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NARRATIVE REVIEW

Preclinical and Human Evidence for MOTS c

OC Wellness Clinical Education

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ARTICLE TYPE	SOURCES	HUMAN STUDIES	U.S. STATUS
Narrative review	48 · PMID linked	18 observational; 0 interventional	Not FDA approved

ABSTRACT

Background. MOTS c (mitochondrial open reading frame of the 12S rRNA type c) is a 16 amino acid mitochondrial derived peptide identified in 2015. It activates AMP activated protein kinase (AMPK) through the folate cycle and, under stress, translocates to the nucleus to regulate antioxidant response genes. Clinicians increasingly field questions about compounded MOTS c, and in October 2026 a federal enforcement discretion policy began to permit its compounding. This review appraises the published evidence.

Methods. A narrative review was conducted in Europe PMC and PubMed through 3 November 2026, supplemented by regulatory and anti doping records obtained directly from the FDA, the Department of Health and Human Services, and the World Anti Doping Agency. Studies were summarized with species, model, dose, route and outcome stated as reported. No formal risk of bias scoring was applied.

Results. The administration evidence is almost entirely rodent and cellular, where MOTS c improved insulin sensitivity, reduced diet induced obesity, enhanced exercise capacity, attenuated bone loss, and protected the myocardium, largely through AMPK. The human evidence comprises studies that measured endogenous circulating or muscle MOTS c, observationally or after exercise, lipid infusion or metformin, and genetic studies of the m.1382A>C (K14Q) variant. No published study has administered MOTS c to humans, and no human pharmacokinetic data exist. One peptide analogue, CB4211, entered a company phase 1 trial without peer reviewed results.

Conclusions. MOTS c is a biologically plausible metabolic regulator supported by consistent preclinical data and coherent human associations, but its efficacy and safety as an administered agent in people are untested. Prescribers should weigh the absence of human administration data against patient demand and the temporary regulatory pathway.

Keywords: MOTS c; mitochondrial derived peptides; AMPK; insulin sensitivity; compounding; enforcement discretion

1 Introduction

Mitochondria were long regarded as effector organelles of energy production, but the discovery of bioactive peptides encoded within the mitochondrial genome reframed them as signaling hubs. The first such peptide, humanin, was followed in 2015 by MOTS c, a 16 amino acid peptide translated from a short open reading frame within the mitochondrial 12S ribosomal RNA, which Lee and colleagues reported to regulate insulin sensitivity and metabolic homeostasis in mice.[1] MOTS c belongs to a small family of mitochondrial derived peptides whose circulating levels decline with age and that have been proposed as mediators of metabolic health and longevity.[2]

The peptide has since moved from the laboratory into direct to patient marketing, where it is promoted for weight loss, metabolic health, physical performance and healthy aging. Narrative reviews aimed at sports medicine and aesthetic practice now place MOTS c among a group of unapproved peptides sold largely outside regulatory oversight, with favourable animal data but scarce human evidence.[3,4] Clinicians at wellness and regenerative medicine practices are therefore asked about MOTS c by patients who have already encountered it online.

This review summarizes the published preclinical and clinical evidence for MOTS c, distinguishes interventional from observational data, and sets out the current United States regulatory and anti doping status, so that a prescriber can frame an evidence based discussion with a patient. It does not recommend a dose, a protocol or a candidate population.

2 Methods

2.1 Search strategy

Europe PMC, which mirrors PubMed, was searched through 3 November 2026 using the terms MOTS c, MOTSc, and mitochondrial open reading frame of the 12S rRNA, combined with filters for human studies, randomized controlled trials, clinical trials, the m.1382A>C and K14Q variants,

pharmacokinetics, doping, and the analogue CB4211. Title and broad text queries returned 177 and 737 records respectively. Reference lists of retrieved reviews were screened for additional primary studies.

2.2 Selection and reporting

Primary studies reporting administration of MOTS c in any species, observational studies of endogenous MOTS c in humans, genetic studies of MOTS c variants, pharmacokinetic reports, and recent narrative reviews were eligible. Studies were read in abstract, and in open access full text where available, and were summarized with species, model, sample size, dose, route, duration and principal outcome as stated in the source. Findings were not carried beyond what each abstract or full text supported. One retracted article on bone fracture healing was identified and excluded. Several hundred records were screened across the queries, and 48 sources are cited.

2.3 Regulatory sources and limitations

Regulatory and anti doping records were obtained directly from the FDA compounding pages and advisory committee materials, the Department of Health and Human Services enforcement discretion policy and its Appendix B, and the World Anti Doping Agency 2026 Prohibited List. This is a narrative review, not a systematic review. No formal risk of bias instrument was applied, no meta analysis was performed, and publication bias and the concentration of early work within a single research group are acknowledged as limitations.

3 Structure, origin and pharmacology

3.1 Structure and origin

MOTS c is a 16 amino acid peptide with the sequence Met Arg Trp Gln Glu Met Gly Tyr Ile Phe Tyr Pro Arg Lys Leu Arg. The free base has a molecular formula of C101H152N28O22S2 and a molecular weight of 2174.6 g/mol; the acetate salt has a molecular weight of 2234.64 g/mol.[5] The peptide is encoded by a 51 base pair short open reading frame within the mitochondrial 12S rRNA and is translated in the cytoplasm, since the mitochondrial genetic code yields tandem start and stop codons; its sequence is highly conserved across species, particularly the first 11 residues.[1] MOTS c is detectable in skeletal muscle, heart, brain and in the systemic circulation of humans and rodents.[56]

3.2 Mechanisms

In cellular and murine models, MOTS c inhibits the folate cycle and the tethered de novo purine biosynthesis pathway, producing an accumulation of 5 aminoimidazole 4 carboxamide ribonucleotide (AICAR), a physiological activator of AMPK; downstream effects include enhanced glucose uptake in skeletal muscle and, in cultured cells, increased fatty acid oxidation.[1] Under glucose restriction and other metabolic stress, MOTS c translocates to the nucleus and regulates genes bearing antioxidant response elements, interacting with the transcription factor NFE2L2 (NRF2).[7] MOTS c has been proposed as an exercise mimetic because it activates AMPK, a regulator of the exercise response, and its benefits in high fat fed mice mirror those of exercise.[6] The FDA noted in its 2026 evaluation that the molecular target through which MOTS c acts remains unknown, which limits prediction of its tissue effects.[5]

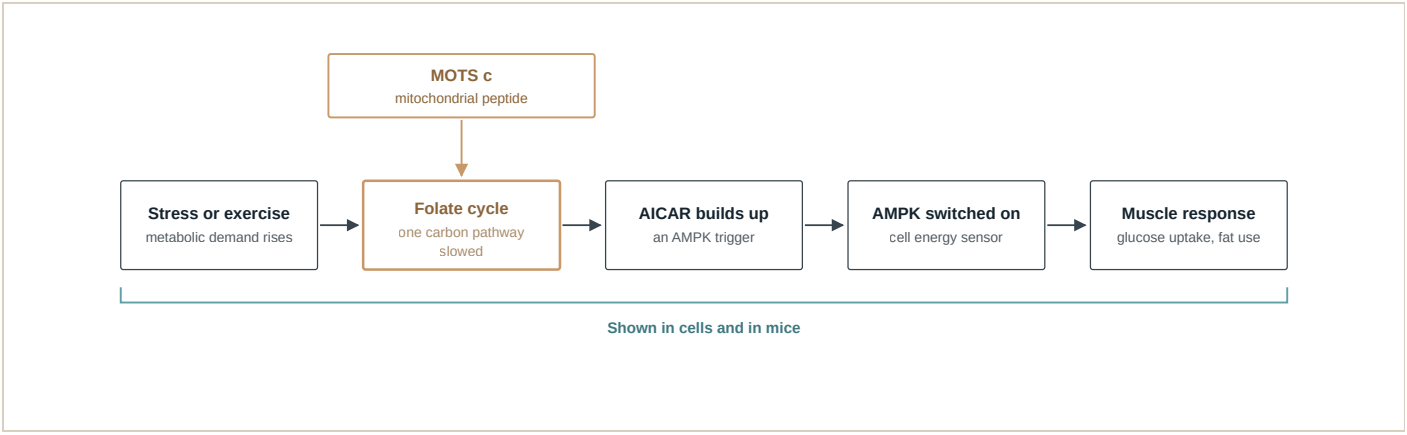


Figure 1. In cells and mice, MOTS c works through the AMPK energy pathway. MOTS c slows the folate cycle, which lets AICAR accumulate and switch on AMPK, the cell's energy sensor, in skeletal muscle.[1] Under stress it can also enter the nucleus and help turn on antioxidant genes.[7] Whether either chain works the same way in the human body has not been measured.

4 Preclinical evidence

4.1 Glucose and lipid metabolism

In the founding study, male CD 1 mice fed a high fat diet and treated with MOTS c at 0.5 mg/kg/day by intraperitoneal injection for 8 weeks gained significantly less weight than untreated mice and were protected from hepatic steatosis and hyperinsulinemia; a 7 day course at 5 mg/kg/day raised whole body insulin sensitivity by approximately 30 percent in hyperinsulinemic euglycemic clamp studies, an effect attributed to AMPK activation in skeletal muscle.[1] Plasma metabolomic analysis in diet induced obese mice showed that MOTS c reduced sphingolipid, monoacylglycerol and dicarboxylate pathways associated with metabolic dysfunction.[8] In ovariectomized mice,

MOTS c at 5 mg/kg/day for 12 weeks prevented weight gain and insulin resistance and increased brown adipose activation,[9] and MOTS c promoted adipose thermogenesis and cold adaptation through the ERK pathway.[10] MOTS c expression interacted with exercise to regulate PGC 1 alpha and improve glucose metabolism in mice.[11]

4.2 Exercise capacity and aging

Reynolds and colleagues reported that MOTS c at 5 or 15 mg/kg improved treadmill performance in young, middle aged and old mice; old mice treated with MOTS c ran approximately twofold longer than untreated old mice.[12] Late life initiated intermittent treatment (15 mg/kg three times weekly from 23.5 months) improved grip strength, gait and walking capacity, and the lifespan curve showed a trend toward increased median (6.4 percent) and maximum (7.0 percent) lifespan that did not reach significance overall.[12]

4.3 Bone

MOTS c attenuated ovariectomy induced bone loss in mice via AMPK dependent inhibition of osteoclastogenesis,[13] reduced particle induced osteolysis in the mouse calvaria by shifting the osteoprotegerin to RANKL ratio,[14] and promoted osteogenic differentiation of rat bone marrow mesenchymal stem cells in vitro through TGF beta/Smad signaling.[15]

4.4 Cardiovascular

In a rat model of vitamin D3 and nicotine induced vascular calcification, MOTS c at 5 mg/kg/day for 4 weeks attenuated calcification and myocardial remodeling through AMPK signaling.[16] MOTS c delivered by subcutaneous osmotic pump prevented pressure overload heart failure in mice[17] and attenuated diabetic cardiomyopathy in a streptozotocin induced type 1 diabetic mouse model over 12 weeks.[18]

4.5 Immune, muscle and a negative finding

MOTS c improved survival and reduced bacterial load in mice infected with methicillin resistant Staphylococcus aureus,[19] and prevented autoimmune beta cell destruction in non obese diabetic mice by modulating T cells.[20] In diet induced obese mice and C2C12 myotubes, MOTS c reduced myostatin and muscle atrophy signaling.[21] Not all findings were positive. In cybrid cells harboring the pathogenic 3243A>G mitochondrial mutation, exogenous MOTS c did not improve mitochondrial respiration or ATP content, which suggests that its effects depend on context.[22]

Table 1. Selected preclinical studies of administered MOTS c, by organ system. All studies were conducted in rodents or cells.

STUDY	MODEL	DOSE AND ROUTE	PRINCIPAL FINDING
Lee 2015[1]	CD 1 and C57BL/6 mice; HEK293/HeLa cells	0.5 mg/kg/day IP 8 wk; 5 mg/kg/day IP 7 d	Prevented diet induced obesity; raised insulin sensitivity ~30 percent; AMPK via folate cycle
Kim 2019[8]	Diet induced obese mice	IP	Reduced plasma lipid pathway metabolites; enhanced insulin sensitivity
Lu 2019[9]	Ovariectomized mice	5 mg/kg/day IP 12 wk	Prevented OVX obesity and insulin resistance; AMPK
Reynolds 2021[12]	CD 1, C57BL/6J, C57BL/6N mice	5 or 15 mg/kg IP; intermittent 15 mg/kg 3x/wk late life	Improved treadmill capacity across ages; old mice ran ~2 fold longer; healthspan improved; lifespan trend not significant
Ming 2016[13]	Ovariectomized mice	5 mg/kg/day injection 12 wk	Reduced bone loss; inhibited osteoclastogenesis via AMPK
Yan 2019[14]	Mouse calvaria osteolysis	1 mM local injection 7 d	Reduced osteolysis; raised OPG/RANKL
Wei 2020[16]	Sprague Dawley rats	5 mg/kg/day IP 4 wk	Attenuated vascular calcification and myocardial remodeling
Zhong 2022[17]	Mice, transverse aortic constriction	SC osmotic pump	Prevented pressure overload heart failure; AMPK
Wu 2025[18]	STZ type 1 diabetic mice	SC osmotic pump 12 wk	Attenuated diabetic cardiomyopathy; AMPK
Kong 2021[20]	Non obese diabetic mice	Injection	Prevented autoimmune beta cell destruction; T cell modulation
Kumagai 2021[21]	Diet induced obese mice; C2C12 cells	Injection; in vitro	Reduced myostatin and atrophy signaling
Ahn 2020[22]	3243A>G cybrid cells	Exogenous peptide; expression vector	No improvement in mitochondrial respiration (negative)

IP, intraperitoneal; SC, subcutaneous; OVX, ovariectomy; STZ, streptozotocin; OPG, osteoprotegerin; RANKL, receptor activator of nuclear factor kappa B ligand.

5 Clinical evidence in humans

5.1 No interventional data

No published study has administered MOTS c, whether as the free base or the acetate salt, to human subjects by any route. The FDA confirmed in its 2026 evaluation that no clinical studies or human exposure data were identified, that outsourcing facilities reported no compounding of MOTS c products between 2017 and 2025, and that its adverse event database held no reports.[5] The human literature therefore consists entirely of studies that measured endogenous MOTS c, either observationally or after an exercise, lipid infusion or drug intervention, and of genetic studies of MOTS c variants.

5.2 Studies of endogenous circulating and muscle MOTS c

Exercise raises endogenous MOTS c. In 10 healthy young men, a single cycling bout increased skeletal muscle MOTS c approximately 11.9 fold and circulating MOTS c approximately 1.5 fold; circulating levels returned to baseline after 4 hours of rest, while muscle levels remained elevated with a trend toward baseline.[12] A randomized acute exercise study in 30 adults found that endurance exercise raised circulating humanin significantly and MOTS c showed a trend to increase, while resting humanin, but not MOTS c, correlated with age.[23] In 104 healthy men, circulating MOTS c decreased with age whereas skeletal muscle MOTS c was higher in older than younger men.[24] Lower circulating MOTS c has been associated with coronary endothelial dysfunction,[25] childhood obesity in boys,[26] and obstructive sleep apnea with a gradient by severity.[27] Associations have been inconsistent in direction across settings. MOTS c correlated positively with insulin resistance in lean but not obese adults,[28] rose after intralipid infusion and was blunted by insulin in PCOS and control women,[29] and was higher, not lower, with metabolic syndrome and with android and liver fat in participants without diabetes.[30] In cross sectional studies, higher serum MOTS c correlated with muscle strength of the legs but not with peak oxygen uptake,[31] and rose progressively from sedentary to recreationally active to elite young men.[32] Among professional athletes, MOTS c was lower than in sedentary controls in one pilot.[33] In hemodialysis patients, higher MOTS c was associated with a composite of death and nonfatal cardiovascular events and refined risk prediction.[34] A 16 week exercise intervention in breast cancer survivors raised MOTS c in non Hispanic White but not Hispanic women, consistent with ethnicity dependent responses.[35] Reported absolute concentrations vary by orders of magnitude between assays, which limits comparison across studies.[36]

5.3 Genetic studies of the m.1382A>C (K14Q) variant

An East Asian specific mitochondrial polymorphism, m.1382A>C (rs111033358), produces a K14Q substitution that yields a less active MOTS c. A meta analysis of three cohorts of Japanese descent, two in Japan and one of Japanese Americans, totaling 27,527 individuals found that men, but not women, carrying the C allele had a higher prevalence of type 2 diabetes, with evidence of interaction with physical activity.[37] The same variant was associated with a higher proportion of fast twitch fibres and greater leg strength in men, and the C allele was more frequent in sprint and power athletes than endurance athletes.[38] In 683 older Korean adults, C allele men had higher muscle mass and grip strength, with no effect in women.[39] These findings have been proposed as a partial explanation for exceptional longevity in some Japanese populations.[40] A randomized substudy found that metformin did not alter circulating MOTS c in breast cancer patients.[36]

Table 2. Human studies of endogenous MOTS c. Some tested exercise, lipid infusion or metformin; none administered MOTS c.

STUDY	N	POPULATION	DESIGN	PRINCIPAL FINDING
Reynolds 2021[12]	10	Healthy young men	Exercise, muscle and plasma	Muscle MOTS c rose ~11.9 fold, plasma ~1.5 fold after one bout
von Walden 2021[23]	30	Adults	Randomized acute exercise	Endurance exercise trend to raise MOTS c; no correlation with age at rest
D'Souza 2020[24]	104	Healthy men, three age bands	Cross sectional	Plasma MOTS c fell with age; muscle MOTS c higher with age
Qin 2018[25]	40	Coronary endothelial testing	Case control	Lower MOTS c with endothelial dysfunction
Du 2018[26]	97	Obese and healthy children	Case control	Lower MOTS c in obese boys; linked to insulin resistance
Cataldo 2018[28]	20	Lean and obese adults	Cross sectional	MOTS c correlated with insulin resistance in lean only
Ramanjaneya 2019[29]	PCOS and controls	Women	Intralipid/insulin clamp	Intralipid raised MOTS c; insulin blunted it
Sequeira 2021[30]	159	Adults without diabetes	Cross sectional, imaging	Higher MOTS c with metabolic syndrome and liver fat
Baylan 2021[27]	90	Obstructive sleep apnea	Case control	Lower MOTS c with apnea, by severity
Dieli Conwright 2021[35]	49	Breast cancer survivors	RCT, exercise substudy	Exercise raised MOTS c in White but not Hispanic women
Alser 2022[33]	105	Athletes and controls	Cross sectional pilot	Lower MOTS c in athletes than controls
Domin 2023[31]	20	Active adults	Preliminary	MOTS c correlated with strength, not peak VO2
Zhang 2026[32]	30	Young men	Cross sectional	MOTS c rose across sedentary to athlete; linked to VO2max
Bolignano 2024[34]	94	Hemodialysis	Observational cohort	Higher MOTS c refined cardiovascular risk prediction
Zempo 2021[37]	27,527	Japanese and Japanese American cohorts	Genetic meta analysis	K14Q C allele: more type 2 diabetes in men

STUDY	N	POPULATION	DESIGN	PRINCIPAL FINDING
Kumagai 2022[38]	211; 86; 1,594	Japanese adults, athletes and controls	Genetic association	C allele: fast twitch fibres, strength, power athletes
Kim 2024[39]	683	Older Korean adults	Cross sectional genetic	C allele men: higher muscle mass and grip strength
Cuyas 2022[36]	38	Breast cancer	RCT substudy	Metformin did not change circulating MOTS c

PCOS, polycystic ovary syndrome; RCT, randomized controlled trial; VO2, oxygen uptake; K14Q, lysine to glutamine substitution at residue 14.

6 Pharmacokinetics, formulation and doses studied

6.1 Pharmacokinetics

No human pharmacokinetic data exist. The FDA identified no in vivo pharmacokinetic or toxicokinetic studies of MOTS c in any species.[5] The only pharmacokinetic related study was an in vitro analysis in which MOTS c incubated in human whole blood was rapidly hydrolyzed to shorter fragments, MOTS c(2 to 16) through MOTS c(5 to 16), raising the question of whether exogenous administration can sustain pharmacologically active concentrations.[41] That study also developed a validated mass spectrometric assay for doping control and found that endogenous ELISA reference ranges could not be confirmed by liquid chromatography mass spectrometry.[41]

6.2 Doses and routes studied

All administration data are preclinical. Murine metabolic studies used intraperitoneal doses of 0.5 to 15 mg/kg/day,[112] cardiovascular studies used intraperitoneal 5 mg/kg/day in rats[16] or subcutaneous osmotic pump delivery in mice,[1718] and an oral MOTS c formulation was ineffective in a colitis model, prompting development of a cell penetrating analogue.[42] The withdrawn compounding nomination proposed 5 mg and 10 mg subcutaneous injection, but the nomination gave no reconstitution volume, so the FDA could not evaluate the final concentration or solubility.[5] No regulator has established a human dose, and none is recommended here.

7 Safety and tolerability

Human safety data are absent. Because no human has been administered MOTS c in a published study, there are no clinical safety observations, no human pharmacokinetics, and no adverse event reports in the FDA Adverse Event Reporting System, which the agency qualified by noting that 503A compounders generally do not report adverse events to it. The FDA also identified no nonclinical toxicity studies of MOTS c.[5] In the one long term mouse study, mice treated intermittently from late life kept a body weight comparable to controls despite reduced total food intake, and showed a nonsignificant trend toward longer lifespan.[12]

Two theoretical concerns bear on prescribing. First, the FDA judged MOTS c to be inadequately characterized for injectable compounding, citing absent impurity, aggregate and endotoxin data and a consequent inability to exclude immunogenicity, a risk that may be heightened by the subcutaneous route.[5] Second, the FDA noted that the molecular target is unknown, which makes it difficult to predict which organs MOTS c affects;[5] because MOTS c acts on the AMPK axis that governs glucose handling in rodents,[1] interactions with glucose lowering therapy are plausible but unstudied. A narrative review of unapproved peptides has noted that a parallel gray market operates largely outside regulatory oversight, with potential for serious harm to patients.[3]

CLINICAL CONSIDERATIONS

- No efficacy or safety outcome has been measured in humans given MOTS c; all benefit data are rodent or cellular.[5]
- Rapid proteolysis in human blood in vitro raises an unresolved question about systemic exposure after injection.[41]
- Product quality is itself a safety variable; the policy requires an FDA registered CGMP source with a certificate of analysis.[43]
- MOTS c is prohibited in sport at all times; athletes should be counseled before any use.[44]

8 Regulatory and anti doping status

MOTS c is not a component of any FDA approved drug and has no United States Pharmacopeia or National Formulary monograph.[5] It was placed in the FDA Category 2 list of bulk substances that may present significant safety risks and was shown as withdrawn from that category as of 22 April 2026.[45] At the Pharmacy Compounding Advisory Committee meeting of 23 to 24 July 2026, MOTS c related bulk drug substances were reviewed for obesity and osteoporosis; FDA staff recommended against inclusion on the 503A bulks list, while the committee voted 7 to 5 in favour. The vote is advisory and neither form is on the final list.[465]

On 30 October 2026 the Department of Health and Human Services published an enforcement discretion policy permitting 503A compounding of certain peptide bulk substances, MOTS c acetate among them, for subcutaneous or intramuscular injection only.[4347] The policy applies to patient specific prescriptions from state licensed pharmacies or physicians, not to 503B outsourcing facilities; it requires a single active ingredient with no combinations, an FDA registered CGMP source with a valid certificate of analysis, the label statement that the product is a compounded drug not for resale, and adverse event reporting to the FDA. It is temporary, pending a final rule, and expressly is not FDA approval; the policy states that compounded drugs are not FDA approved and that the FDA does not review their safety, effectiveness or quality before sale.[43] The HHS rationale for MOTS c acetate cited updated lot specific certificates of analysis, documented single ingredient historical use, and a randomized

placebo controlled trial of a MOTS c analogue reporting no serious adverse events, for which no citation was provided in the policy.[47]

Under the World Anti Doping Agency 2026 Prohibited List, in force from 1 January 2026, MOTS c is named explicitly in section S4.4.1 among activators of the AMP activated protein kinase (AMPK). Section S4, hormone and metabolic modulators, is prohibited at all times, in and out of competition; substances in S4.4 are non specified substances. MOTS c is not listed under S0.[44]

9 Discussion

The preclinical case for MOTS c is coherent and has been reproduced across laboratories and organ systems. A plausible mechanism, AMPK activation through folate cycle inhibition with a distinct nuclear role under stress, links its metabolic, musculoskeletal and cardiovascular effects, and the observation that endogenous MOTS c rises with exercise and falls with age gives the biology face validity in humans. The genetic data on the K14Q variant add a second, independent line of human evidence that a less active MOTS c tracks with metabolic and muscular phenotypes.[3738]

The translational gap, however, is wide and specific. No human has been administered MOTS c in any published study, so every statement about benefit in people is an extrapolation from rodents.[5] The human literature on endogenous MOTS c is associative, is drawn from heterogeneous assays whose absolute values disagree by orders of magnitude, and at times points in opposing directions, with MOTS c lower in some metabolic disease states and higher in others.[3041] The molecular target remains unknown, and the rapid hydrolysis of MOTS c in human blood in vitro raises a pharmacokinetic doubt about whether an injected dose achieves sustained activity.[41] The only human exposure to a related molecule is the CohBar analogue CB4211, which entered a randomized phase 1 trial in healthy subjects and nonalcoholic fatty liver disease (NCT03998514) but has no peer reviewed results; any inference from it applies to the analogue, not to MOTS c.[248] A substantial share of the founding literature originates from a single group whose principal investigators hold a financial interest in CohBar, and independent replication of the main findings is still needed.[112]

This review has limitations. It is narrative, did not apply a risk of bias instrument, and relied in places on abstracts. It did not quantitatively pool the observational data, which the assay heterogeneity would in any case render unreliable. Research priorities include validated and harmonized MOTS c assays, human pharmacokinetic studies of an injected preparation, and adequately powered randomized trials with defined metabolic or performance endpoints before efficacy claims can be made.

10 Conclusions

MOTS c is a mitochondrial derived peptide with a consistent preclinical profile as an AMPK linked metabolic and exercise related regulator, and with coherent human observational and genetic associations. It has never been administered to humans in a published study, has no human pharmacokinetic or safety data, and is prohibited in sport at all times.

Until human administration data exist, MOTS c should be regarded as an investigational agent supported by animal evidence, without established therapeutic benefit. The temporary HHS enforcement discretion policy permits compounding of MOTS c acetate for subcutaneous or intramuscular use under defined conditions but is not FDA approval and does not substitute for the clinical evidence that remains to be generated. Prescribing decisions rest with the treating physician and should be grounded in an accurate account of the evidence.

DECLARATIONS

Purpose. This is an internal evidence review prepared for clinicians; it has not been externally peer reviewed and is not a clinical guideline or a protocol. **Funding.** None. **Competing interests.** OC Wellness provides clinical services that may include prescribing compounded preparations of the peptide reviewed. **Data availability.** All sources are listed in the references. **Use of sources.** Findings are reported as stated in the cited abstracts or full texts.

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ABOUT THIS REVIEW

This is an internal evidence review prepared by OC Wellness for licensed clinicians. It summarizes published literature and public regulatory records; it has not been through external peer review and is not a clinical guideline, a protocol, or medical advice for any individual patient. MOTS c is not approved by the U.S. Food and Drug Administration for any indication; since 30 October 2026 a temporary HHS enforcement discretion policy has permitted 503A compounding of MOTS c acetate for subcutaneous or intramuscular use, which is not an FDA approval. Treatment decisions rest with the treating physician.

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