CLEAN PEPTIDES

MOTS-c Dosage Guide

Mitochondrial-derived peptide — AMPK activation, insulin sensitivity, metabolic optimization, exercise-mimetic research and longevity.

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What Is MOTS-c?

MOTS-c is a 16-amino-acid mitochondria-derived peptide (MDP) discovered in 2015 (Dr. Changhan David Lee, USC). Encoded in the mitochondrial genome's 12S rRNA gene, it acts as a retrograde signaling molecule — translocating to the nucleus under metabolic stress to regulate gene expression. Its primary target is AMPK, the master metabolic energy sensor also activated by exercise, caloric restriction and metformin. This has led to it being described as an "exercise mimetic."

Dosing derives from animal studies, early human research and community protocols.

Key Characteristics

- **Mitochondria-derived peptide** — encoded in mitochondrial DNA (12S rRNA gene).
- **16-amino-acid peptide** — sequence MRWQEMGYIFYPRKLR.
- **AMPK activator** — same pathway as exercise and metformin.
- **Retrograde signaling** — translocates cytoplasm → nucleus under metabolic stress.
- **Exercise-mimetic properties** — enhanced glucose metabolism, fatty-acid oxidation, insulin sensitivity.
- **Age-related decline** — endogenous levels fall with age, correlating with metabolic dysfunction.

How Dosage Is Determined

Relatively recent (2015); the 5–10 mg daily range derives from animal dose extrapolation, early human research and community experience. Landmark studies (Lee et al., 2015) showed prevention of age-dependent insulin resistance and diet-induced obesity in mice. **Strength of evidence: emerging.**

Standard Dosage Ranges

Level	Dose/Injection	Frequency	Weekly Total	Notes
Beginner	5 mg	3x per week	15 mg	Assess tolerance; lower-cost entry
Intermediate	5 mg	Daily (7x/week)	35 mg	Most common community dosing
Advanced	10 mg	Daily or 5x/week	50–70 mg	Targeted metabolic goals

Dosed in milligrams, not micrograms — a standard 5 mg dose is 5,000 mcg. Morning administration preferred; fasting not required; some inject 30–60 min pre-exercise.

AMPK Activation & Metabolic Pathway

MOTS-c activates AMPK (the cellular energy sensor), shifting cells from anabolic to catabolic mode. Effects: enhanced glucose uptake (GLUT4), improved insulin sensitivity, fatty-acid oxidation (ACC inhibition), mitochondrial biogenesis (PGC-1α), cellular stress-response activation, and folate-cycle regulation. It complements — not replaces — exercise-induced AMPK activation.

Reconstitution & Dosing (with the supplied 3 ml)

Every Clean Peptides vial ships with **3 ml of bacteriostatic water** (0.9% benzyl alcohol). All figures below assume you reconstitute with the **full 3 ml**. On a standard U-100 insulin syringe, **100 units = 1 ml**.

Quick formula: concentration = vial strength ÷ 3 ml, and **units to draw = dose (mg) × 300 ÷ vial strength (mg)**.

How to reconstitute

1. **Wash your hands** and lay out the vial, the 3 ml bacteriostatic water, an insulin syringe and alcohol swabs on a clean surface.
2. **Flip off the caps** and swab both rubber stoppers with alcohol; let them air-dry 10–15 seconds.
3. **Draw the full 3 ml** of bacteriostatic water (in three 1 ml passes with an insulin syringe, or in one pass with a 3 ml syringe).
4. **Add the water slowly**, angling the needle so it runs down the inside glass wall — never squirt it directly onto the powder cake.
5. **Dissolve gently** — let the vial sit 1–2 minutes, then swirl or roll it between your palms until the solution is clear. Never shake.
6. **Label and refrigerate** at 2–8 °C. Resulting concentration: 10 mg → 3.33 mg/mL.

Storage: unreconstituted powder refrigerated (2–8 °C); reconstituted solution refrigerated and used within 28–30 days; do not freeze; protect from light and heat.

Draw volumes with 3 ml — MOTS-c

Vial (Clean Peptides)	Concentration	5 mg	10 mg
10 mg	3.33 mg/mL	150 u*	300 u*

* This volume exceeds the 100-unit (1 mL) capacity of a standard insulin syringe — split it into two injections, or draw it with a 3 mL syringe.

Dosage by Goal

- **Metabolic optimization & insulin sensitivity:** 5 mg SubQ daily; 8 wk on, 4 wk off. Monitor fasting glucose/insulin, HbA1c, HOMA-IR.
- **Fat loss & body composition:** 5–10 mg daily or 5x/week; 6–8 wk on, 4 wk off. Combine with exercise and caloric management.
- **Exercise performance & endurance:** 5 mg daily or on training days; 30–60 min pre-exercise; 4–8

wk.
- **Longevity & anti-aging:** 5 mg 3–5x/week; 8 wk on, 4 wk off, repeated.

All goals benefit from concurrent exercise (synergistic AMPK activation).

Cycling Protocols

Protocol	On-Cycle	Off-Cycle	Best For
Standard	4–8 weeks daily	4 weeks	Most users
Extended	8–12 weeks daily	4–6 weeks	Maximum metabolic adaptation
Maintenance	Continuous, 3x/wk	None	Long-term longevity
Training-Aligned	Training days only	Rest days	Exercise-performance focus

Cycling is precautionary (no documented desensitization) — it aids assessment and cost management.

Stacking Protocols

- **MOTS-c + 5-Amino-1MQ** — metabolic synergy (AMPK + NNMT inhibition).
- **MOTS-c + GLP-1 agonist** (Tirzepatide/Semaglutide) — weight management.
- **MOTS-c + AOD-9604** — fat loss (300 mcg SubQ daily).
- **MOTS-c + Tesamorelin** — metabolic & body composition.

Introduce compounds one at a time to attribute effects.

Safety, Side Effects & Contraindications

Limited published human safety data; favorable animal profile; generally well-tolerated.

Mild, self-limiting: injection-site reactions, occasional GI discomfort, rare headache, transient fatigue. **Theoretical:** blood-glucose changes (monitor if diabetic or on glucose-lowering meds). No cortisol/prolactin/appetite effects, no water retention.

Contraindications: active cancer or history of cancer; pregnancy/breastfeeding; type 1/insulin-dependent diabetes; concurrent glucose-lowering meds (hypoglycemia risk); severe hepatic/renal impairment.

Monitor: fasting glucose, fasting insulin, HbA1c, HOMA-IR, lipid panel, body composition. Not FDA-approved.

Common Mistakes

- Treating MOTS-c as a direct fat burner (it optimizes metabolism over time).
- Using oral administration (zero bioavailability — must inject SubQ).
- Expecting immediate results (2–4 weeks typical).
- Not combining with exercise and nutrition.
- Storing reconstituted MOTS-c at room temperature.
- Exceeding 10 mg daily (no proportional benefit).
- Neglecting metabolic blood work.
- Stacking too many metabolic compounds at once.

Key Takeaways

- Mitochondria-derived peptide acting via nuclear retrograde signaling.
- Standard dose 5–10 mg SubQ daily or 3–5x/week (milligrams, not micrograms).
- Primary mechanism: AMPK activation (like exercise, fasting, metformin).
- Best paired with exercise; top stacks 5-Amino-1MQ, GLP-1 agonists, AOD-9604.
- Cycle 4–8 wk on / 4 wk off; mild side effects; not FDA-approved (emerging evidence).

References

1. Lee C, Zeng J, Drew BG, et al. "MOTS-c promotes metabolic homeostasis and reduces obesity and insulin resistance." *Cell Metab.* 2015;21(3):443-454.
2. Lee C, Kim KH, Cohen P. "MOTS-c: a novel mitochondrial-derived peptide regulating muscle and fat metabolism." *Free Radic Biol Med.* 2016;100:182-187.
3. Kim KH, et al. "MOTS-c translocates to the nucleus to regulate gene expression under metabolic stress." *Cell Metab.* 2018;28(3):516-524.
4. Reynolds JC, et al. "MOTS-c is an exercise-induced regulator of age-dependent physical decline." *Nat Commun.* 2021;12(1):470.
5. Yin X, et al. "MOTS-c relieves hyperglycemia and insulin resistance in gestational diabetes." *Pharmacol Res.* 2022;175:105987.