Peptide Perspectives™

BEYOND GLP-1

Peptide & Supplement Combinations for Metabolic Health

A BROADER METABOLIC APPROACH

GLP-1 drugs are powerful tools for glucose and weight management, but metabolic health goes beyond appetite. A multi-pathway approach can also support insulin sensitivity, mitochondrial function, muscle health, liver function, and inflammation.

- Glucose control (e.g., HbA1c, CGM)
- Healthy body composition (fat vs. muscle)
- Metabolic flexibility (fuel use and energy)
- Mitochondrial health (cellular energy)
- Liver health (e.g., fatty liver support)
- Lower chronic inflammation
- Cardiovascular and kidney health

KEY BIOLOGICAL PATHWAYS FOR METABOLIC HEALTH

1. GLP-1 / GIP / AMYLIN (SATIETY & PANCREAS)



- Regulate appetite and fullness
- Enhance insulin release (glucose-dependent)
- Slow gastric emptying
- Improve post-meal glucose control

2. INSULIN SENSITIVITY & METABOLIC FLEXIBILITY



- Improve how muscle and liver use glucose and fat for energy
- Support healthier body composition
- May reduce liver fat (e.g., MASLD)
- Enhance overall metabolic efficiency

3. MITOCHONDRIA, ATP & CARDIOLIPIN



- Support cellular energy (ATP)
- Maintain cardiolipin (mitochondrial membrane health)
- Reduce mitochondrial stress
- May improve exercise capacity and fatigue

4. INFLAMMATION & STRESS SIGNALING



- Modulate inflammatory pathways (e.g., NF-κB, IL-6, TNF-α)
- Support immune balance
- May improve insulin sensitivity
- Influence recovery and metabolic resilience

RESEARCHED PEPTIDE STACKS & DOSING CONTEXT

1. SEMAGLUTIDE + CAGRILINTIDE (CagriSema)

- **What it is:** Dual incretin + amylin analog combination studied for greater weight loss and metabolic effects.
- **Evidence:** Phase 3 clinical data (e.g., REDEFINE trials) showed greater A1c reduction and weight loss than either

STUDIED DOSE (PHASE 3)

Semaglutide: 2.4 mg once weekly
Cagrilintide: 2.4 mg once weekly (after stepwise escalation)

Investigational combination. Not an approved DIY mixed-vial regimen.

2. TIRZEPATIDE + SS-31 (Conceptual)

- **What it is:** GLP-1/GIP dual agonist (tirzepatide) with a mitochondrial peptide (SS-31).
- **Evidence:** Tirzepatide is FDA-approved for diabetes and weight management. No controlled trials of the combination with SS-31, and no validated stack dose.

LABELED / APPROVED DOSE

Tirzepatide: Start 2.5 mg once weekly for 4 weeks, then 5 mg weekly; may increase by 2.5 mg increments ≥ 4 weeks apart (approved indications).
SS-31: 40 mg subcutaneous daily (FDA-approved only for eligible Barth syndrome patients).

3. MOTS-c + SS-31

- **What it is:** Mitochondrial peptides that may support energy, metabolic flexibility, and cellular stress resistance.
- **Evidence:** Preclinical (animal and cellular) data suggest complementary mitochondrial benefits. No validated human combination dose.

COMMUNITY-REPORTED CONTEXT (NOT VALIDATED)

MOTS-c: ~5–10 mg, 2–3×/week
SS-31: ~25 mg daily (Elamipretide)

Experimental use; no proven human regimen.

4. MOTS-c + HUMANIN (Experimental)

- **What it is:** Mitochondrial-derived peptides studied for metabolic, cellular protection, and longevity pathways.
- **Evidence:** Preclinical research suggests benefits for insulin sensitivity, stress resistance, and mitochondrial function. No validated human dose or humanin regimen.

COMMUNITY-REPORTED CONTEXT (NOT VALIDATED)

MOTS-c: ~5–10 mg, 2–3×/week
Humanin: No established dose (research use only).

Experimental; human data are limited.

5. MOTS-c + HUMANIN + SS-31

- **What it is:** A broader mitochondrial stack targeting energy, resilience, and metabolic health.
- **Evidence:** Theoretical and preclinical rationale only. No human trials or verified dosing for the combination.

EXPERIMENTAL CONCEPT (No Verified Regimen)

MOTS-c: ~5–10 mg, 2–3×/week
Humanin: No established dose
SS-31: ~2–5 mg daily

Highly experimental; research only.

SUPPORTIVE SUPPLEMENTS & NUTRITIONAL STRATEGIES

Creatine Monohydrate



- 3–5 g/day

Supports strength, muscle and metabolic health.

Psyllium / Soluble Fiber



- No universal dose (e.g., 5–10 g/day is commonly used).

Supports satiety, weight and glucose.

Protein



- Individualized (≈1.2–1.6 g/kg/day depending on goals).

Supports muscle and metabolic health.

Berberine



- No standard adjunct dose (often 500 mg 1–2×/day in studies).

May support glucose and lipid metabolism. Check for drug interactions.

Magnesium



- If deficient (≈200–400 mg/day, e.g., glycinate).

Supports glucose metabolism, sleep, and muscle function.

Omega-3s (EPA/DHA)



- ≈1–4 g/day (especially for high triglycerides).

Supports cardiometabolic health.

Alpha-Lipoic Acid (ALA)



- ≈300–600 mg/day

Studied for diabetic neuropathy and oxidative stress. Not proven to improve HbA1c.

EVIDENCE HIERARCHY (HOW TO INTERPRET THE DATA)

- **Phase 3 Clinical Trial:** High-quality human evidence (e.g., CagriSema).
- **FDA-Approved (Separate Indication):** Proven use, but not for the specific stack (e.g., tirzepatide, SS-31).
- **Early / Preclinical:** Animal or cellular data showing potential (e.g., MOTS-c, humanin stacks).
- **Theoretical / No Trials:** Plausible rationale, but no human combination data.

MEANINGFUL OUTCOMES TO TRACK

- **HbA1c** (longer-term glucose control)
- **CGM metrics** (time in range, variability)
- **Body composition** (fat mass vs. lean mass)
- **Muscle function** (strength, power, recovery)
- **Exercise capacity** (endurance and performance)
- **Adverse events** (GI, tolerability, other)
- **Longer-term risks and benefits** (cardiovascular and kidney outcomes)



THE FOUNDATION STILL MATTERS



- **Resistance training:** 2–3× per week (maintain & build muscle)
- **Aerobic activity:** 150+ minutes/week (e.g., walking, cycling, zone 2)
- **Adequate protein:** individualized intake (≈1.2–1.6 g/kg/day)
- **Quality sleep:** 7–9 hours/night (hormones, appetite, insulin sensitivity)

COMPLEMENTARY PATHWAYS DO NOT PROVE COMBINATION BENEFIT. RESEARCH DOSING IS NOT RECOMMENDATION.

Educational research overview | November 2026 | Not medical advice