P.O. Box 144345 Austin, TX 78714-4345 ▪ 512.926.4900 ▪ Fax: 512.926.2345 ▪ www.herbalgram.org

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File: ■ Hibiscus (*Hibiscus sabdariffa*, Malvaceae)
■ Type 2 Diabetes
■ Systematic Review/Meta-analysis

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RE: Meta-analysis of Hibiscus Studies Show Improves Glucose Levels in People with Diabetes

Bule M, Albelbeisi AH, Nikfar S, Amini M, Abdollahi M. The antidiabetic and antilipidemic effects of *Hibiscus sabdariffa*: a systematic review and meta-analysis of randomized clinical trials. *Food Res Int*. April 2020;130:108980. doi:10.1016/j.foodres.2020.108980.

Type 2 diabetes (T2D) is a chronic disease caused by inability to produce sufficient insulin or to utilize it properly. T2D is characterized by high postprandial and fasting blood glucose, insulin resistance, and low insulin production. Sedentary lifestyles and the use of refined foods are risk factors for obesity and contribute to rising incidence of T2D in developing or urbanizing areas. Social and health costs of T2D and often severe complications are immense, with direct medical expenses alone >US $825 billion annually. Oral hypoglycemics and other medications are available, but most people with T2D do not achieve optimal glucose control and may experience adverse effects (AEs).

High costs and, in many areas, limited access to pharmaceuticals raise interest in herbal alternatives. Hibiscus (HS; *Hibiscus sabdariffa*, Malvaceae) flowers and calyxes, in hot and cold beverages. are used traditionally for T2D, high blood pressure, liver diseases, fever and inflammation, and conditions symptomatic of hyperlipidemia around the world.

Effects of HS in T2D are not well-studied, in contrast to those in hypertension and hyperlipidemia. The authors searched electronic databases from inception to October 28, 2019, for human trials of such effects, excluding in vitro, in vivo, and ex vivo studies; review articles; conference abstracts; and abstracts lacking details. Of 1038 records retrieved, 421 were duplicates. Of 617 unique results, 597 were excluded on the basis of title or abstract. Of 20 full-text articles assessed, 12 were excluded, and eight included in this systematic review and meta-analysis.* Studies were conducted in Egypt (n = 1), Mexico (1), Iran (4), India (1), and the UK (1). All were randomized placebo-controlled clinical trials (RCTs) but not all were double-blinded. They involved 492 participants, ranging from eight to 129 in number. All but one included men and women; one, men only. Most included participants 25-65 years of age; one was a pediatric study in young teenagers (~ 14 years old). Interventions lasted six to 90 days. All used oral HS infusions as the active substance, in doses of 15-10,000 mg/kg/body weight (BW) given one-three times daily.

Unclear risk of bias was found for most trials in randomization, blinding, and/or allocation. In two trials, dropout rates ≤ 20% potentially affected treatment estimates.

Endpoints included in the meta-analysis were HS effects on fasting plasma glucose (FPG), total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides (TGs). All studies reported baseline and post-treatment levels and gave results as means ± standard deviation (SD). Pooled results showed significant mean reductions in FPG (P = 0.001) and LDL (P = 0.018) vs. placebo. All seven RCTs reporting FPG used HS at different doses (30 – 10,000 mg/d). Overall heterogeneity for these studies was 25.5% (P = 0.217). Significant decreases were not seen for TC (P = 0.102), HDL (P = 0.944), or TG (P = 0.102) vs. placebo. Statistical analysis found significant heterogeneity in studies reporting TC or TG (P = 0.000 for each), but not in those reporting HDL (P = 0.535) or LDL (P = 0.312).

Subgroup analyses based on HS doses administered found that only < 500 mg/kg/d had no statistically significant effects on glycemic or lipid profile endpoints except for TC, significantly affected at < 500 mg/kg/d (P = 0.037) with less between-study heterogeneity. No statistically significant decrease in TG was seen at any dose studied; however, univariate meta-regression analysis found a dose-response association (P = 0.03) for TG. No dose-response association was seen for FPG or TC. Sensitivity analyses using the leave-one-out method found no undue effect of any study. Funnel plots and Egger's regression analysis revealed no publication bias for FPG (P = 0.664), HDL (P = 0.065), LDL (P = 0.677), or TG (P = 0.232) results, but a statistically significant potential bias for TC (P = 0.056) was seen.

HS' benefits to FPG are most convincingly supported. Potential mechanisms of action include reducing α-glucosidase and α-amylase enzymatic activity, downregulating advanced glycation end-products levels, and reducing the oxidative stress of hyperglycemia. All of these proposed mechanisms have supporting in vivo and/or in vitro reports, suggesting that HS' antidiabetic effects (e.g., regulation of signaling and energy-sensitive pathways, oxidative and inflammatory processes, mitochondrial functionality, and membrane-dependent processes) are multi-targeted.

A 2013 meta-analysis found statistically significant HS effects on LDL, HDL, TC, and TG. Differences may result from different levels of HS' active compounds in specific formulations used, attributable to many variables from plant characteristics to processing and storage. More studies of HS potential antihyperlipidemic effects, as well as of other indications of hyperglycemia, are needed.

—Mariann Garner-Wizard

*Of the 12 excluded after full-text assessment, all but three were for lack of detail or data. Those three were excluded as being in "other languages," but no language limitation is specified in study criteria reported.

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