Monique M. Moona, MD; Richard Smits, MD; Joseph Kertesz, MA; Albert Meyer, MD
New Hanover Regional Medical Center Residency in Family Medicine, Wilmington, NC

Leslie Mackler, MSLS
Moses Cone Medical Center, Greensboro, NC

ASSISTANT EDITOR
Anne Mounsey, MD
University of North Carolina School of Medicine, Chapel Hill

Q/ Do complementary agents lower HbA1c when used with standard type 2 diabetes therapy?

EVIDENCE-BASED ANSWER

A/ **No, there is no high-quality evidence** that supports using complementary or alternative agents to lower hemoglobin A1c (HbA1c) in patients with noninsulin-dependent type 2 diabetes. Oral chromium in widely varying doses reduces HbA1c a small amount (strength of recommendation [SOR]: **C,** meta-analysis of low-quality randomized, controlled trials [RCTs] of disease-oriented outcomes, with inconsistent results).

Oral cinnamon 1 to 3 g/d causes a small (<0.1%) drop in HbA1c (SOR: **C,** meta-analysis of low-quality RCTs of disease-oriented outcomes).

Fenugreek, milk thistle, safflower oil, and sweet potato extract may also reduce HbA1c (SOR: **C,** small, low-quality RCTs of disease-oriented outcomes).

Evidence summary

Almost all complementary and alternative agents reviewed here were tested against placebo, and most were used in combination with standard therapy, usually identified as diet with or without oral hypoglycemic agents (**TABLE**).[1-8]

Meta-analyses evaluate effects of chromium and cinnamon

A meta-analysis of 13 RCTs evaluating the effect of oral chromium in patients with type 2 diabetes (age range not given) found a small improvement in HbA1c.[1] Limitations of the meta-analysis included a wide range of chromium dosages and preparations. Ten studies showed no benefit, and of the 3 showing improvement, the researchers rated 2 as poor-quality.

A meta-analysis of 5 RCTs assessing the effect of oral cinnamon in patients with type 2 diabetes, 42 to 71 years of age, found that cinnamon produced a clinically irrelevant but statistically significant decrease in mean HbA1c.[2] After analyzing the 2 RCTs with the largest effects, the researchers concluded that cinnamon might have a greater effect in patients with poorly controlled diabetes (baseline HbA1c>8.2%).

When they evaluated these RCTs for study homogeneity, they found significant differences among the studies in subject age, gender, ethnicity, body mass index, disease duration, concurrent medications, and baseline HbA1c levels, as well as variations in cinnamon dose, preparation, and therapy duration. Furthermore, only one of the studies reported randomization methods and whether allocation was concealed.

What about caiapo, fenugreek, milk thistle, and safflower oil?

Two small, moderate-quality RCTs of caiapo (sweet potato skin extract) in diet-controlled patients with diabetes demonstrated small but possibly clinically significant reductions in HbA1c between the intervention and control groups.[3,4]

Four small, placebo-controlled RCTs of fenugreek, milk thistle, and safflower oil

TABLE

Effect of complementary or alternative agents on HbA1c in type 2 diabetes

CAA*	Dose/ day	Concurrent diabetes therapy	Study type	Study size	Study duration	Difference in HbA1c (in HbA1c units)	95% CI or *P* value
Chromium[1]	1.28-1000 mcg	Not given	Meta-analysis of 13 RCTs	381	3 wk-8 mo	-0.6†	-0.9 to -0.2
Cinnamon[2]	1-3 g	Various oral hypoglycemic agents‡	Meta-analysis of 5 RCTs	315	1.5-4 mo	-0.09 (WMD)†	-0.14 to -0.04
Caiapo[3]	4 g	Diet only	RCT	61	5 mo	-0.21 (caiapo)§	*P*=.08
						+0.25 (placebo)§	*P*=.0001
Caiapo[4]	4 g	Diet only	RCT	61	3 mo	-0.53 (caiapo)§	*P*<.001
						+0.06 (placebo)§	*P*=.23
Trigonella foenum-graecum (fenugreek)[5]	6.84 g	Sulfonylurea	RCT	69	3 mo	-1.46 (fenugreek)§	*P*<.05
						-0.41 (placebo)§	*P*<.05
Silybum marianum (milk thistle)[6]	200 mg	Metformin and sulfonylurea	RCT	51	4 mo	-1.0 (milk thistle)§	*P*<.001
						+1.2 (placebo)§	*P*<.0001
Silybum marianum (milk thistle)[7]	200 mg	Sulfonylurea	RCT	38	4 mo	-1.5 (milk thistle)§	*P*<.05
						-0.5 (placebo)§	*P*=NS
Safflower oil vs conjugated linoleic acid[8]	8 g	Various oral hypoglycemic agents‡	DBRCD	35	4 mo	-0.6 (safflower oil)§	*P*=.0007
						+0.1 (conjugated linoleic acid)§	*P*=NS

CAA, complementary or alternative agents; CI, confidence interval; DBRCD, double-blind, randomized, crossover design; HbA1c, glycosylated hemoglobin A1c; NS, not significant; RCT, randomized controlled trial; WMD, weighted mean difference.

*All CAAs were compared against placebo, with the exception of safflower oil, which was compared against conjugated linoleic acid supplementation.

† Change in HbA1c means at study endpoint; the difference in HbA1c in intervention vs placebo groups.

‡ Oral hypoglycemic agents included α-glucosidase inhibitors, biguanides, glinides, glitazones, sulfonylureas, and thiazolidinediones.

§ Change in HbA1c means at study endpoint; the change in HbA1c from baseline.

found statistically and clinically significant reductions in HbA1c, but all these studies were of poor quality with unclear methods of randomization, threats to blinding, and a lack of baseline demographics.[5-8]

Recommendations

Both the American Diabetes Association (ADA) and the Diabetes UK Nutrition Working Group state that, "there is no clear evidence of benefit from vitamin or mineral supplementation in people with diabetes (compared with the general population), who do not have underlying deficiencies."[9,10] The ADA specifically states that chromium cannot be recommended because it lacks any clear benefit.[9] JFP

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