (IRB No. H-0907-038-286; http://cris.snuh.org) and consistent with the Declaration of Helsinki.

Materials

The Aloe QDM complex used as the intervention material was a 700-mg soft capsule composed of processed aloe vera gel 147 mg/cap [18] and aloesin powder (95% aloesin) 3 mg/cap [19], yeast chromone 125 mg/cap, and excipients (soy bean oil, yellow beeswax, and lecithin) 425 mg/cap. The control material was a 700-mg soft capsule composed of natural pigment 4.2 mg/cap and excipients (soybean oil, yellow beeswax, and lecithin) 695.8 mg/cap.

Procedures

This was a double-blind, RCT. Participants were screened and then assigned to the intervention or control group by block randomization, with the randomization code generated by SAS 9.2 (SAS Institute, Cary, NC).

Participants took the Aloe QDM complex or placebo orally, two capsules after breakfast and two after dinner, for 8 wk. They visited the center at the day of recruitment (baseline) and 4 and 8 wk after randomization for physical examinations, laboratory tests, and evaluation of adverse effects. Fasting (≥8 h) blood samples were taken and body fat was measured with a bioimpedence analyzer (InBody720, Biospace, Seoul, South Korea).

Variables measured for the evaluation of efficacy were weight, body fat mass (BFM), lean body mass (LBM), FBG, fasting serum insulin, HOMA-IR, HbA_{1c}, total cholesterol, triglycerides, low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein cholesterol. Safety was assessed by adverse effects, abnormal laboratory tests, and vital sign changes.

Participants were lost when there were adverse reactions, withdrawals of consent, medication compliance <75%, or follow-up loss, and the reasons were recorded on a case report form.

Statistical analysis

Using descriptive statistics, we assessed efficacy by measuring the change in each variable 4 and 8 wk from baseline. We used analysis of variance (ANOVA) to compare the mean difference between baseline and 4 wk and the mean difference between baseline and 8 wk for each variable. We performed all statistical analyses with SAS version 9.2, considering a two-sided $P < 0.05$ statistically significant. For safety analysis, we noted all reported adverse reactions at every visit, and we used ANOVA, the Fisher exact test, or the χ^2 test to evaluate adverse events and abnormal laboratory results.

Results

Table 1 shows the baseline characteristics of the study participants in the intention-to-treat protocol. The intervention and control groups did not differ significantly in age, sex, BMI, height, weight, LBM, BFM, FBG, fasting serum insulin, or HOMA-IR.

We enrolled 136 participants and randomly assigned 68 to each group. There was a loss of 6 participants in the control group and 8 in the intervention group, leaving 62 in the control group and 60 in the intervention group (Fig. 1).

Table 1
Baseline characteristics of study participants

	Placebo (n = 68)	Aloe QDM complex (n = 68)	*P*-value
	Number (%) or Mean ± SD	Number (%) or Mean ± SD	
Age group (y)			0.71*
30–39	2 (2.9%)	1 (1.5%)	
40–49	7 (10.3%)	8 (11.8%)	
50–59	21 (30.9%)	25 (36.8%)	
60–69	26 (38.2%)	19 (27.9%)	
≥70	12 (17.6%)	15 (22.1%)	
Age (y)	60.7 ± 10	60.4 ± 10	0.85
Men	49 (72.1%)	47 (69.1%)	0.71*
Women	19 (27.9%)	21 (30.9%)	
Body mass index (kg/m^2)	27.3 ± 2.6	27.5 ± 2.1	0.65
Height (cm)	164.1 ± 8.6	162.7 ± 9.2	0.39
Weight (kg)	73.7 ± 11.1	73 ± 10.5	0.69
Body fat mass (kg)	23.7 ± 5.5	23.4 ± 5.0	0.77
Lean body mass (kg)	50.0 ± 9.0	49.5 ± 10.0	0.79
FBG (mg/dL)	116.9 ± 11.6	115.5 ± 11.9	0.49
Insulin (μIU/mL)	11.5 ± 4.3	11.8 ± 5.3	0.72
HOMA-IR	3.3 ± 1.2	3.4 ± 1.6	0.79
Hemoglobin A_{1c}	6.2 ± 0.4	6.2 ± 0.4	0.50
Total cholesterol	182 ± 33†	181.7 ± 33.1	0.96
Triglycerides	176.3 ± 100.6†	141.6 ± 72.7	0.02
HDL cholesterol	49.7 ± 10†	49.7 ± 10.4	0.99
LDL cholesterol	108.1 ± 30.1†	112.7 ± 27.8	0.35

FBG, fasting blood glucose; HDL, high-density lipoprotein; HOMA-IR, Homeostasis Model of Assessment-Insulin Resistance; LDL, low-density lipoprotein
One-way analysis of variance with treatment group as factor
* Pearson χ^2.
† n = 67.

The two groups did not differ at baseline or at 4 or 8 wk in their intake of fiber and calorie from carbohydrate, protein, or fat (Table 2).

Analysis within groups

In the intervention group, compared with baseline values, body weights at 4 ($P = 0.05$) and 8 wk ($P = 0.05$) decreased with borderline significance, whereas BFM decreased significantly at both 4 ($P = 0.02$) and 8 ($P < 0.01$) wk. LBM increased insignificantly at 4 wk ($P = 0.16$) but significantly at 8 wk ($P = 0.04$), whereas weight, BFM, and LBM did not change significantly in the control group (Table 3).

FBG decreased significantly at 4 ($P < 0.01$) and 8 ($P = 0.02$) wk in the intervention group and only at 4 wk in the control group ($P < 0.01$). Fasting serum insulin level ($P = 0.01$) and HOMA-IR ($P < 0.01$) decreased significantly at 4 wk in the intervention group but at neither time in the control group (Table 3).

Analysis between groups

Between-group weight differences were evident at 4 wk and significant at 8 wk (mean difference 0.6 kg; $P = 0.02$). The BFM decrease at 8 wk was greater in the intervention group (mean difference 0.9 kg; $P = 0.03$), as was the LBM increase, but not to a level of significance (mean difference 0.3 kg; $P = 0.39$). The tendency of BFM to decrease and LBM to increase was more notable at 8 wk than at 4 wk (Fig. 2).

Between-group differences in FBG increased with time but were not significant. Differences in serum insulin concentration ($P = 0.04$) and HOMA-IR ($P = 0.047$) were significant at 4 wk with low levels in the intervention group, and the same was true at

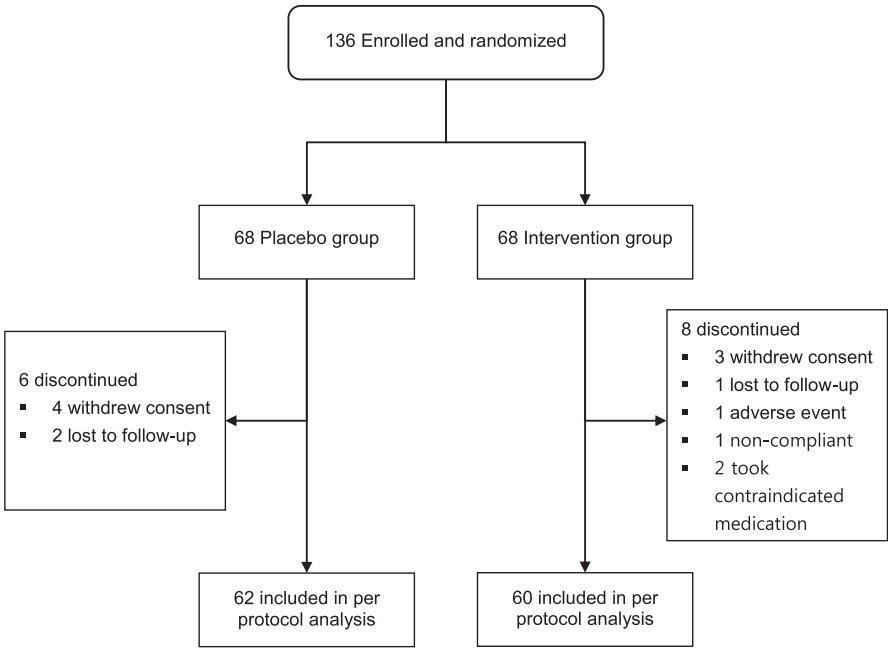

Fig. 1. Study population and data collection algorithm.

8 wk with borderline significance ($P = 0.09$; $P = 0.08$, respectively) (Fig. 2).

Discussion

In this placebo-controlled, double-blind, randomized trial examining the effect of Aloe QDM complex on obesity-related biomarkers (body weight, BFM, and LBM) and DM-related biomarker (FBG, fasting serum insulin, and HOMA-IR) on prediabetic patients or non-medicated patients with early DM, we found small but significant effects. Because the two groups did not differ in nutritional intake, the weight reduction in the intervention group was likely caused by a metabolic effect specific for BFM reduction. The LBM increase, which reflects an increase in skeletal muscle, improves insulin sensitivity [20,21], whereas excess adiposity decreases it [22]. Thus, the BFM reduction and the tendency toward an LBM increase suggest metabolic benefits rather than simple weight loss, and those metabolic benefits contributed to insulin sensitivity and FBG reduction.

The between-group difference in HOMA-IR was paralleled by a difference in serum insulin concentration. The calorie changes shown in Table 2 suggest that nutrition could have influenced the within-group DM biomarker changes because the calorie intake decreased at 4 wk and returned to the baseline value at 8 wk. The calorie intakes within each group, however, did not show significant changes and the differences relative to baseline were maintained. Therefore, the mean between-group biomarker differences seem to reflect an effect of the Aloe QDM complex.

Our findings are consistent with animal studies. Aloe vera gel improved insulin sensitivity, had hypoglycemic and hypolipidemic effects, and decreased the size of adipocytes in type 2 DM mice [18]. In a rat study, aloe vera phytosterols decreased blood glucose and lipid levels and significantly reduced visceral fat weight by altering the expression of genes related to glucose and lipid metabolism [23]. When fed to obese mice, Aloe QDM complex reduced body fat and improved insulin sensitivity by activating AMP-activated muscle protein kinase, which is important in the regulation of glucose and lipid metabolism [24,25]. The consistency of those results with ours suggests that the Aloe QDM complex causes weight reduction and improves insulin sensitivity in humans by similar mechanisms. Additional research is needed.

In our study, in contrast to animal studies, aloe vera complex did not significantly affect some metabolic biomarkers, possibly because we were not able to strictly control variables such as nutrition, medication, and physical activity or other healthy behaviors, as can be done in an animal study, and although the trial was randomized, confounding factors might have affected

Table 2
Calorie and fiber from dietary intake

	Baseline	Week 4	Week 8
Total dietary calorie (kcal)			
Placebo	1585 ± 59	1474 ± 61	1526 ± 53
ACTIValoe	1531 ± 49	1470 ± 52	1492 ± 52
P-value	0.49	0.96	0.65
Carbohydrate (%)			
Placebo	60.5 ± 1.2	61.4 ± 1.4	61.6 ± 1.1
ACTIValoe	60.6 ± 1.2	62.1 ± 0.9	61.0 ± 1.1
P-value	0.92	0.66	0.73
Protein (%)			
Placebo	17.4 ± 0.4	17.5 ± 0.5	17.0 ± 0.4
ACTIValoe	17.4 ± 0.5	17.5 ± 0.5	17.6 ± 0.6
P-value	0.99	0.94	0.37
Fat (%)			
Placebo	22.4 ± 1.1	21.5 ± 1.3	21.3 ± 1.0
ACTIValoe	22.7 ± 1.0	21.6 ± 1.2	22.7 ± 1.1
P-value	0.81	0.93	0.34
Fiber (g)			
Placebo	20.0 ± 1.1	20.5 ± 1.1	22.5 ± 1.3
ACTIValoe	20.4 ± 1.0	21.7 ± 1.1	20.4 ± 0.9
P-value	0.83	0.43	0.18

Values are means ± SE
One-way analysis of variance with treatment group as factor

Table 3
Metabolic biomarkers within placebo and treatment groups

Variable	Time	Placebo group (n = 62)	*P*-value	Treatment group (n = 60)	*P*-value
Weight (kg)	Baseline	74.0 ± 1.4		73.0 ± 1.4	
	Week 4	74.0 ± 1.5	0.98	72.7 ± 1.3	0.05
	Week 8	74.2 ± 1.5	0.18	72.6 ± 1.3	0.05
Body fat mass (kg)	Baseline	23.9 ± 0.7		23.4 ± 0.7	
	Week 4	23.6 ± 0.7	0.20	22.8 ± 0.6	0.02
	Week 8	23.9 ± 0.8	0.90	22.4 ± 0.7	<0.01
Lean body mass (kg)	Baseline	50.1 ± 1.2		49.6 ± 1.3	
	Week 4	50.4 ± 1.2	0.12	49.9 ± 1.3	0.16
	Week 8	50.4 ± 1.2	0.15	50.2 ± 1.2	0.04
HOMA-IR	Baseline	3.3 ± 0.2		3.5 ± 0.2	
	Week 4	3.2 ± 0.2	0.69*	2.8 ± 0.2	<0.01
	Week 8	3.5 ± 0.2	0.20	3.1 ± 0.2	0.16
FBG (mg/dL)	Baseline	117.3 ± 1.5		115.2 ± 1.5	
	Week 4	111.5 ± 1.8	<0.01	108.5 ± 2.0	<0.01
	Week 8	116.6 ± 2.1	0.60	112.1 ± 1.5	0.02
Insulin (μIU/mL)	Baseline	11.3 ± 0.5		12.1 ± 0.7	
	Week 4	11.5 ± 0.7	0.70*	10.3 ± 0.5	0.01
	Week 8	12.2 ± 0.7	0.16	11.1 ± 0.7	0.20

FBG, fasting blood glucose; HOMA-IR, Homeostasis Model of Assessment-Insulin Resistance
Values are means ± SE
Outcome variables between baseline and at 4 wk, and between baseline and at 8 wk were evaluated for *P*-values from paired *t* test
* n = 61.

the results. Also, we determined the dose and duration of treatment by the extrapolation from an animal study [26] because no human dose-finding study has yet been carried out. Studies with suitable doses, however, would demonstrate the effect of the complex more precisely, and because of the tendency of mean differences in body weight, BFM, LBM, and FBG to increase with time, longer treatment periods might show more significant differences in those variables; in other words, we would see dose–time response gradients. Finally, the medical effects of aloe vera might be more evident in participants with overt DM than they were in those with prediabetes or early DM. Indeed, in an Iranian RCT, aloe complex significantly reduced fasting glucose, HbA_{1c}, total cholesterol, and LDL levels in patients with overt disease (type 2 DM and dyslipidemia) [27]. But evidence for a cascade mechanism involving weight reduction and increased insulin sensitivity is insufficient because obesity markers such as body weight, BFM, and LBM were not analyzed.

This study has several limitations. Information about nutritional calorie intake was reported by 24-h recall, which might not be precise, and information about physical activity might not be reliable because there was no hard data from devices such as an activity tracker. Also, we estimated BFM and LBM by bioimpedence analysis, but modalities such as dual-energy X-ray absorptiometry, computed tomography, and magnetic resonance yield more reliable data. Additionally, some studies showed the effects of gender on DM [28], but we did not perform subgroup analysis according to gender because there were not enough participants to do so.

In conclusion, Aloe QDM complex reduced body weight and BFM and improved insulin sensitivity in obese patients with prediabetic and early untreated DM. Studies are needed to evaluate the effects of the long-term use of the Aloe QDM complex in patients with overt DM.

Conclusion

In obese patients with prediabetes or early untreated DM, Aloe QDM complex can reduce body weight, BFM, and insulin resistance.

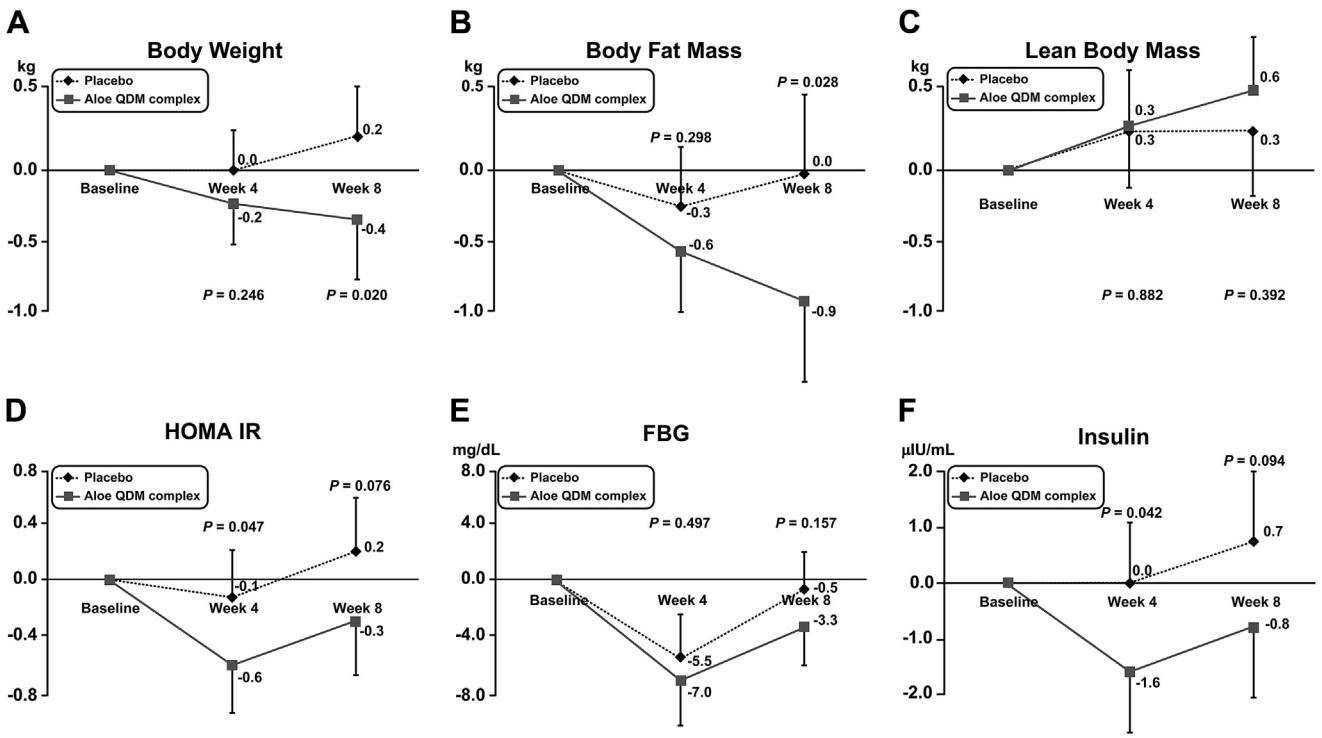

Fig. 2. Changes in body weight (A), fat mass (B), lean body mass (C), HOMA-IR (D), fasting glucose (E), and insulin (F) in Aloe QDM complex group and placebo group. FBG, fasting blood glucose; HOMA-IR, Homeostasis Model Assessment-Insulin Resistance. *P* = value from ANCOVA with treatment as factor and baseline value as covariate.

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