SUPPLEMENTS TO LOWER BLOOD SUGAR

Hundreds of dietary supplements including herbals, vitamins and minerals have been reported to have beneficial anti-glycemic effects for patients with diabetes though, in most cases, evidence is of poor quality. The best current evidence on supplements is presented below.

Note: Please refer to the *Passport to Whole Health*, Chapter 15 on Dietary Supplements for more information about how to determine whether or not a specific supplement is appropriate for a given individual. Supplements are not regulated with the same degree of oversight as medications, and it is important that clinicians keep this in mind. Products vary greatly in terms of accuracy of labeling, presence of adulterants, and the legitimacy of claims made by the manufacturer.

HERBAL SUPPLEMENTS

Many modern pharmaceuticals have natural plant origins. Among them, metformin was derived from *Galega officinalis* (goat's rue or French lilac), a traditional remedy for diabetes used in Europe since the Middle Ages. Many botanicals are used for glycemic control and management of diabetic complications. Below are two examples of botanicals, cinnamon and *Nigella sativa*, that have more than one review/meta-analysis to support their efficacy in diabetes. Some botanical supplements have one recent review/meta-analysis supporting their role in diabetes. These include:

- Milk thistle[1]
- Purslane[2]
- Ginseng-related therapies[3]
- Nettle[4]

Other botanicals that have less robust evidence supporting their use in managing blood sugars include the following:

- Bitter melon
- Fenugreek
- Gymnema
- Pycnogenol
- Prickly pear

CINNAMON

True cinnamon (Cinnamomum *zeylanicum),* Chinese cinnamon (Cinnamomum *cassia)* and Indonesian cinnamon (Cinnamomum *burmanni)* are among 300 species of *Cinnamomum* that belong to the Lauraceae family. Pooled results from a 2012 Cochrane Review showed no effect on HbA1c of these three types of cinnamon on patients with type 1 or type 2 diabetes mellitus.[5] These results are in conflict with a 2011 meta-analysis demonstrating a significant improvement in fasting blood glucose (FBG) with whole and extract Cinnamon

cassia.[6] A 2019 review and meta-analysis of 18 studies showed that cinnamon did significantly reduce fasting blood sugar by an average of 19.26 mg/dL; however, there was no significant change in hemoglobin A1c, body weight, body mass index, or waist circumference. Due to the heterogeneity of the studies, the evidence is still inconclusive.[7]

NIGELLA SATIVA (FENNEL FLOWER, BLACK SEED, BLACK CUMIN)

Nigella is a plant that belongs to the family *Raninculaceae* and has been used in medicine for centuries, especially in Southeast Asia and the Middle East. While the optimal dosage and formulation are yet to be determined, there have been three systematic reviews/meta-analyses that have provided encouraging evidence to support Nigella's health benefits for people who have been diagnosed with diabetes. A 2016 review of 23 articles including 1,531 participants showed that fasting blood sugar (FBS) was reduced significantly in 13 studies.[8] A 2017 review and meta-analysis suggested effectiveness in glucose homeostasis and improvement in serum lipids.[9] Lastly, a 2019 review and meta-analysis concluded that Nigella significantly benefits glycemic status.[10] If this were to be considered as part of a treatment plan, the Natural Medicines Food, Herbs, and Supplements Database suggests that black seed powder be dosed at 1 gm twice daily for 3-12 months, based on what has been used in the literature. Black seed oil 450mg three times daily for 12 weeks has also been used.[11]

VITAMINS AND MINERALS

Although the ADA does not generally support the use of micronutrient supplements for people with diabetes, they recommend that people who are at increased risk for micronutrient deficiencies (e.g., those following very-low-calorie diets, the elderly, and strict vegetarians) may benefit from multivitamin supplements.

MAGNESIUM

Magnesium deficiency is seen with decreased absorption (as in patients with poor diets high in processed food) or increased elimination (as in people who use alcohol, caffeine, or take diuretics or birth control pills). Dietary sources include whole grains, leafy green vegetables, legumes, and nuts. Magnesium is involved in insulin secretion, binding, and activity. Results of a 2006 meta-analysis support improvement in FBS but not HbA1c.[12] A 2017 review and meta-analysis concluded that magnesium supplementation can lead to improved FBG, HDL, LDL, triglycerides, and systolic blood pressure in people diagnosed with diabetes, suggesting it may be beneficial in mitigating cardiovascular disease associated with diabetes. [13]

ALPHA-LIPOIC ACID (ALA)

Alpha-Lipoic Acid (ALA) is an antioxidant made by the body and also found in very small amounts in foods. ALA is widely used in Europe and shows promise in the treatment of diabetic neuropathy. Small studies show ALA may reduce oxidative stress and improve insulin sensitivity in patients with diabetes[14] and a recent small randomized controlled

trial (RCT) showed a statistically significant decrease in FBG and post-prandial glucose after eight weeks.[15]. A 2019 systematic review and meta-analysis of 31 trials demonstrated that ALA significantly improves hemoglobin A1c (decreased by 0.35% on average) FBS, in addition to other inflammatory biomarkers such including tumor necrosis factor alpha, interleukin 6, and C-reactive protein.[16]

VITAMIN D

Individuals with the highest vitamin D status (>25 ng/ml) have a 43% lower risk of developing type 2 diabetes mellitus (T2DM) compared with those in the lowest group (<14 ng/ml).[17] Recent studies have suggested that vitamin D supplementation may confer a positive effect on glycemic control. One 2017 review and meta-analysis of 29 trials including 3324 participants found a modest reduction in A1c (decreased by 0.32% on average)[18]. Another meta-analysis in 2018 suggested that vitamin D supplementation may reduce insulin resistance, especially in people who are vitamin D deficient and have well-controlled A1c at baseline.[19] In addition, several reviews and meta-analyses have been published on the benefits vitamin D supplementation may have in improving lipid profile,[20] diastolic blood pressure[21], and chronic inflammation[22], though the results are still not conclusive.[23] While there have been studies on very high dose vitamin D as a treatment for diabetes, data are not sufficient at this time to support this treatment approach.[24]

ZINC

Zinc has an interesting relationship with the body's glucose metabolism. First, zinc plays a key role in the production and secretion of insulin. In addition, zinc is excreted in the urine when blood glucose levels are high, so people with diabetes often have lower zinc serum levels than those without diabetes.[25] Therefore, to support the body's natural insulin function, it can be helpful to consider zinc supplementation.[26] That being said, a 2015 Cochrane review of three trials with a total of 128 participants concluded that as of that time there was no evidence on which to base the use of zinc in the prevention of type 2 diabetes.[27] More recently, a 2017 systematic review of 15 original studies demonstrated a negative correlation between hemoglobin A1c percentage and plasma zinc levels, concluding that zinc supplementation in people with type 2 diabetes did, in fact, improve glycemic control.[28] A recommended dose of zinc in people diagnosed with diabetes would be zinc gluconate 25mg twice daily.[29]

FOLATE

Higher levels of homocysteine have been associated with higher insulin resistance and risk of type 2 diabetes. As folate supplementation is one way of lowering homocysteine, it is thought to be a way to mitigate elevated blood glucose levels. A 2019 meta-analysis concluded that folate may be beneficial in supporting glucose homeostasis and lowering insulin resistance, decreasing A1c by 0.46% on average.[30] A 2018 review and meta-analysis of 18 trials including 21,081 participants showed a decrease in fasting glucose by 0.15mmol/L but no significant effect on A1c.[31] There is no standard dose of folate

recommended for blood sugar management at this time; however, Natural Medicines Food, Herbs and Supplements Database lists 1mg of folic acid once daily as a dose that has been studied to support people with diabetic neuropathy.[32]

OMEGA-3 POLYUNSATURATED FATTY ACIDS (PUFAS)

There has been much attention given to the role PUFAs play in the prevention and treatment of diseases related to inflammation. Authors of a 2009 Cochrane Review found no significant change in HbA1c, fasting glucose, or fasting insulin although triglyceride (TG) and very low density lipid (VLDL) levels were significantly improved.[33] There are no data supporting reduced risk of macrovascular outcomes or mortality from PUFA supplementation.[33] Additionally, a recent meta-analysis of 18 separate cohorts (n= 540,184 individuals and 25,670 cases of incident T2DM) found no harms or benefits associated with fish/seafood or omega-3 (fatty acids EPA and DHA) supplementation on the development of T2DM.[34] A 2015 meta-analysis of 20 RCTs found that omega-3 supplementation only significantly decreased triglyceride levels in participants diagnosed with Type 2 diabetes.[35]

FIBER SUPPLEMENTATION

The ADA recommends a goal of 25-35 gm of dietary fiber daily for a healthy diet. Dietary fiber supplementation has been shown to improve glucose control.[36] Other review studies have shown that non-oil seed pulses, either alone or in combination with a high fiber diet, improve glycemic control in patients with T2DM, although significant inter-study heterogeneity exists.[37] A 2015 meta-analysis showed that psyllium fiber showed the greatest improvement in glycemic control in people who were already being actively treated for T2DM, as opposed to people with prediabetes or those who were euglycemic.[38]

PROBIOTICS

A 2016 systematic review and meta-analysis demonstrated that probiotics seem to have a beneficial role in managing type 2 diabetes, significantly decreasing fasting blood glucose and hemoglobin A1c.[39] A 2015 meta-analysis showed an average reduction of A1c by 0.81% with probiotic supplementation.[40] Another 2016 review and meta-analysis showed significant reduction of fasting blood glucose by 0.98 mmol/L (though it did not corroborate a significant decrease in A1c) with probiotic consumption.[41] In addition, a 2017 meta-analysis demonstrated that probiotic supplementation in people with type 2 diabetes was associated with a significant improvement in both A1c and fasting insulin.[42] One meta-analysis concluded that the beneficial effect of probiotics on glucose metabolism was greatest when the duration of supplementation was greater than or equal to 8 weeks and when multiple probiotic species were consumed.[43] Another 2017 meta-analysis suggested that probiotics may also be an effective way to decrease cholesterol levels and blood pressure in addition to FBG.

TABLE 1. EVIDENCE OF EFFECTS OF DIETARY SUPPLEMENTS ON GLYCEMIC CONTROL IN PATIENTS WITH TYPE 2 DIABETES

Supplement and Study Design	Dose and How Long Supplement Taken	Findings
Cinnamon[5] • Meta-analysis • 10 RCTs • 577 participants	<1-3 g, average 2g daily for 4-16 weeks	• No effect on HbA1c (-0.06%; 95% CI -0.29 to 0.18; P = 0.63; n = 405; 6 trials) • Borderline effect FBG (-0.83 mmol/L; 95% CI -1.67 to 0.02; P = 0.06; n = 388; 8 trials.)
Cinnamon[6] • Meta-analysis • 8 RCTs • 369 participants	250 mg-6 g daily for 4-16 weeks	• Significant improvement in FBG (–0.49 – 0.2 mmol/L; P = .025; n=369; 8 trials)
Magnesium[12] • Meta-analysis • 9 RCTs • 370 participants	360 mg daily median dose for 4-16 weeks	• Significant improvement FBG (−0.56 mmol/l; 95% CI 1.10 to −0.01) • Nonsignificant improvement in HbA1c (−0.31%; 95% CI −0.81 to 0.19)
Alpha-Lipoic Acid (ALA)[15] • RCT • 57 participants	300 mg daily for 8 weeks	• Significant improvement FBG (185mg/dl vs.156mg/dl; p<0.0001) and PPG (278mg/dl vs. 238mg/dl; p<0.023)
Vitamin D[17] Systematic review • 8 RCTs with no DM • 3 trials with type 2 DM	400 IU-8600 IU daily for 6 weeks-7 years	• No glycemic effect on patients with normal glucose tolerance at baseline • No effect on glycemic control in Type 2 DM
Omega-3 Fatty Acids/Fish Oil[33] • Meta-analysis • 23 RCTs • 1075 participants	Average of 3.5 g daily for a mean of 8.9 weeks	• No significant change HbA1c, FBG, HDL • TG Decreased (-0.45 mmol/L; 95% CI -0.58 to -0.32, P < 0.00001) • VLDL Decreased -0.07 mmol/L (95% CI -0.13 to 0.00, P = 0.04) • LDL Increased+ 0.11 mmol/L (95% CI 0.00 to 0.22, P = 0.05)
Dietary Fiber Supplementation[36] • Meta-analysis • 15 RCTs	4-40 gm fiber daily. Avg 15 gm daily, total soluble and insoluble fiber	• Significant improvement in HbA1c (-0.26%; 95% CI 0.02 to – 0.51)

Supplement and Study Design	Dose and How Long Supplement Taken	Findings
		• Significant improvement in FBG (-85 mmol/L; 95% CI, 0.46 to –1.25)

DM = Diabetes mellitus; FBG = Fasting blood glucose; HbA1c = Hemoglobin A1c
HDL = High Density Lipoprotein; IU = International Units; LDL = Low Density Lipoprotein
RCT = Randomized Controlled Trial; TG = Triglycerides; VLDL = Very Low Density Lipoprotein

RESOURCE LINKS

- *Passport to Whole Health*: https://www.va.gov/WHOLEHEALTHLIBRARY/docs/Passport_to_WholeHealth_FY2020_508.pdf
- Natural Medicines Database: https://naturalmedicines.therapeuticresearch.com/

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