ECHO IDAHO

Diabetes and Metabolic Conditions

Role of Supplements in Diabetes Care

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None of the planners or presenters for this educational activity have relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

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Learning Objectives



List the most common supplements consumed for the treatment of diabetes



Evaluate evidence for supplements used in the treatment of diabetes



Summarize steps to ensure patients are using appropriate products

Common Supplements used in Diabetes

Dietary Supplements

- *Chromium*
- Magnesium
- Alpha- Lipoic Acid (ALA)
- *Vitamin D*
- Probiotics
- Coenzyme Q10 (CoQ10)

Herbal Supplements

- *Cinnamon*
- Ginger
- *Berberine*
- *Fenugreek*
- *Bitter melon*
- Curcumin
- *Black seed*

https://www.t2dnetwork.ca/post/t2d-supplements

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Chromium (4)

- Chromium picolinate activates insulin receptors
- Dose commonly used: 200 mcg daily
- Results inconsistent

Study or Subgroup	chromium Mean	SD	Total	placebo Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Chen 2014	-0.4	8.63	38	0.3	7.46	28	1.2%	-0.70 [-4.59, 3.19]
Guimaraes 2013	0.19	1.24	16	-0.32	1.44	13	9.5%	0.51 [-0.48, 1.50]
Hosseinzadeh 2013	-1	1.55	42	-0.1	1.71	42	12.4%	-0.90 [-1.60, -0.20]
Kleefstra 2007	0.51	0.64	29	0.26	0.47	28	16.6%	0.25 [-0.04, 0.54]
Martin 2006	-1.16	1.42	14	-0.44	1.43	11	8.4%	-0.72 [-1.85, 0.41]
Paiva 2015	-1.7	1.65	39	-0.8	1.34	32	12.5%	-0.90 [-1.60, -0.20]
Pei 2006	-0.21	0.2	30	0.1	0.2	30	17.7%	-0.31 [-0.41, -0.21]
Racek 2006	-0.03	1.59	19	0.17	1.64	17	8.9%	-0.20 [-1.26, 0.86]
Sharma 2011	-2.65	1.21	20	-0.59	0.94	20	12.7%	-2.06 [-2.73, -1.39]
Total (95% CI)			**247**			**221**	**100.0%**	**-0.54 [-0.98, -0.09]**

Heterogeneity: $Tau^2 = 0.29$; $Chi^2 = 49.04$, df = 8 ($P < 0.00001$); $I^2 = 84\%$
Test for overall effect: $Z = 2.36$ ($P = 0.02$)

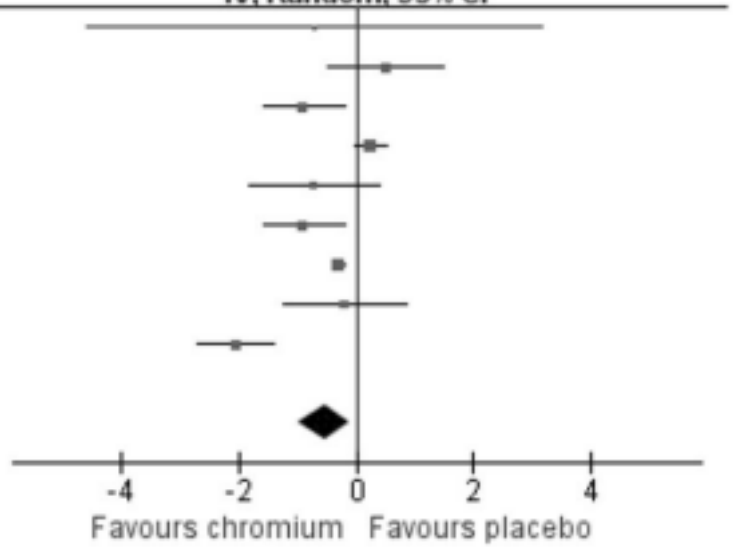
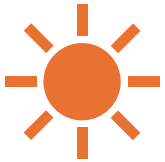


Fig. 2 Forest plot of glycosylated hemoglobin comparison after chromium supplementation

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Vitamin D (6-7)



Two forms

Cholecalciferol (Vitamin D3)- skin exposure to solar ultraviolet B radiation

Ergocalciferol (Vitamin D2)- synthesized by plants



Food sources

Fish (tuna, sardines, salmon), Meat (beef, liver)

Dairy

Green leafy veggies (spinach, okra, kale), Beans (soy, white)



Low Vitamin D levels

Impaired fasting glucose, HTN, obesity, glucose intolerance, development of DM2



Clinical Trial

RCT, double blind: Vitamin D 4000 IU vs placebo for 6 months

- Significant improvement in insulin sensitivity

Vitamin D (7)

Table 2 Levels of FBG, FI, HbA_{1c}, Vit. D and Ca in the patients' subgroups after treatment

Parameters	Group A (Mean ± SD)	Group B (Mean ± SD)	Group C (Mean ± SD)	Group D (Mean ± SD)	*p*-value	Reference range
FBG (mg/dL)	116.9 ± 3.4	108.1 ± 2.2	94.2 ± 4.4	90.5 ± 5.7	0.000*	70–100
FI (μIU/mL)	5.2 ± 1.9	7.8 ± 1.4	10.7 ± 1.5	9.9 ± 1.8	0.000*	4.03–23.46
HbA_{1c} (%)	6.2 ± 0.6	5.8 ± 0.3	5.2 ± 0.1	4.7 ± 0.3	0.000*	3.8–5.8
Vit. D (ng/mL)	10.1 ± 4.4	32.3 ± 0.7	34.1 ± 1.7	36.4 ± 3.2	0.000*	30–100
Ca (mg/dL)	7.9 ± 0.2	8.6 ± 0.3	9.7 ± 0.4	9.3 ± 0.6	0.000*	8.2–10.4

*Significant at the levels of ($p \leq 0.05$)

- 300 patients, with Vit D deficiency, T2DM, ages 36-48, x 6 months
  - Instructed to follow health and balanced diet with restriction of sugars and carbohydrates
  - Group A- Metformin only (500 mg BID)
  - Group B- Metformin and Vitamin D (50,000 IU weekly x2 mo, then 2000 IU daily)
  - Group C- Metformin, Vitamin D, Calcium (1000 mg Ca citrate daily)
  - Group D- Control
  - Baseline A1c in treatment group 8.6 ± 1.2, control group 4.8 ± 0.3

Cinnamon (1, 2)

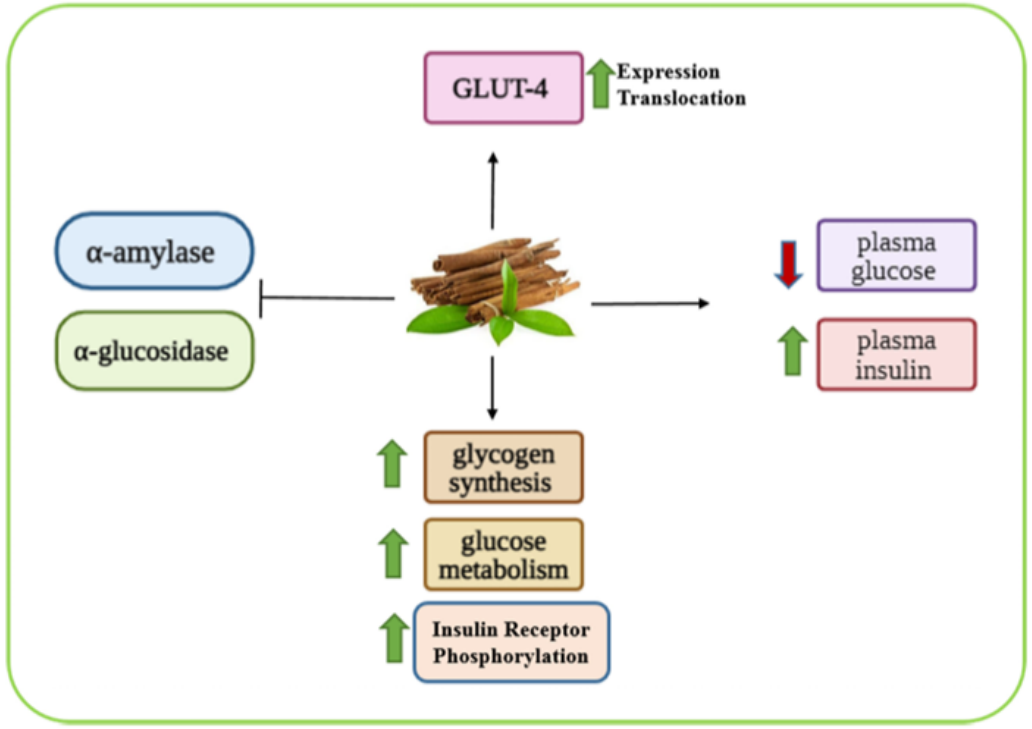


Figure 3. A graphical representation of the molecular mechanism of cinnamon inhibiting α-amylase, α-glucosidase, and plasma glucose, and stimulating plasma insulin, glycogen synthesis, glucose metabolism, and insulin receptor phosphorylation. Green and red arrows indicate increase and decrease, respectively. Image was created using BioRender.com.

- True cinnamon or Ceylon cinnamon
- Dose 1-6 grams daily
- Contains coumarin which can cause liver damage when consumed in excess
  - Tolerable daily intake is 0.1 mg/kg
  - Cassia cinnamon contains 0.1-3.5 mg per gram
  - 1 tsp cinnamon = ~2.5 g of cinnamon

Cinnamon Efficacy (2)

Select Studies on Cassia Cinnamon for Type 2 Diabetes		
Population & Study Design	**Intervention vs. Comparison**	**Outcomes**
Adults with prediabetes (N=54) RCT	Oral cassia cinnamon 1500 mg daily for 12 weeks vs. placebo	↓ Postprandial glucose by 20 mg/dL ↓ HbA1c by 0.2% Stabilizes fasting blood glucose (cassia cinnamon group remained stable; placebo group ↑ by ~5 mg/dL)
Adults with type 2 diabetes (N=543) Meta-analysis of 10 RCTs	Oral cassia cinnamon 120 mg to 6 g daily for 4 to 18 weeks vs. placebo or standard diabetes medications	↓ Fasting blood glucose by 25 mg/dL ↔ HbA1c

Berberine (2)

- Mechanism of Action
  - ↑ glucose uptake in muscle cells
  - ↑ glycolysis (breakdown of glucose)
  - ↑ insulin sensitivity
  - ↓ hepatic gluconeogenesis (production of glucose by the liver)
- Dose 500 mg 2-3 times daily (max 1500 mg daily)
- Common side effects
  - Abdominal pain and distension, constipation, diarrhea, gas, nausea and vomiting
- Drug Interactions
  - Inhibits CYP 2C9, 2D6 and 3A4



Image from: https://www.webmd.com/obesity/berberine-health-benefits

Berberine Efficacy (2)

Select Studies on Berberine in Adults with Type 2 Diabetes		
Population & Study Design	**Intervention vs. Comparison**	**Outcomes**
Adults with type 2 diabetes or prediabetes (N=4158) Meta-analysis of 46 randomized controlled trials (RCTs)	Oral berberine 600-1500 mg daily for 4-24 weeks alone or in combination with standard diabetes medications vs. placebo, lifestyle interventions, or standard diabetes medications	↓ HbA1c 0.7% ↓ Fasting blood glucose by ~16 mg/dL ↓ Postprandial glucose by ~23 mg/dL
Adults with type 2 diabetes, hyperlipidemia, and/or hypertension (N=2569) Meta-analysis of 27 RCTs	Oral berberine 500-1500 mg daily for 2 weeks to 6 months, alone or in combination with lifestyle intervention or standard diabetes medications vs. placebo, lifestyle interventions, or standard diabetes medications	↓ HbA1c 0.7% ↓ Fasting glucose by ~18 mg/dL ↓ Postprandial glucose by ~36 mg/dL
Adults with type 2 diabetes and dyslipidemia (N=116) RCT	Oral berberine 1000 mg daily for 3 months vs. placebo	↓ HbA1c 0.9% ↓ Fasting glucose by ~25 mg/dL ↓ Postprandial glucose by ~56 mg/dL

Fenugreek (2)

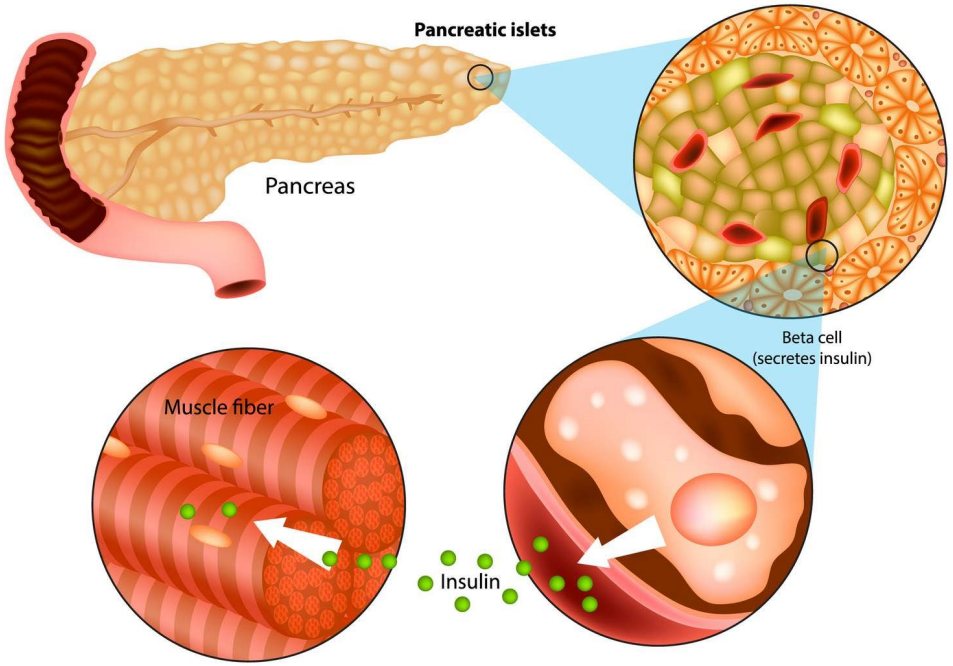




Image from: https://aanmc.org/naturopathic-kitchen/naturopathic-kitchen-fenugreek/

- Dose 5-10 grams daily
- Efficacy in 8-16 week trials
  - ↓ FBS by 27 mg/dL
  - ↓ PPG by 30 mg/dL
  - ↓ A1c by 0.5%
- Common side effects
  - Abdominal pain, bloating, diarrhea, dyspepsia, gas, nausea
    - High fiber food 50-65% fiber by weight

Bitter Melon (5-6)



Image from: https://www.healthline.com/nutrition/bitter-melon

- Mechanism of action
  - Inhibit intestinal absorption of glucose
  - Suppress glycogenic enzymes
  - Decrease hepatic gluconeogenesis
- Contains Polypeptide-P
  - Resembles bovine insulin
- Evidence
  - SubQ injections of polypeptide-p more effective than oral administration
  - Very few randomized controlled trials conducted
    - 90 subjects (in final analysis) over 12 weeks- treatment group had lower fasting BG, no difference in A1c
  - Various forms
- As a food source
  - Caution against hypoglycemia
  - Monitor blood sugars more consistently

Nopal (5)



Image from: https://www.growveg.com/plants/us-and-canada/how-to-grow-prickly-pear-cactus/

- Prickly pear cactus
- Rich in soluble fiber and pectin
  - Reduces intestinal glucose uptake
- Very few well designed trials conducted in human subjects

Black Seed (Nigella sativa) (2)

- Mechanism of action
  - ↑ insulin sensitivity
  - ↓ insulin resistance
  - ↑ insulin secretion
  - ↑ glucose uptake
  - ↓ hepatic gluconeogenesis
- Dose
  - Powder – up to 2 grams daily
  - Oil – up to 5 mL (5 grams) daily
- Common side effects
  - Constipation, gastric burning or discomfort, nausea, vomiting



Image from: https://loveorganics.net.au/wp-content/uploads/2023/12/Black-Cumin-Nigella-scaled-1.jpg

Black Seed Efficacy (2)

Population & Study Design	Intervention vs. Comparator	Outcomes
Adults with type 2 diabetes (N=706) Meta-analysis of 7 RCTs	Oral black seed oil 1 gram daily or powder 1-3 grams daily for 2-12 months vs. placebo or standard care	↓ Fasting blood glucose by ~18 mg/dL ↓ HbA1c by ~0.7%
Adults with type 2 diabetes (N=43) RCT	Oral black seed oil 1 gram daily for 8 weeks vs. placebo	↓ Fasting blood glucose by ~23 mg/dL ↓ HbA1c by ~0.7%

Steps to Choose an Appropriate Product

- Talk with your provider first
  - Medication interactions
  - Medical conditions
  - Upcoming procedures
  - Safety
- Select a reputable company using Good Manufacturing Practices (GMPs)
  - ConsumerLab.com
  - NSF International
  - U.S. Pharmacopeia (USP)

https://www.nccih.nih.gov/health/dietary-and-herbal-supplements
https://ods.od.nih.gov/factsheets/WYNTK-Consumer/

Key Points and Patient Education

- Not all supplements are created equally
- Encourage patients to talk with providers before starting supplements
- Monitor blood glucose levels more closely
- Adjustments to other medications may be needed
- If using food source, start low and go slow

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