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File: ■ Aloe (*Aloe vera*)
■ Type 2 Diabetes
■ Hypercholesterolemia
■ Glycemia

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RE: Aloe Gel in the Treatment of Diabetic Hyperlipidemia: More Study Needed

Huseini HF, Kianbakht S, Hajiaghaee R, Dabaghian FH. Anti-hyperglycemic and anti-hypercholesterolemic effects of *Aloe vera* leaf gel in hyperlipidemic type 2 diabetic patients: a randomized double-blind placebo-controlled clinical trial. *Planta Med*. March 2012;78(4):311-316.

Type 2 diabetes mellitus (T2DM) is a prevalent disease worldwide, in part characterized by elevated low-density lipoprotein (LDL) cholesterol, very low-density lipoprotein (VLDL) cholesterol, and triglycerides, as well as lower than normal high-density lipoprotein (HDL) cholesterol. Pharmaceutical agents used to treat this hyperlipidemic condition in T2DM vary in mechanisms of action and are typically used concurrently; many are also associated with adverse side effects. This necessitates the search for broader and safer agents for both hyperglycemia and hyperlipidemia. Aloe (*Aloe vera*) has been used traditionally for wound healing and as a laxative.[1] In addition, the acetylated polymannose compound known as acemannan is thought to largely account for aloe's bioactivity.[1] Although many previous studies have shown aloe to be effective in lowering glucose, lipids, and cholesterol both clinically and in vivo, there is a need for more rigorous studies with specific endpoints. This randomized, double-blind, placebo-controlled clinical trial investigates aloe gel for treating hyperlipidemia in T2DM patients.

The aloe was procured from the Research Institute of Medicinal Plants in Karaj, Iran. The gel was manually extracted from the inside of a washed aloe leaf. The bioactive compounds aloin and anthraquinone were removed and the gel was freeze-dried. The acemannan was quantified using high-performance thin layer chromatography (HPTLC) with an acemannan standard. Gelatin capsules were filled with 300 mg of aloe gel powder each or "toast powder" as a placebo. No other description of the placebo is provided.

Included patients were Iranian men and women with T2DM who were between 40-60 years of age. The 3 main criteria were patients with fasting blood glucose concentrations of 150 mg/dl to 200 mg/dl, hemoglobin A1c (HbA1c) levels from 7-9%, and who were taking glyburide (10 mg/day) and metformin (1000 mg/day); those that only took

glyburide (10 mg/day) and metformin (1000 mg/day); and patients recently diagnosed with T2DM that had fasting blood concentrations of LDL cholesterol and/or triglycerides between 100 mg/dl and 150 mg/dl. Those on other diabetes pharmaceuticals (including insulin); who had other serious health conditions; who were using estrogen, steroids, beta-blockers, or thiazide; or who were pregnant, trying to get pregnant, or breastfeeding were excluded.

A total of 67 patients were randomized to either the aloe (n=33) or placebo group (n=34), with 7 patients lost to follow-up, resulting in n=30 for each group completing the study. Patients took either 300 mg of aloe or placebo every 12-hour period for 2 months. They were also counselled on a healthy diet, kept a food diary for 3 days of each week, and were asked to return unconsumed capsules at the end of the study to ensure compliance. The primary endpoints were changes in fasting blood concentrations of glucose, HbA1c, and lipids, which were taken at baseline and at the end of the study. Secondary endpoints included fasting blood concentrations of lipids, bilirubin, blood urea nitrogen, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), γ-glutamyl transpeptidase (GGT), and peptidase.

The demographic data and all blood measures were not significantly different between the aloe and placebo groups at baseline. There were no adverse effects reported. Patients in the aloe group had lower glucose concentrations at the end of the study than at baseline; these were significantly lower than those in the placebo group (167.8 ± 8 mg/dl vs. 191.2 ± 42.9 mg/dl, P=0.036). At the end of the study, the aloe group also had significantly decreased HbA1c concentrations as compared to placebo (6.6 ± 1.1% vs. 7.8 ± 1.8%, P=0.036). Although the total cholesterol of the aloe group decreased over the course of the study, it was significantly higher than that of the placebo group at the end of the study (217.9 ± 28.2 mg/dl vs. 181.0 ± 42.9 mg/dl, P=0.006). No corresponding increase in HDL cholesterol was seen in either group. Also, the aloe group's LDL cholesterol concentrations were higher than the placebo group's at the end of the study (125.7 ± 15.2 mg/dl vs. 100.6 ± 25.4 mg/dl, P=0.004). None of the other parameters measured were significantly different, and patients did not report any adverse side effects.

In summary, this study reports that aloe gel supplements led to decreased blood glucose, total cholesterol, and LDL cholesterol concentrations, but baseline and endpoint measurements were not statistically compared. As this would seem an obvious analysis, omitting this data is unusual and makes assessing the bioactivity difficult. The results of this study somewhat agree with previous reports, and discrepancies are thought to be due to a small sample size. One major problem with this study is the failure to ensure the intake of glyburide and metformin in all patients. Included patients should be on the same dosage of both agents in order to assess any drug-herb interaction effects and to standardize any variation from this; the authors are unclear as to whether this was done. Despite this, standardizing the aloe gel to acemannan adds rigor to the material used, and aloe gel is worthy of future clinical trials in T2DM patients.

—Amy C. Keller, PhD

Reference

[1]Engels G. Aloe. *HerbalGram*. 2010;(87):1-5.