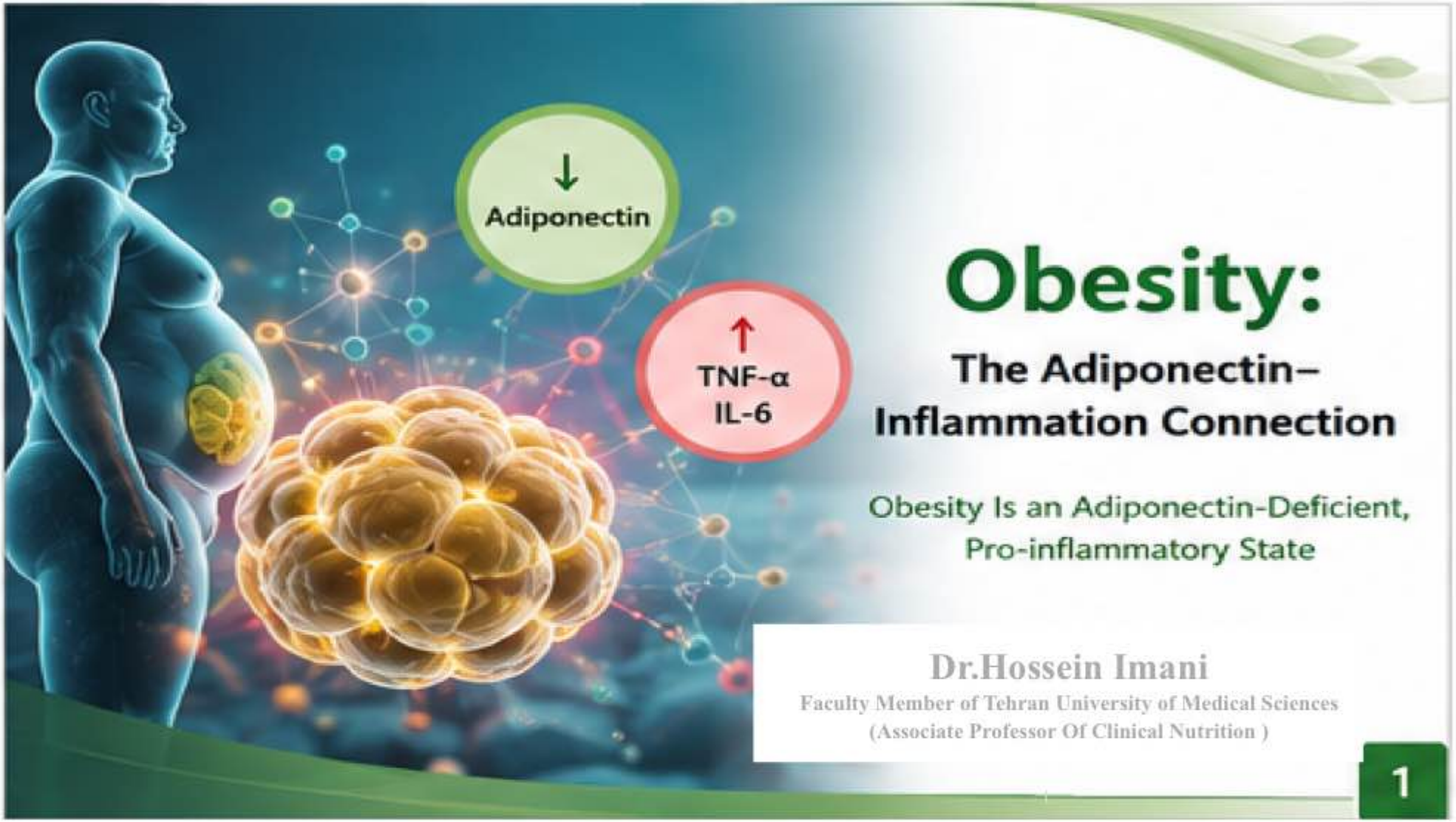


Obesity:

The Adiponectin–Inflammation Connection

Obesity Is an Adiponectin-Deficient, Pro-inflammatory State

Dr.Hossein Imani
Faculty Member of Tehran University of Medical Sciences
(Associate Professor Of Clinical Nutrition)

Obesity: The Adiponectin–Inflammation Connection

OBESITY IS AN ADIPONECTIN-DEFICIENT, PRO-INFLAMMATORY STATE

Visceral adiposity → **TNF-α ↑ / adiponectin ↓** → **Inflammation** → **Insulin resistance** → **Metabolic syndrome**

Obesity is characterized not only by excess adipose tissue, but by adipose tissue dysfunction.

Expansion of visceral adipose tissue is associated with: ↓ adiponectin; ↑ TNF-α; ↑ IL-6; chronic low-grade systemic inflammation; impaired insulin signaling

Therefore, nutritional treatment should target both adiposity and the inflammatory/adipokine phenotype.

Source: Sunita S, et al. Obes Sci Pract. 2026.
Source: Zhuang R, et al. Front Nutr. 2026.

Obesity: The Adiponectin–Inflammation Connection

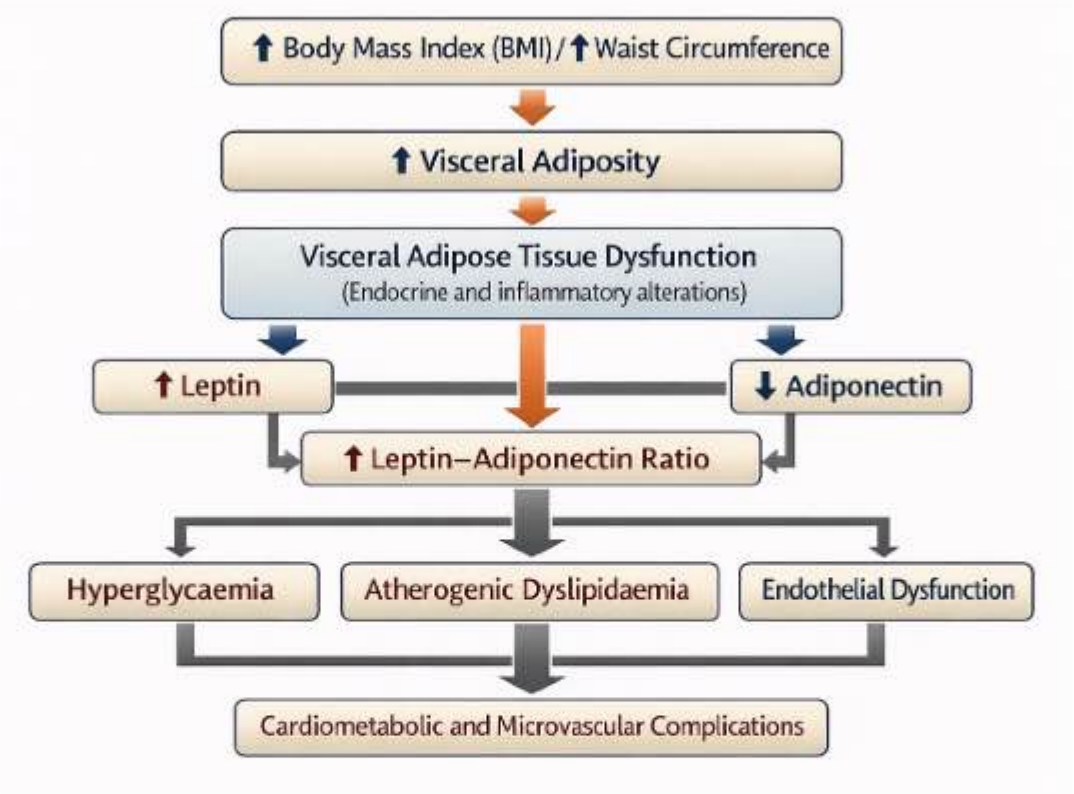
Evidence

- 2026 systematic review/meta-analysis: adiponectin was lower and TNF-α higher in obesity.

2026 exercise network meta-analysis: aerobic exercise + energy restriction reduced TNF-α by SMD −0.48 and IL-6 by SMD −0.35.

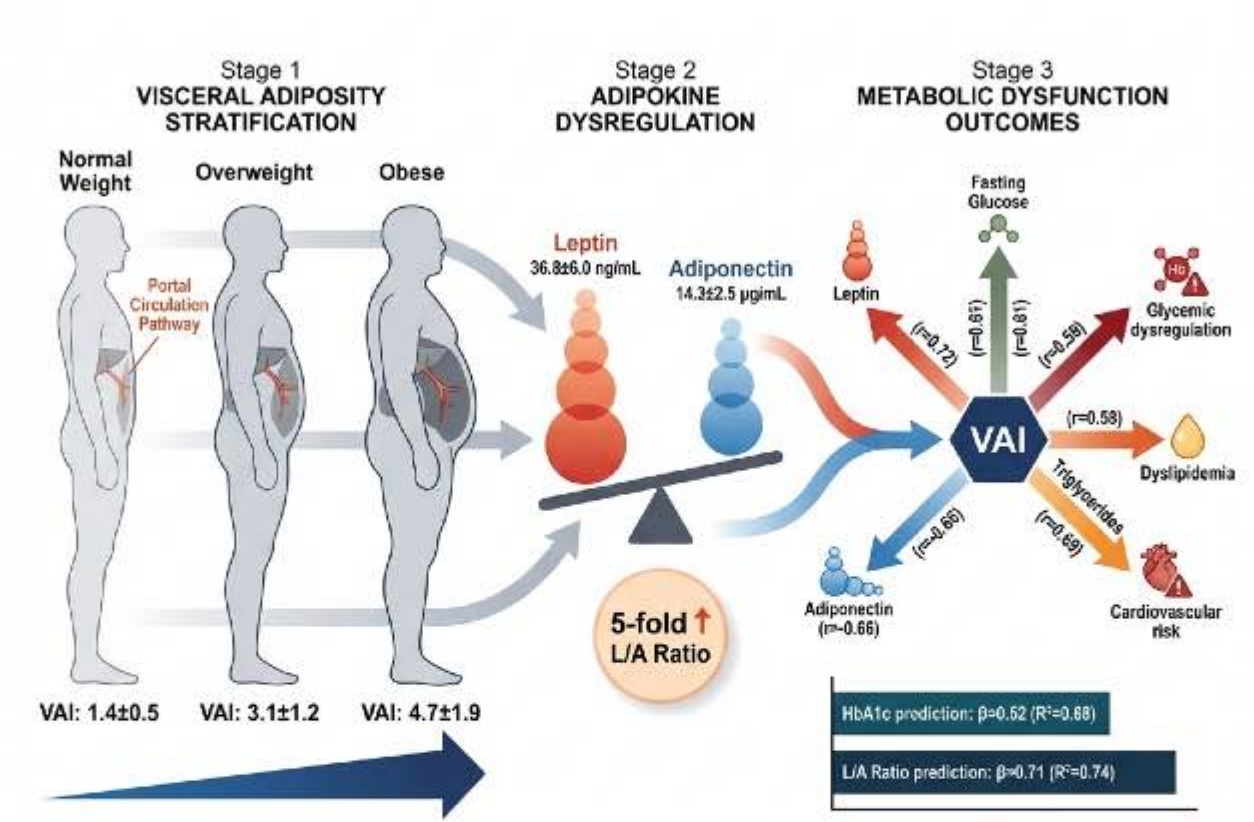
Sunita S, et al. Recent insights into circulating adipokines in obesity: systematic review and meta-analysis. Obes Sci Pract. 2026.
Zhuang R, Xia T, Shao Z, Zhang S. Comparative efficacy of exercise modalities added to energy restriction on inflammatory markers in obesity: a systematic review and network meta-analysis. Front Nutr. 2026. Full text: https://www.frontiersin.org/journals/nutrition/articles/10.3389/fnut.2026.1879890/full

Obesity , Adiponectin and Metabolic syndrome



Shaheer, A. ., Akhtar, S. ., & Jallo, M. . (2026). Integrated evaluation of visceral adiposity indices and markers in adults with type 2 diabetes mellitus: A cross-sectional analytical study. *Biomedical Research and Therapy*, *13*(3), 8426-8436. https://doi.org/10.15419/zze3qf71

Visceral Fat AND Metabolic Syndrome



Shaheer, A. ., Akhtar, S. ., & Jallo, M. . (2026). Integrated evaluation of visceral adiposity indices and markers in adults with type 2 diabetes mellitus: A cross-sectional analytical study. *Biomedical Research and Therapy, 13*(3), 8426-8436. https://doi.org/10.15419/zze3qf71

Why TNF-α Is Clinically Important

TNF-α ↑

- TNF receptor signaling
- activation of inflammatory pathways
- inhibitory phosphorylation of IRS
- i
- ↓
- ↓
- –

Adiponectin ↓

- ↓ AdipoR1/AdipoR2 signaling
- ↓ AMPK activation
- ↓ fatty-acid oxidation
- impaired metabolic flexibility
- further insulin resistance

Nutritional target: reduce the TNF-α-dominant inflammatory environment while restoring adiponectin signaling.

Sunita S, et al. Obes Sci Pract. 2026.
Razmpoosh E, et al. Br J Nutr. 2023.

Practical Inflammatory Assessment in Obesity

Is TNF-α the Best Clinical Inflammatory Marker?

- Mechanistically important in obesity-associated adipose inflammation and insulin resistance.
- However, it is **not the most practical routine biomarker** for clinical monitoring because cytokine assays are relatively expensive and have greater analytical/biological variability.
- Best suited to **research/mechanistic assessment**, rather than routine nutritional follow-up.

- Pischon T, Nimptsch K. Blood-based obesity biomarkers and their relevance for disease risk. Nat Rev Endocrinol. 2026;22:338-355. Full text
- Yang Y, Wang J, Cai J, et al. Association between immune-inflammatory biomarkers (NLR, PLR, SII, SIRI) and obesity in adults: a systematic review and meta-analysis. Int J Obes (Lond). 2026;50:1380-1397. Full text
- Ren Z, Xia T, Shao Z, et al. Comparative efficacy of exercise modalities added to energy restriction on inflammatory markers in obesity: a systematic review and network meta-analysis. Front Nutr. 2026;13:1879890. Full tex

Practical Inflammatory Assessment in Obesity

Marker	What it reflects	Clinical usefulness
hs-CRP	Liver-derived systemic inflammatory response; integrates adipose–IL-6–liver signaling	Best practical choice for systemic low-grade inflammation and longitudinal monitoring
NLR	Neutrophil/lymphocyte balance	Very cheap; useful as an additional systemic inflammation/risk marker
SII	Platelets × neutrophils / lymphocytes	Low-cost composite marker; potentially useful for MetS risk stratification
SIRI	Neutrophils × monocytes / lymphocytes	Low-cost systemic inflammatory index; promising but less clinically established

Use hs-CRP as the practical systemic inflammation marker; use NLR/SII as inexpensive adjuncts; reserve TNF-α/IL-6 mainly for specialized or research assessment.

- Pischon T, Nimptsch K. Blood-based obesity biomarkers and their relevance for disease risk. Nat Rev Endocrinol. 2026;22:338-355. Full text
- Yang Y, Wang J, Cai J, et al. Association between immune-inflammatory biomarkers (NLR, PLR, SII, SIRI) and obesity in adults: a systematic review and meta-analysis. Int J Obes (Lond). 2026;50:1380-1397. Full text
- Ren Z, Xia T, Shao Z, et al. Comparative efficacy of exercise modalities added to energy restriction on inflammatory markers in obesity: a systematic review and network meta-analysis. Front Nutr. 2026;13:1879890. Full tex

Insulin Resistance Is Tissue-Specific

"Insulin resistance" is not a single metabolic defect

HOMA-IR should not be considered equivalent to "whole-body insulin resistance." Insulin resistance can vary across the **liver, skeletal muscle, and adipose tissue**.
A 2026 human study showed that 42% of individuals exhibited discordant patterns between adipose-IR and muscle-IR.

Tissue	What insulin normally does	What changes with insulin resistance	Practical clinical consequence
Skeletal muscle	↑ GLUT4-mediated glucose uptake → ↑ glycogen synthesis	↓ glucose uptake and ↓ glycogen synthesis	Postprandial hyperglycemia; reduced glucose disposal
Liver	Suppresses gluconeogenesis + regulates lipid metabolism	Failure to suppress hepatic glucose production; persistent lipogenesis	↑ fasting glucose, hypertriglyceridemia, MASLD
Adipose tissue	Suppresses lipolysis and promotes appropriate nutrient storage	Inadequate suppression of lipolysis	↑ free fatty acids → hepatic & muscular lipotoxicity
Pancreatic β-cell	Compensatory insulin secretion	Progressive β-cell stress/failure	Transition toward T2D

- Insulin resistance: mechanisms and therapeutic interventions. *Mol Biomed*. 2026.
- Choo YN, Ravi RN, Subramaniyan V. Insulin resistance induced by obesity: mechanisms, metabolic implications and therapeutic approaches. *Mol Biol Rep*. 2026;53:357.

Insulin Resistance Is Tissue-Specific

Key point: Skeletal muscle accounts for appr
disposal in healthy individuals; therefore, mus
determinant of whole-body glucose intoleranc

Clinical interpretation:

A patient may have relatively normal fasting glucose but already have **muscle insulin resistance**, whereas predominant hepatic insulin resistance is more strongly reflected by **fasting hyperglycemia and impaired suppression of hepatic glucose production**.

- Insulin resistance: mechanisms and therapeutic interventions. *Mol Biomed*. 2026.
- Choo YN, Ravi RN, Subramaniyan V. Insulin resistance induced by obesity: mechanisms, metabolic implications and therapeutic approaches. *Mol Biol Rep*. 2026;53:357.

Which Test for Which Type of Insulin Resistance

Test / Marker	Main Tissue / Process Represented	Practical Interpretation
HOMA-IR	Mainly **hepatic / fasting insulin resistance**	Simple and practical marker for **fasting insulin resistance**; useful for screening and follow-up
TyG Index	**Systemic IR; strongly reflects hepatic/metabolic IR**	Highly practical and inexpensive when fasting insulin is unavailable
TG/HDL-C Ratio	**Systemic / metabolic IR**	One of the simplest surrogate markers, particularly when fasting insulin is not available
OGTT	**Dynamic glucose/insulin handling**	More informative than fasting indices when assessing **dynamic glucose metabolism**
Fasting insulin	**Fasting compensatory hyperinsulinemia; mainly hepatic IR context**	Can identify **hyperinsulinemia despite normal glucose**, but should be interpreted cautiously because insulin assays lack standardization.

- Choo YN, Ravi RN, Subramaniyan V. Insulin resistance induced by obesity: mechanisms, metabolic implications and therapeutic approaches. *Mol Biol Rep.* 2026;53:357. Full text
- Meshkat K, Gijbels A, Afman LA, et al. Adipose tissue insulin resistance, not muscle insulin resistance, is associated with impaired metabolic health in humans. *Diabetes Res Clin Pract.* 2026;113480. PubMed
- Mustakin, Arief M, Nurahmi, Kurniawan LB. Diagnostic accuracy of FGF-21 and GDF-15 for predicting insulin resistance: a systematic review and bivariate diagnostic test accuracy meta-analysis. *Diabetes Res Clin Pract.* 2026;113318. PubMed

Nutrition therapy for Hepatic IR

Nutrition strategy

- **Primary target: reduce hepatic fat and energy surplus**, rather than simply lowering fasting glucose.
- **Mediterranean-style dietary pattern:** vegetables, legumes, whole grains, nuts, fish, extra-virgin olive oil; minimize refined carbohydrates, sugar-sweetened beverages, and ultra-processed foods.
- Prefer **low-GI/high-fiber carbohydrate sources** and replace saturated fat with unsaturated fat.

- Comparative efficacy of different exercise interventions on intrahepatic lipid content, glucose homeostasis, and liver function in adults with and without nonalcoholic fatty liver disease: a systematic review with pairwise and network meta-analyses. *Obes Rev*. 2026;27:e70052. PubMed
- Dose-response relationship between exercise and hepatic steatosis: a systematic review with Bayesian network meta-analysis of randomized controlled trials. 2026. PubMed

Nutrition therapy for Hepatic IR

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- Dose-response relationship between exercise and hepatic steatosis: a systematic review with Bayesian network meta-analysis of randomized controlled trials. 2026. PubMed

Nutrition therapy for Hepatic IR

2025 dose–response meta-analysis: 24 RCTs, **961 adults with MASLD** → combined aerobic + resistance exercise ranked highest; hepatic-steatosis benefit plateaued at **630 MET-min/week** and peaked around **850 MET-min/week**.

2026 network meta-analysis: 38 studies, **1,880 adults** → exercise **reduced** intrahepatic lipid (**SMD −0.33**), fasting insulin (**SMD −0.16**), fasting glucose (**−2.27 mg/dL**), ALT (**−3.72 U/L**) and AST (**−3.51 U/L**).

- Comparative efficacy of different exercise interventions on intrahepatic lipid content, glucose homeostasis, and liver function in adults with and without nonalcoholic fatty liver disease: a systematic review with pairwise and network meta-analyses. *Obes Rev*. 2026;27:e70052. PubMed
- Dose-response relationship between exercise and hepatic steatosis: a systematic review with Bayesian network meta-analysis of randomized controlled trials. 2026. PubMed

Nutrition therapy for Skeletal Muscle IR

- Resistance training enhances metabolic and muscular health and reduces systemic inflammation in middle-aged and older adults with type 2 diabetes: a meta-analysis. 2026. PubMed
- Impact of resistance training on cardiometabolic health-related indices in patients with type 2 diabetes and overweight/obesity: a systematic review and meta-analysis of randomised controlled trials. 2025. PubMed

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- Impact of resistance training on cardiometabolic health-related indices in patients with type 2 diabetes and overweight/obesity: a systematic review and meta-analysis of randomised controlled trials. 2025. PubMed

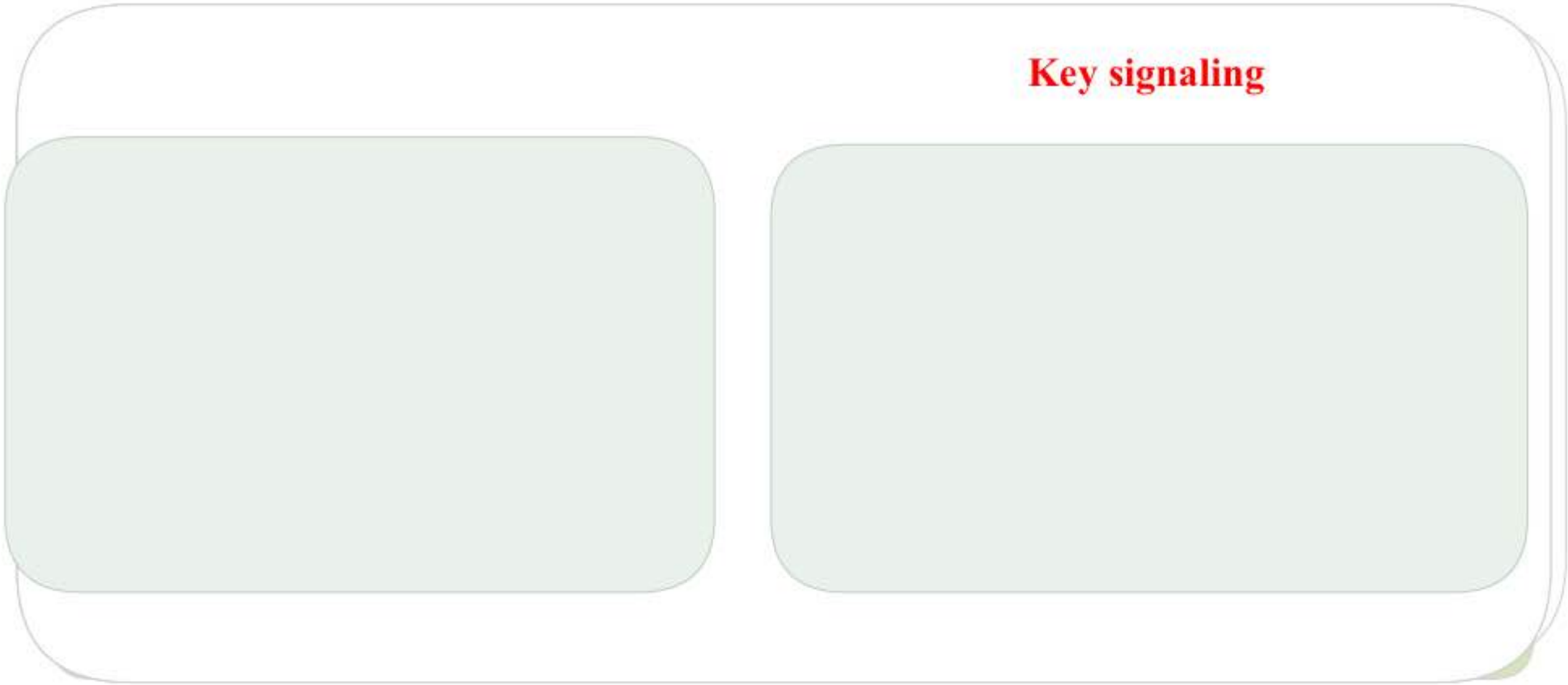
Nutrition therapy for Skeletal Muscle IR

Why resistance training matters during weight loss?

Less muscle → less glucose-disposal capacity.
Therefore, in patients losing weight, especially those at risk of sarcopenia:
Caloric deficit + adequate protein + resistance exercise → fat loss while preserving muscle → better insulin sensitivity.

- Resistance training enhances metabolic and muscular health and reduces systemic inflammation in middle-aged and older adults with type 2 diabetes: a meta-analysis. 2026. PubMed
- Impact of resistance training on cardiometabolic health-related indices in patients with type 2 diabetes and overweight/obesity: a systematic review and meta-analysis of randomised controlled trials. 2025. PubMed

Adiponectin in Skeletal Muscle



- Surina S, Scisciola L, Basilicata MG, et al. Age-related adiponectin resistance in human skeletal muscle dysfunction: in vivo and in vitro evidence. *J Transl Med.* 2026. PubMed
- Prokopidis K, Duque G. Association of intermuscular and intramuscular fat with insulin resistance, type 2 diabetes, and metabolic syndrome: a systematic review. *Clin Nutr.* 2026;64:106727. PubMed

Adiponectin in Skeletal Muscle

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- Prokopidis K, Duque G. Association of intermuscular and intramuscular fat with insulin resistance, type 2 diabetes, and metabolic syndrome: a systematic review. *Clin Nutr.* 2026;64:106727. PubMed

Adiponectin–Liver Axis

- Gastaldelli A, Scoditti E, Macedo MP. Metabolic drivers of MASLD and MASH: from hormonal imbalance to fibrosis. *Diabetologia.* 2026. Full text
- Tontikidou C, et al. Circulating adiponectin in patients with nonalcoholic fatty liver disease-related liver fibrosis: a systematic review and meta-analysis. *J Gastroenterol Hepatol.* 2022. Full text

Adiponectin–Liver Axis

Low adiponectin should not be interpreted simply as "another obesity marker"; it reflects dysfunctional adipose–liver metabolic communication.

nction, impaired lipolysis, insulin resistance and adipokine

d that adiponectin was **lower in patients with fibrosis** in adult/non-morbidly obese subgroups: **SMD −0.23 to −0.30**, depending on the sensitivity analysis

- Gastaldelli A, Scoditti E, Macedo MP. Metabolic drivers of MASLD and MASH: from hormonal imbalance to fibrosis. *Diabetologia*. 2026. Full text
- Tontikidou C, et al. Circulating adiponectin in patients with nonalcoholic fatty liver disease-related liver fibrosis: a systematic review and meta-analysis. *J Gastroenterol Hepatol*. 2022. Full text

• Diabetol Metab Syndr. 2025 May 13;17:152. doi: 10.1186/s13098-025-01721-9

Low fat-diet and circulating adipokines concentrations: a systematic review and meta-analysis of randomized controlled trials

Sepideh Soltani [1], Fatemeh Meshkini [2], Kimia Torabinasab [3], Elham Razmpoosh [4], Omid Toupchian [5], Sheida ...ollahi [5,✉]

Dietary pattern	Adiponectin	Other adipokines	Clinical interpretation
Low-fat vs high-fat diet	**+0.07 ng/mL**	Leptin: **+0.06 ng/mL**; Resistin: **−0.67 ng/mL**	**No significant overall effect**
Low-fat + higher protein	**+1.78 ng/mL**	—	**Most favorable dietary signal for adiponectin**
Female-only studies	**−0.47 ng/mL** (95% CI −0.85 to −0.08; *P*=0.02)	—	Fat restriction alone may **not** increase adiponectin
Sensitivity analysis	**+1.09 ng/mL** (95% CI 0.33–2.14; *P*=0.04)	Resistin: **−0.93 ng/mL**	Effect becomes significant after excluding higher-risk

Practical dietary implication: prioritize a **high-quality, protein-adequate diet with controlled total fat**, rather than simply prescribing an aggressively low-fat diet to increase adiponectin.

• Soltani S, Meshkini F, Torabinasab K, Razmpoosh E, Toupchian O, Zeraattalab-Motlagh S, et al. Low fat-diet and circulating adipokines concentrations: a systematic review and meta-analysis of randomized controlled trials. **Diabetol Metab Syndr. 2025;17:152.** doi:10.1186/s13098-025-01721-9.

Exercise: A Concrete Human RCT

6 WEEKS • 3 × 60 MIN/WEEK AEROBIC–RESISTANCE TRAINING

Adiponectin

3 → 3.97 ng/mL
≈ +15.7%

1 → 5.32 ng/mL
3%; reported +15%

−48%

−30%

Key message: adding dietary quality to exercise produced a stronger anti-inflammatory and adiponectin response than exercise alone.

Source: Makiel K, Targosz A, Kosowski P, Suder A. Int J Mol Sci. 2025;26:9500.

Diet + Exercise Beats Exercise Alone

A Practical High-Protein, Low-GI Strategy

6-week intervention

and fish

Outcome	Exercise only	Exercise + diet
Adiponectin	+15.7%	≈ +18% / reported +15%
IL-6	−30%	−48%
hs-CRP	Not significant	−30%
Body composition	Improved	Greater improvement
Protein	—	+23%
Fiber	—	+50%

Makiel K, Targosz A, Kosowski P, Suder A. Int J Mol Sci. 2025;26:9500.

What About Protein, GI and Fat Quality?

Wu Z, et al. Front Nutr. 2026.
Makiel K, et al. Int J Mol Sci. 2025;26:9500.

Mediterranean Diet: The Core Anti-inflammatory Diet

Mediterranean Diet for Obesity + Metabolic Syndrome

whole grains + nuts + EVOO

poultry

grains + sweets + ultra-processed foods

Practical composition

Total fat	SFA	MUFA	PUFA	Protein	Carbohydrate	EVOO
25–40%	8–10%	10–20%	≈10%	15–30%	40–65%	≈20–40 g/day when replacing other fats

Reyneke GL, Lambert K, Beck EJ. Nutr Rev. 2026;84:1187-1192; lifestyle recommendations for metabolic syndrome.

Mediterranean Diet: Numerical Metabolic Effects

Outcome	Change
Body weight	−1.72 kg
	/m²
	n
	dL
	dL
	/L

across intervention meta-analyses

Reyneke GL, Lambert K, Beck EJ. Nutr Rev. 2026;84:1167-1192.
Mediterranean diet controlled-trial meta-analysis.

Why Mediterranean Diet matters for adiponectin?

MEDINA RCT — 12 weeks, adults with NAFLD:
Mediterranean diet: adiponectin **13.7 → 17.0 µg/mL**, **+24%**, *P*=0.016, **despite no weight loss**; the low-fat diet did not significantly increase adiponectin.

Clinical message:
Do not prescribe "low-fat" simply to increase adiponectin.
The more defensible approach is a **Mediterranean dietary pattern + energy deficit when weight loss is indicated + high dietary fiber + unsaturated fat predominance + minimally processed foods.**

- Keshani M, et al. Mediterranean Diet Reduces Inflammation in Adults: A Systematic Review and Meta-analysis of Randomized Controlled Trials. **Nutr Rev. 2025.** doi:10.1093/nutrit/nuaf213.
- *Dietary Patterns Associated With Anti-inflammatory Effects: An Umbrella Review of Systematic Reviews and Meta-analyses.* **Nutr Rev. 2026;84(6):1167-1185.**
- *Adherence to a Mediterranean diet may improve serum adiponectin in adults with nonalcoholic fatty liver disease: The MEDINA randomized controlled trial.* **J Acad Nutr Diet. 2023**

Food Components With the Best Anti-inflammatory Rationale

P

Food/component	Nutritional rationale
Extra-virgin olive oil	MUFA + polyphenols; characteristic Mediterranean fat source
Fatty fish	EPA/DHA → pro-resolution lipid mediators + possible adiponectin increase
Nuts & seeds	Unsaturated fats, magnesium, fiber and polyphenols
Legumes	Fiber + plant protein + low glycemic carbohydrate
Whole grains	Fiber + micronutrients; replace refined starch
Vegetables & berries/fruit	Polyphenols, carotenoids, vitamin C and fiber
Fermented foods / selected probiotics	Potential gut-microbiota and metabolic-inflammatory effects
Turmeric/curcumin-containing foods	Curcuminoids with anti-inflammatory signaling activity

- *Dietary Patterns Associated With Anti-inflammatory Effects: An Umbrella Review of Systematic Reviews and Meta-analyses.* **Nutr Rev. 2026;84(6):1167-1185.**
- Keshani M, et al. **Nutr Rev. 2025.** doi:10.1093/nutrit/nuaf213.

When Lifestyle Does Not Fully Correct the Metabolic Phenotype

Weight Loss ≠ Complete Metabolic Recovery

Wu Z, et al. Front Nutr. 2026.
Zhuang R, Xia T, Shao Z, Zhang S. Front Nutr. 2026.

Nutritional Modulators of Adiponectin: What Is Clinically Actionable?

n-3

Intervention	Proposed mechanism relevant to adiponectin	Dose / duration studied	Human evidence
Curcumin	Suppresses inflammatory signaling (including NF-κB) and may improve adipocyte function → ↑ **adiponectin** / ↓ **leptin**	Usually **500–1500 mg/day curcuminoids**, ~8–12 wk; bioavailable formulations may require lower doses	**Adiponectin ↑ SMD 0.86** (95% CI 0.33–1.39) across 13 RCTs
Lactobacillus probiotics	Gut microbiota modulation → reduced metabolic inflammation and improved adipose signaling	Variable strains/doses; studies generally **<10 to >10 billion CFU/day**, several weeks–months	**Adiponectin +0.71 µg/mL** (95% CI 0.22–1.20)

- Denzad MJ, et al. The effect of curcumin supplementation on circulating adiponectin and leptin concentration in adults: a GRADE-assessed systematic review and meta-analysis of randomised controlled trials. **Br J Nutr. 2024;131:1050-1062.**
- Lele JAJ, et al. Probiotic *Lactobacillus* sp. as a strategy for modulation of non-comorbid obesity: a systematic meta-analysis and GRADE assessment of randomized controlled trials. **Narra J. 2025;5:e1630.**
- Kim J, et al. The benefits of ω-3 supplementation depend on adiponectin basal level and adiponectin increase after the supplementation: a randomized clinical trial. **Nutrition. 2016;32:1061-1066.**
- Dastani M, et al. Can vitamin D be considered an adiponectin secretagogue? A systematic review and meta-analysis. **J Steroid Biochem Mol Biol. 2021;211:105896.**

Nutritional Modulators of Adiponectin: What Is Clinically Actionable?

Intervention	Proposed mechanism relevant to adiponectin	Dose / duration studied	Human evidence
n-3 PUFA (EPA+DHA)	Improves lipid handling and inflammatory signaling; adiponectin appears to mediate part of the cardiometabolic response	**~2–3 g/day fish oil** in clinical trials; ~2 months in one RCT	Increased adiponectin; magnitude depends on baseline adiponectin
Vitamin D	Possible adipocyte/adiponectin regulation, particularly when deficiency/diabetes is present	**50,000 IU/week × 8 wk** studied in deficient T2D	Evidence inconsistent; **not recommended solely to raise adiponectin**

Clinical priority: Correct obesity/visceral adiposity and dietary quality first; supplements are adjuncts, not substitutes for weight loss and dietary treatment.

- Dehzad MJ, et al. The effect of curcumin supplementation on circulating adiponectin and leptin concentration in adults: a GRADE-assessed systematic review and meta-analysis of randomised controlled trials. **Br J Nutr. 2024;131:1050-1062.**
- Lele JAJ, et al. Probiotic *Lactobacillus* sp. as a strategy for modulation of non-comorbid obesity: a systematic meta-analysis and GRADE assessment of randomized controlled trials. **Narra J. 2025;5:e1630.**
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- Dastani M, et al. Can vitamin D be considered an adiponectin secretagogue? A systematic review and meta-analysis. **J Steroid Biochem Mol Biol. 2021;211:105896.**

Nutraceuticals That May Increase Adiponectin

Not Every "Anti-inflammatory" Supplement Is an Adiponectin Agonist

		weeks
		−29.3% vs −8.6%
2 g/day, 8 weeks × 2 periods; 4-week washout	Cohen's d=0.88	TNF-α 29.8 vs 36.1 pg/mL; AdipoR1 +0.77-fold; body weight d=0.60

Clinical position: Promising adjunct — not first-line obesity treatment.

Mahdavi R, et al. J Herbal Med. 2016;6:67-72.
Razmpoosh E, et al. Br J Nutr. 2023;129:627-636.

Adiponectin Receptor Agonists: A Different Strategy

Increase Adiponectin vs Activate Adiponectin Signaling

Adiponectin secretagogue
↑ endogenous adiponectin

Adiponectin receptor agonist
Directly activates AdipoR1/AdipoR2

PEG-BHD1028 mechanistic/preclinical study: PMC7830917; receptor signaling and mitochondrial pathways as described in the provided source.

Deglusterol: What Is It and Where Does It Fit?

Deglusterol — A Peptide Approach to Insulin Resistance

ited

140% increase in circulating adiponectin in humans.

EFSA Journal. 2026; nonapeptide–pentapeptide mixture assessment.
PubMed 35148196.

Deglusterol Directly Upregulates Adiponectin Expression: The Mechanistic Evidence

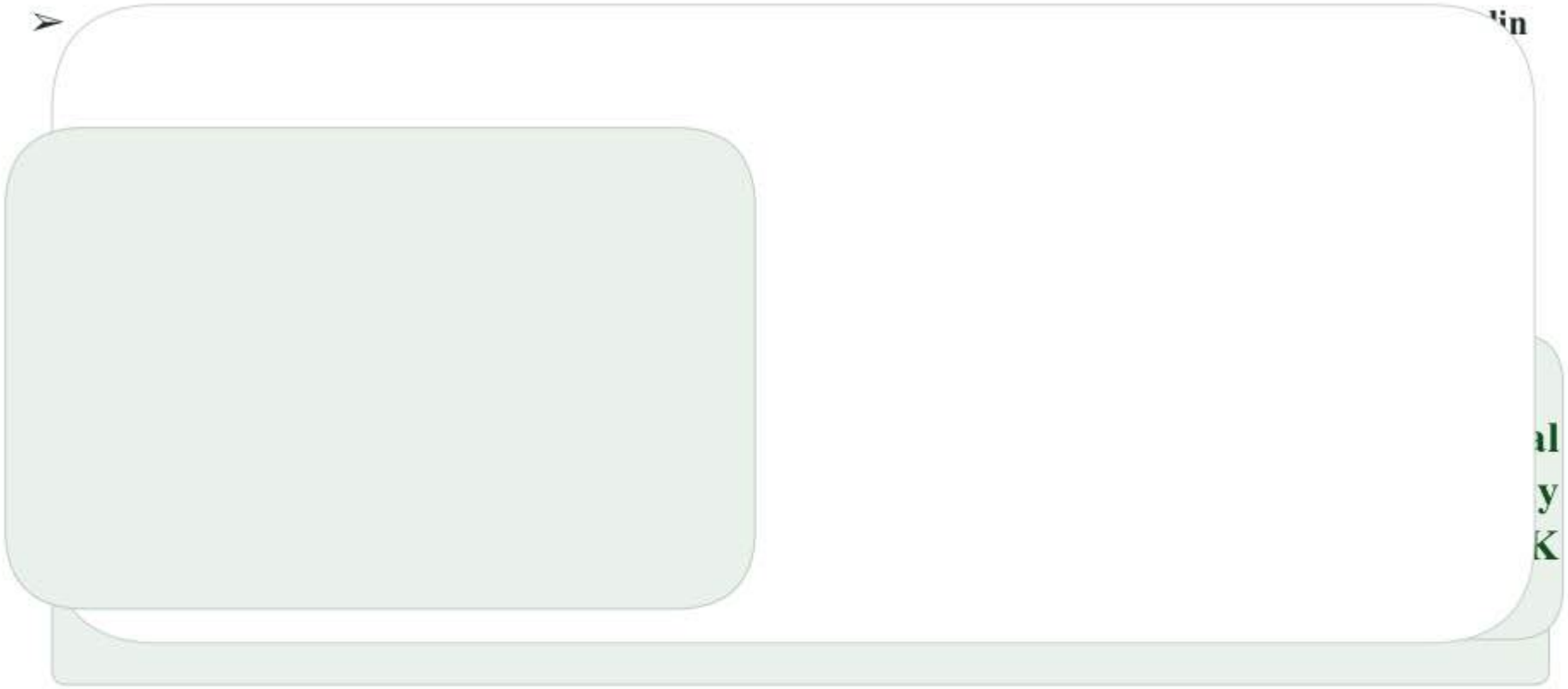
- **Deglusterol treatment results in a significant 140% increase in adiponectin mRNA expression.**
- **This adiponectin elevation is mechanistically linked to the AMPK pathway:**

- Deglusterol induces AMPK phosphorylation .

- AMPK activation, in turn, enhances adiponectin signaling and insulin sensitivity .

Kim EM, Kim SS, Chung YJ. Lowering of Blood Glucose Levels with the Peptide Mixture Deglusterol in In Vitro and In Vivo Models. **J Med Food**. 2022;25(2):166-176. doi:10.1089/jmf.2021.K.0159

Deglusterol Directly Upregulates Adiponectin Expression: The Mechanistic Evidence



Kim EM, Kim SS, Chung YJ. Lowering of Blood Glucose Levels with the Peptide Mixture Deglusterol in In Vitro and In Vivo Models. **J Med Food**. 2022;25(2):166-176. doi:10.1089/jmf.2021.K.0159

Deglusterol: Dose & Safety — What Should You Say?

Dose

Scientifically defensible wording:
“Studied dose: 30 mg/day × 12 weeks. EFSA 2026 concluded safety up to 14 mg/day for adults under its assessed conditions.”

EFSA Journal. 2026;10098. Safety assessment of nonapeptide–pentapeptide mixture as a novel food.

Deglusterol (ProGsterol) Improves Glycemic Control and Insulin Sensitivity

12-Week Human Study RCT

I for diabetes/prediabetes

I 9 | **Duration:** 12 weeks

	Deglusterol	Placebo
[illegible]	**−6.7 ± 8.6 mg/dL**	—
HbA1c	**−0.31 ± 0.26%**	−0.01 ± 0.24%
Fasting insulin	**−1.03 ± 2.69 µU/mL**	+1.89 ± 4.56 µU/mL
HOMA-IR	**−0.43 ± 0.94**	+0.44 ± 1.11
C-peptide	**−0.12 ± 0.51 ng/mL**	+0.24 ± 0.40 ng/mL

Deglusterol supplementation was associated with improved fasting glycemia, HbA1c, insulin levels and HOMA-IR, suggesting improved insulin sensitivity after 12 weeks.

- Kim EM, Kim SS, Chung YJ. Lowering of Blood Glucose Levels with the Peptide Mixture Deglusterol in In Vitro and In Vivo Models. **J Med Food**. 2022;25(2):166-176. doi:10.1089/jmf.2021.K.0159

The Final Clinical Algorithm

	Fat: replace SFA with MU
4. Exercise	Aerobic + resistance → a
5. If metabolic inflammation	
6–7. Emerging strategies	AdipoR agonism / emerging peptides: PEG-BHD1028 and Deglusterol remain emerging; not yet established anti-obesity/adiponectin-raising therapies.

Sunita S, et al. 2026.
Zhuang R, et al. 2026.
Reyneke GL, et al. 2026.
Lapuerta P, Kim BB. 2026.
EFSA 2026.

Which Intervention Gives the Best Adiponectin–Inflammation Response?

Intervention	Duration	Adipo
Aerobic-resistance exercise	6 wk	+15
Exercise + high-protein/low-GI diet	6 wk	≈ +15
Mediterranean diet	≥12 wk	+0.59 to +
Low-GI/LGL diet	RCTs, variable	No signific
Nigella sativa + calorie restriction	8 wk	+87.5% v
Deglusterol	12 wk human study	imp

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Maleki et al. 2025.
Reynaka et al. 2024.
Wu et al. 2020.
Malahavi et al. 2016.
Razmpoosh et al. 2025.
Laprairie & Kim 2026.

Thank you for your attention