Vitamin E, Vitamin C, Zinc, & Chromium in diabetes

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American Diabetes Association

Standards of Care in Diabetes

01

Supplements have not been proven to be an effective option for lowering blood sugar or supporting diabetes management

02

For some people may be necessary (deficiency, pregnant or breastfeeding, elderly, vegetarians, following very low-calorie or low-carbohydrate diets)

- The relationship between (E/C/Cr/Zn) and the risk of diabetes
- The role of (E/C/Cr/Zn) in glycemic control
- The prevalence of (E/C/Cr/Zn) deficiencies in diabetic patients
- The intake, absorption, metabolism, and excretion of (E/C/Cr/Zn) in diabetic patients
- Supplementation of (E/C/Cr/Zn)

Vitamin C

Intake
(Moderate certainty)

at the RDA level (70 mg/day)

↓24% risk of DM

Serum
(Lack of evidence)

65 μmol/l VS 17 μmol/L

↓42% risk of DM

Supplement **(Lack of evidence)**

Lampousi A, et al.2024
Sun H, et al.2022
Li Z, et al.2025

The role of Vit C in glycemic control

- Vitamin C can compete with glucose for binding to hemoglobin, HbA1C
- Translocation of Glut4
- Antioxidant

Liu j, et al.2023
Alberts A, et al. 2025
Undurty N, et al. 2019

Vitamin C status based on plasma concentration

Saturated
≥ 70 µmol/L
≥ 170 Toxicity

Adequate
≥ 50-69 µmol/L
(0.8-1.2 mg/dl)

insufficient
(hypovitaminosis)
< 50-23 µmol/L
(0.4-0.8 mg/dl)
deficient
< 23 µmol/L

Lunt H, et al.2023

Vitamin C deficiency in diabetic patients

Diabetics have (30% & 5 µmol/L) lower serum vitamin C VS healthy people

Diabetics who are overweight, obese, or older have lower vitamin C levels

Prevalence of deficiency; 12–38%, hypovitaminosis C ≥ 50%

Car AC, et al.2023
Car AC, et al. 2024
Car AC, et al.2022
Liu J et al.2023
Ebenuwa I, et al. 2022

Renal leak of vitamin C

01

Renal leak of vitamin C

dysregulation of the vitamin C transporter in the kidneys (SLC23A1) or damage to the renal tubules

02

Prevalence of vitamin C renal leak in diabetics: 33%

Lunt H, et al.2023
Ebenuwa I, et al. 2022

To achieve normal vitamin C

In healthy individuals; consuming 65 to 90 mg vitamin C

In diabetic individuals; consuming 125 to 166 mg vitamin C (approximately 1.5 times that of healthy individuals)

Car AC, et al.2023

Vitamin C supplementation

Meta-analyses of RCTs: **(Low certainty)**

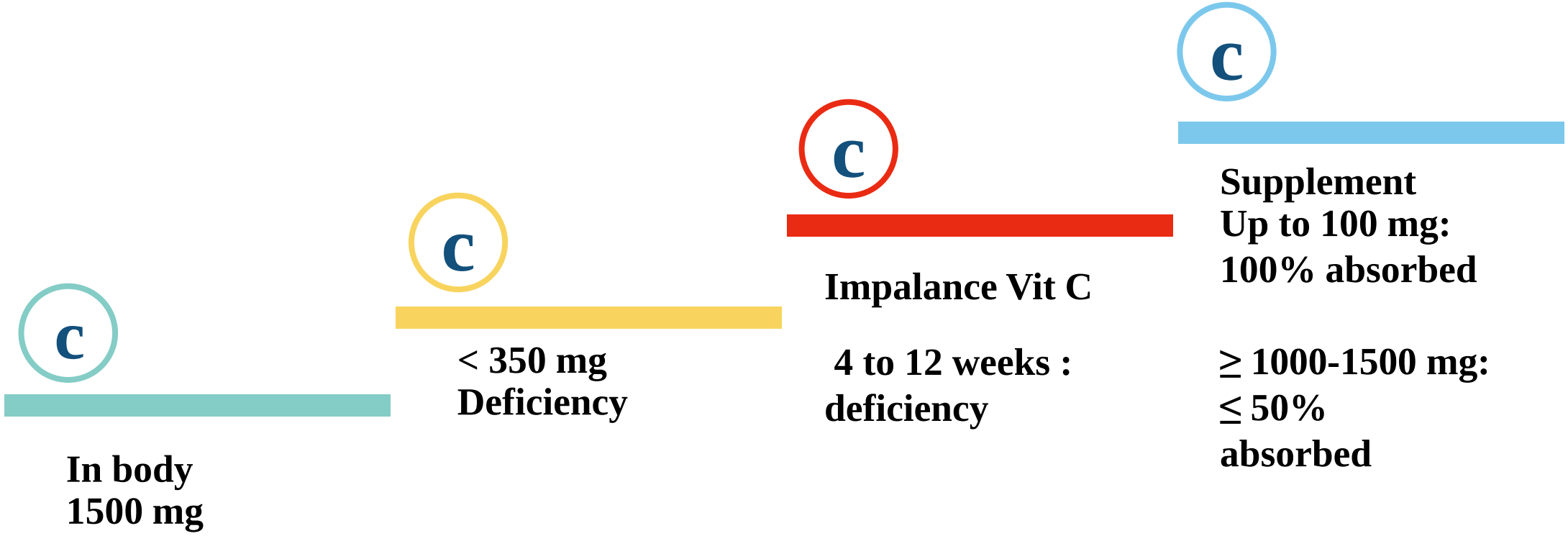
↓ FBS, HbA1c (especially in younger patients)

Long-term interventions are more beneficial

DFU

Rabizadeh S, et al. 2023
Mohammadi A,et al. 2023
Namkhah Z,et al. 2021
Das UN, et al. 2019
Liu J, et al. 2023

More information



Maxfield L, et al. 2023

RDA (C)

Age	Male	Female	Pregnancy	Lactation
0–6 months	40 mg*	40 mg*		
7–12 months	50 mg*	50 mg*		
1–3 years	15 mg	15 mg		
4–8 years	25 mg	25 mg		
9–13 years	45 mg	45 mg		
14–18 years	75 mg	65 mg	80 mg	115 mg
19+ years	90 mg	75 mg	85 mg	120 mg
Smokers	Individuals who smoke require 35 mg/day more vitamin C than nonsmokers.			

UL (C)

Age	Male	Female	Pregnancy	Lactation
0–12 months	Not possible to establish*	Not possible to establish*		
1–3 years	400 mg	400 mg		
4–8 years	650 mg	650 mg		
9–13 years	1,200 mg	1,200 mg		
14–18 years	1,800 mg	1,800 mg	1,800 mg	1,800 mg
19+ years	2,000 mg	2,000 mg	2,000 mg	2,000 mg

Vitamin C

1/2 cup red pepper: 95 mg
1/2 sweet green peppers: 60 mg
1 medium orange: 70 mg
1/2 cup strawberries: 50 mg
1/2 cup broccoli: 50 mg
1/2 cup cantaloupe: 30 mg
1 baked potato: 17 mg
1 tomato: 17 mg

Practical instructions

- **Nutritional: Fruit and vegetable intake status**
- **History (**Alcohol use disorder, Smoking, Bariatric surgery, Iron-overload conditions, Restrictive or low carbohydrate diets, Food allergies, mental illness, Hemodialysis)
- **Serum Vit C**
- **diabetic retinopathy (C+statins)**

Supplementation:
* 500 mg/d for 1 to 3 months
* 2 g/d for the initial 3 days, 500 mg/d for 1 week, and 100 mg/d for 1 to 3 months

Diet: 125-165 mg/d (5 servings of fruits and vegetables provides about 200 mg of vitamin C)

Reger D, et al. 2008
Maxfield L, et al. 2023
Thosar SS, et al. 2015
Park SW, et al. 2019
Gurreei A, et al. 2019
Shi C, et al. 2020

Vitamin E

Intake
(High certainty)

At the RDA level (12 mg/day)
↓ 28% risk of DM (no smoker)

Serum
(Very low certainty)

High VS Low : ↓risk of DM
Deficiency: ↑risk of DM

Supplement
(Moderate certainty)

No effect

Lampousi A, et al.2024
Valdes-Romas R, et al.2015

The role of Vit E in glycemic control

Structural change in the insulin monomer and facilitation of receptor binding

Effect downstream signaling molecules in the insulin pathway

Expression of genes involved in glucose metabolism & Antioxidant

Enhances glutathione levels and protective role in magnesium deficiency

Balbi ME, et al. 2018
Bhatti JS, et al. 2022
Lee S, et al. 2024
Zaulkffali AS,et al. 2019
Lin B, et al. 2023

Vitamin E status based on plasma concentration

Toxicity: rare

Supplement:30

Adequate

5.5 to 20 mg/l

deficiency

< 5 mg/l

In patients with extremely high or extremely low cholesterol levels, the levels of circulating alpha-tocopherol are not an accurate measure of vitamin E

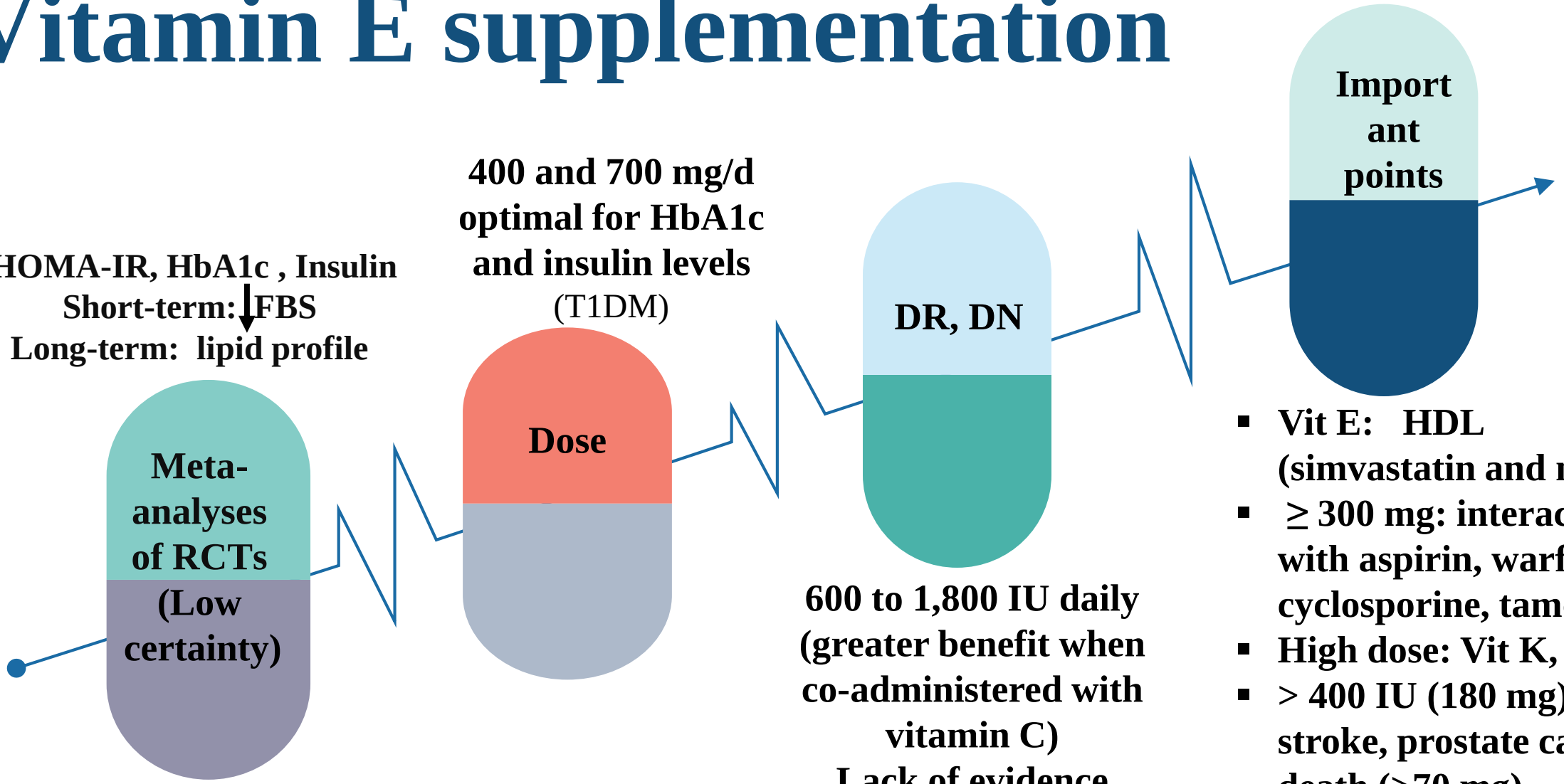
Owen KN, et al. 2023
Kemnic TR, et al. 2023

Vitamin E deficiency in diabetic patients

- Diabetics have (4 μg/ml) lower serum vitamin E VS healthy people. women or older have lower vitamin E levels
- Prevalence of Vit E in healthy: 0.1% VS in diabetics: 36%
- longer duration
- Peripheral neuropathy

Ripon MI, et al.2025
Illison VK, et al. 2010
Valdes-Romas R, et al.2015

Vitamin E supplementation



Asbaghi O, et al. 2023
Jin Z,et al.2023
Mohammad A,et al.2021
Zheng PP, et al. 2024
Matough FA, et al. 2012

Emami MR, et al. 2019
Liu l, ET AL.2020
Ghatziralli.2017
Shi C, et al. 2020

RDA (E)

Age	Males	Females	Pregnancy	Lactation
0–6 months*	4 mg	4 mg		
7–12 months*	5 mg	5 mg		
1–3 years	6 mg	6 mg		
4–8 years	7 mg	7 mg		
9–13 years	11 mg	11 mg		
14+ years	15 mg	15 mg	15 mg	19 mg

UL (E)

Age	Male	Female	Pregnancy	Lactation
1–3 years	200 mg	200 mg		
4–8 years	300 mg	300 mg		
9–13 years	600 mg	600 mg		
14–18 years	800 mg	800 mg	800 mg	800 mg
19+ years	1,000 mg	1,000 mg	1,000 mg	1,000 mg

To convert from mg to IU:

1 mg of alpha-tocopherol is equivalent to 1.49 IU of the natural form or 2.22 IU of the synthetic form.

To convert from IU to mg:

1 IU of the natural form is equivalent to 0.67 mg of alpha-tocopherol.

1 IU of the synthetic form is equivalent to 0.45 mg of alpha-tocopherol.

Vitamin E

1 tbsp wheat germ oil: 20 mg
30 g sunflower seeds: 7.5 mg
1 tbsp sunflower oil: 5.5 mg
1 tbsp corn oil: 2 mg
1 kiwi: 1.1 mg
1 tomato: 0.7 mg

Practical instructions

- **Nutritional**
- **women or older**
- **Other comorbidity or secondary condition:**

  (Abetalipoproteinemia 100 to 200 IU/kg/d, Chronic cholestasis 15 to 25 IU/kg/d, Cystic fibrosis 5 to 10 IU/kg/d, Short-bowel syndrome 200 to 3600 IU/d, Isolated vitamin E deficiency 800 to 3600 IU/d)
- **Serum α-Tocopherol**
- **diabetic retinopathy (C+E)**

Supplementation?

Chromium

Intake highly uncertain

Serum Deficiency: ↑risk of DM

Supplement ↓ 25-30% risk of DM
Not recommended.

Chen J, et al.2022
Chen S, et al. 2017
Mclver DJ, et al.2015
Trumbo P, et al.2008
Afzal S, et al.2024

The role of chromium in glycemic control

The exact biological function of chromium is still unknown

Activates insulin receptor

Expression of glucose transporters, specifically GLUT1 and GLUT4

Enhancing the interaction between insulin and receptors (chromodulin has not been identified)

Decreased inflammatory markers (CRP)(<400 ug, ≤12 weeks)

Anderson R.2000

Chromium status

Cr6+

Adequate (serum)
<1.4 µg/L (0.5-5).

Urine
5 to 10 µg/L

Chromium deficiency in diabetes

there is no evidence of chromium deficiency in humans who consume a typical oral diet.

A compounding factor for this lack of clinical cases is that the methods available for evaluating chromium levels are unreliable

TPN,SBS

Berger MM, et al.2022
Afzal S, et al.2024

Chromium supplementation

- Meta-analyses of RCTs: **(Low certainty)**

↓HOMA-IR (1.5), HbA1c (0.7-0.5), FBS (20)

Short-term: ↓ FBS

Long-term: ↓TG, ↑ HDL

- Evidence is inconsistent or insufficient to definitively confirm chromium as an essential or therapeutically beneficial nutrient in non-deficient individuals.

*Not recommended

Georgaki MN, et al.2024
Asbaghi O, et al. 2020
Suksomboon N, et al. 2014
Asbaghi O, et al.2021
Zhao F, et al. 2022
Ebenuwa I, et al. 2024
Alkhalidi F, et al. 2024
Tirona M, et al. 2023
Berger MM, et al.2022
Afzal S, et al.2024

Chromium supplementation

- **0.5% of Cr of diet is absorbed, (30 µg/d → 0.15 µg)**
- **Supplement: higher compared to what is typically obtained from a typical diet (pharmacological effects)**
- **Renal and hepatic failure with high-dose oral chromium supplementation, ranging from 600 to 2400 µg/d, have been reported**

Berger MM, et al.2022
Afzal S, et al.2024

AI (Cr)

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months*	0.2 mcg	0.2 mcg		
7–12 months*	5.5 mcg	5.5 mcg		
1–3 years	11 mcg	11 mcg		
4–8 years	15 mcg	15 mcg		
9–13 years	25 mcg	21 mcg		
14–18 years	35 mcg	24 mcg	29 mcg	44 mcg
19–50 years	35 mcg	25 mcg	30 mcg	45 mcg
51+ years	30 mcg	20 mcg		

Practical instructions

- **Routine monitoring is not recommended**
- **Nutritional:** Diverse diet, Vitamin C increases the absorption of chromium.
- **Deficiency is suspected:** glucose tolerance testing before and after chromium administration
- **Routine supplementation: not recommended**
- **+ <u>Metformin/ insulin</u>: Hypoglycemia**
- **<u>Levothyroxine</u>: 6 hours**

Zinc

Intake

- **High VS Low : ↓ 12-20 % risk of DM**
- **A moderately higher than DRI: ↓ 13-41%**

Serum

- **High VS Low : ↑ 64% risk of DM**

Supplement

- **No effect (lack of evidence)**

low-dose and long-duration

Fernandez-cao J. et al. 2019
Dib RE, et al. 2015
Pompano ML, et al.2021
Shi C, et al. 2020

The role of zinc in glycemic control

01 **Synthesis, storage, secretion, action of insulin**

02 **Translocation of GLUT4 to the cell surface**

03 A lower gene expression in **ZnT & ZIP** was observed in diabetics compared to controls. (disturbances T2DM-associated zinc dyshomeostasis at the cellular level)

Fernandez- Cao JC, et al. 2019

Zinc status based on plasma concentration

Saturated
≥ 120 µg/dl
Toxicity
≥ 160

Adequate
≥ 70-120 µg/dl

insufficient
< 70-30 µg/dl
deficient
< 30 µmol/L

Yanagisawa H, et al. 2004

Zinc deficiency in diabetes

- **Diabetics have lower serum Zinc VS healthy people (In Asia no Austria & Italy, Age)**
- **The duration of diabetes associated with the concentration of zinc in blood, is not explained by a lower of dietary zinc intake. Exception in DM complications (nephropathy) (3mg/dl)**

Prevalence of deficiency: 30-50 %

Farooq DM, et al.2020
Takuisso, et al. 2025
Fernandez- Cao JC, et al. 2019

Urinary zinc excretion

- RDA of Zn: 8-11 mg - 33% absorption: 2-3 mg (0.5 mg excreted in urine) in diabetes (urinary excretion doubles)
- Daily intake of Zn in diabetes: 10-13 mg

Yazigi AE, et al.1993
Afridi HI, et al.2009
Xu J, et al.2013

Zinc supplementation (clinically significant) (low quality of evidence)

Meta-analyses of RCTs: **(Low certainty)**

↓ HOMA-IR (0.5-0.7), HbA1c (0.3-0.5), FBS (14-23), 2hBS (34-37) Ins (0.6-1.8), Chol (13-16), LDL (6-10), TG (13-18)

↑ total antioxidant capacity, HDL (+4)

Daneshvar M, et al.2024
Nazem MR, et al.2023
Wang X, et al.2019
Heidari M, et al.2023
Nazari M, et al. 2024
Ghaedi K, et al.2024

RDA (Zn)

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months*	2 mg	2 mg		
7–12 months	3 mg	3 mg		
1–3 years	3 mg	3 mg		
4–8 years	5 mg	5 mg		
9–13 years	8 mg	8 mg		
14–18 years	11 mg	9 mg	12 mg	13 mg
19+ years	11 mg	8 mg	11 mg	12 mg

UL (Zn)

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months	4 mg	4 mg		
7–12 months	5 mg	5 mg		
1–3 years	7 mg	7 mg		
4–8 years	12 mg	12 mg		
9–13 years	23 mg	23 mg		
14–18 years	34 mg	34 mg	34 mg	34 mg
19+ years	40 mg	40 mg	40 mg	40 mg

Zinc

90g beef: 3-4 mg
30g pumpkin seeds: 2.2 mg
50g cheddar cheese: 1.5 mg
90g fish: 0.5-1 mg
One egg: 0.6 mg
Half a cup of rice: 0.3-0.7 mg
Half a cup of cooked broccoli: 0.4 mg

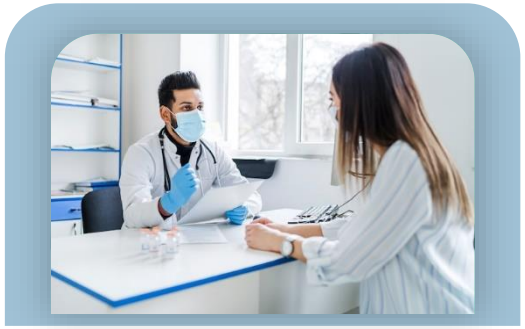
Practical instructions

- **Duration of diabetes**
- **Other comorbidity or secondary condition: IBD, BS, Celiac, vegan**
- **Nutritional:** lack of meat intake, excess phytates (present in legumes, seeds, soy products, and whole grains), or oxalates (found in spinach, okra, nuts, and tea), Alcohol use disorder.
- Iron supplement ≥ 25 mg elemental iron
- **Thiazide diuretics**
- **Serum zinc** (Checking zinc levels each 3-6 months) (No in Infectious, cachectic, hormone therapy conditions)
- **Supplementation (2-6 h- tetracycline, ciprofloxacin)(1 h- Penicillamine)**

*** 5 mg/QOD elemental zinc**

*** 0.5-1 mg/kg (30 mg/d) elemental zinc, 3-4 month**

- **Serum cu: check, if < 70 µg/dl; (For every 30 mg of zinc, 2 mg of copper)**



Thank You

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