2.0

MODULE 3 OF 5 · UU LIFE PEPTIDES 2.0

SHIELDING

Recovery and protection. Tissue repair, gut integrity, immune modulation and connective tissue: BPC-157, TB-500, GHK-Cu, KPV, LL-37, thymic peptides and ARA-290.

Module 3 | UU LIFE PEPTIDES 2.0 | Verified references | Reported doses with provenance

A UU LIFE PRODUCT · UU.LIFE

Cards in this module

01	**BPC-157** Gastric pentadecapeptide	Evidence C
02	**TB-500** Actin-binding peptide fragment	Evidence C
03	**GHK-Cu** Copper-binding tripeptide	Evidence C
04	**KPV** C-terminal alpha-MSH tripeptide	Evidence C
05	**LL-37** Human antimicrobial peptide	Evidence A
06	**Thymosin Alpha-1** Thymic immunomodulatory peptide	Evidence A
07	**Thymalin** Thymic peptide complex	Evidence A
08	**ARA-290** Erythropoietin-derived innate repair receptor agonist	Evidence B

Each card: what it is, mechanism, evidence grade, regulatory and sport status, reported doses with provenance, stacking, safety, reconstitution with a worked calculation, buying notes, common mistakes and the references you can verify.

BPC-157

Body Protection Compound 157, Pentadecapeptide BPC 157

Gastric pentadecapeptide | Module 3 · Shielding | Goals: Recovery, Gut | Route: SC or oral

WADA prohibited

An investigational synthetic pentadecapeptide with extensive preclinical healing research, limited human studies, and no established clinical regimen for injury recovery.

WHAT IT IS

BPC-157 is a synthetic peptide containing 15 amino acids, with the sequence GEPPPGKPADDAGLV and a molecular weight of approximately 1419 Da. Its name expands to Body Protection Compound 157. Publications describe it as a fragment associated with a protein isolated from human gastric juice. That description does not establish a normal physiological role for administered synthetic BPC-157 (PMIDs 14554208, 42198317).

The literature reports stability in gastric juice and biological activity through several experimental routes. Gastric stability alone does not establish absorption, systemic exposure, or clinical effectiveness after oral administration. These require separate measurements using a characterized formulation.

Class: investigational gastric pentadecapeptide. BPC-157 is not a growth hormone secretagogue, steroid, or approved replacement hormone. Its direct molecular target remains incompletely characterized. Changes in receptor expression and downstream signaling have been demonstrated experimentally, but a selective receptor-binding mechanism has not been established. Mechanistic findings explain why researchers study it; they do not establish a treatment for an injured person.

MECHANISM

A well-characterized preclinical finding concerns angiogenesis. In cultured human vascular endothelial cells, BPC-157 increased VEGFR2 expression without increasing VEGF-A expression. It also increased VEGFR2 internalization and activated signaling involving Akt and endothelial nitric oxide synthase, or eNOS. Dynasore, an endocytosis inhibitor, suppressed receptor internalization, downstream signaling, and endothelial tube formation. Rat hindlimb ischemia experiments showed improved blood-flow recovery and increased vessel formation (PMID 27847966).

These experiments support involvement of receptor trafficking and VEGFR2-associated signaling in those models. They do not demonstrate direct binding of BPC-157 to VEGFR2. Dynasore is also not a selective probe for one receptor. The findings therefore support a pathway-level mechanism rather than definitive identification of a unique drug target.

Reviews describe effects involving nitric oxide signaling, ERK1/2, inflammatory mediators, fibroblast activity, and neuromuscular stabilization. Much of this evidence comes from experimentally induced injury in animals. Activity during nitric oxide synthase inhibition or substrate supplementation suggests context-dependent interactions with the nitric oxide system. It does not establish that BPC-157 automatically normalizes nitric oxide production in humans (PMID 40789979).

A separate experiment examined cultured fibroblasts from rat Achilles tendons. BPC-157 increased growth hormone receptor expression at the messenger RNA and protein levels. Adding growth hormone to pretreated cells increased proliferation and activated Janus kinase 2 signaling. This provides a cellular hypothesis about growth hormone responsiveness, not evidence that BPC-157 increases circulating growth hormone or improves a secretagogue combination (PMID 25415472).

Another tendon-cell study found increased explant outgrowth, migration, spreading, and survival during hydrogen peroxide stress. Phosphorylation of focal adhesion kinase and paxillin increased, while direct proliferation of cultured fibroblasts was not increased in the assay used (PMID 21030672). Migration, stress resistance, and proliferation are different outcomes. They should not be collapsed into a single claim that BPC-157 grows or repairs human tendons.

Broader claims that BPC-157 explains cytoprotection across many organs remain hypotheses. Much of the foundational literature comes from overlapping investigator networks, although independent groups have also published mechanistic and animal studies. Repeated positive experiments within one network are less informative about reproducibility than independent confirmation.

The relationship between exposure and effect remains unresolved. Short persistence of intact peptide in animal plasma contrasts with effects measured later in injury models. Downstream signaling could contribute, but a validated human exposure-response model does not exist. Neither frequent administration nor prolonged effects can be inferred reliably from the plasma half-life alone (PMIDs 36588717, 42198317).

EVIDENCE · GRADE C

Grade C for clinical healing, recovery, and gastrointestinal efficacy claims. Human evidence exists, but its design and reporting are too weak to establish these benefits. A systematic review searching through June 2024 identified 544 articles and included 36 studies, comprising 35 preclinical studies and one clinical report (PMID 40756949). That search cutoff matters: its clinical-study count is not a complete description of subsequent publications. Small uncontrolled studies provide signals for further investigation, not a reliable treatment effect. Older controlled gastrointestinal research is reported in meeting abstracts with substantial reporting limitations.

Human data. The knee-pain report identified 17 treated patients, with 16 reached for telephone follow-up. Twelve received BPC-157 alone; 11 reported improvement. Seven reported relief lasting six months to one year. The study lacked a control group, standardized functional outcomes, and follow-up imaging demonstrating structural repair. The paper reports administered doses (PMID 34324435). A second pilot enrolled 12 women with interstitial cystitis who had not responded to pentosan polysulfate. BPC-157 was administered during cystoscopy. Participants reported substantial symptom improvement on questionnaires, but the study was uncontrolled and could not separate treatment effects from procedural effects, expectations, or symptom fluctuation (PMID 39325560). The intravenous pilot enrolled two adults who had already received intravenous BPC-157 before the study. Investigators monitored selected laboratory markers, vital signs, and reported symptoms over three days. They reported no meaningful changes in the measured markers and no reported side effects. Prior exposure introduces selection bias, and this design cannot establish general tolerability, uncommon harms, or long-term safety (PMID 40131143). These three reports account for 31 enrolled or identified participants, or 30 when the unreachable knee patient is excluded. They do not support the repeated claim that fewer than 30 humans have ever been studied. FDA's 2026 review also identified older rectal-administration studies, including a randomized ulcerative-colitis trial reported as a meeting abstract. That trial randomized 53

Animal and mechanistic data. Animal research includes tendon transection, muscle injury, ligament injury, bone defects, gastrointestinal injury, and vascular ischemia. Studies report functional, mechanical, histological, and biochemical outcomes. These endpoints are informative within their models, but they do not establish return-to-training outcomes in humans (PMIDs 40756949, 40789979). The 2003 Achilles study reported improved mechanical properties, functional index, and tissue organization after tendon transection. Assessments extended through day 14. It tested several widely separated dose levels, but positive findings across those levels do not prove identical effects or a flat human dose-response relationship (PMID 14554208). An independent 2026 study randomized 32 rats to control, BPC-157, TB-500, or both after Achilles transection and repair. At four weeks, BPC-157 showed numerically improved maximum load to failure without statistical significance. Its total Bonar and Movin histology scores also did not reach significance. TB-500 reached significance for maximum load to failure, and the combination provided no additional benefit over the individual treatments (PMID 42542926). Surgical repair, assessment timing, sample size, and outcome selection affect interpretation. Chronic tendinopathy in a training adult also differs substantially from an acutely transected rat tendon.

participants, with 46 completing it. Reporting was insufficient, and the reported between-group confidence interval crossed zero. Thus, saying that no Phase II study exists is incorrect. These historical data do not establish efficacy. [FDA BPC-157 briefing document](https://www.fda.gov/media/193343/download). No adequately reported controlled human evidence reviewed here establishes faster tendon healing, cartilage regeneration, improved athletic performance, or an effective subcutaneous recovery regimen.

REGULATORY STATUS AND SPORT

STATUS

BPC-157 remains investigational, with no approved therapeutic formulation identified in the reviewed sources (PMID 42198317). An identifier in a substance database, a prescription, or research-use labeling does not constitute marketing authorization. The FDA category document retrieved for this review, updated May 14, 2026, does not list BPC-157 in Categories 1, 2, or 3. Removal from a nomination category does not establish authorization for compounding. [FDA bulk substances category document](https://www.fda.gov/media/94155/download?attachment=). FDA convened its July 2026 advisory review to consider BPC-157-related substances for the 503A bulks list. Advisory consideration or a favorable committee recommendation is distinct from a final agency determination and from drug approval. The materials reviewed here do not establish a newly authorized compounding pathway. [FDA July 2026 advisory meeting](https://www.fda.gov/advisory-committees/advisory-committee-calendar/july-23-24-2026-meeting-pharmacy-compounding-advisory-committee-07232026). Regulatory status is jurisdiction-specific and can change. Claims that all commercial material shares one legal status or manufacturing standard are not justified. Regulatory review also does not resolve the missing evidence for clinical benefit, validated dosing, or long-term harms.

WADA

Prohibited at all times under S0, Non-Approved Substances. WADA explicitly names BPC-157 in this category. The prohibition applies in competition and out of competition. Its status does not depend on whether an article describes it as a growth factor or signaling modifier. [WADA Prohibited List](https://www.wada-ama.org/en/prohibited-list). A prescription, research-use label, or compounding claim does not by itself authorize use under anti-doping rules. Exemption decisions require the applicable anti-doping authority's criteria; no exemption is established here.

RESEARCH USE · REPORTED, NOT RECOMMENDED

ROUTES

Animal studies have used intraperitoneal, intravenous, intramuscular, oral or intragastric, topical, and local administration. Route-specific results should not be treated as equivalent exposure or interchangeable efficacy (PMIDs 36588717, 40756949). The three recent human reports used intra-articular injection, bladder-wall injections during cystoscopy, and intravenous infusion. These are different procedures in different populations, not interchangeable demonstrations of a general recovery regimen (PMIDs 34324435, 39325560, 40131143). Subcutaneous and oral administration appear in non-clinical use descriptions. The reviewed evidence does not establish human subcutaneous bioavailability, a benefit from administration near an injury, or an effective oral regimen for gastrointestinal disease. Stability in gastric juice does not establish passage across the intestinal barrier or delivery to an injured tendon.

HALF-LIFE

A formal study found an elimination half-life of intact BPC-157 below 30 minutes after intravenous and intramuscular administration in rats and beagle dogs. Intramuscular absolute bioavailability was approximately 14 to 19 percent in rats and 45 to 51 percent in dogs. Intact peptide degraded into smaller fragments and amino acids, with radiolabeled material eliminated through urine and bile (PMID 36588717). These are animal results. A defensible human half-life is not established by the two-person intravenous safety report. Its reported methods do not provide a validated human pharmacokinetic profile. The later review's stronger human half-life claim is therefore not adopted here (PMIDs 40131143, 42198317). Measurements of intact peptide, degradation products, and total radioactivity answer different questions. None supplies a validated dosing interval for human tissue repair.

TIMING

No validated human timing rule relates BPC-157 administration to meals, training, sleep, or injury location. The early postoperative administration in the rat tendon study was part of that experiment, not evidence for a human treatment window (PMID 14554208). A short animal plasma half-life does not establish that dividing human exposure improves effectiveness. That inference would require

human pharmacokinetic and exposure-response data. Similarly, delivering a preparation near perceived pain does not establish preferential delivery to the injured structure.

CYCLE LENGTH

A 4 to 8 week course followed by a break is commonly cited in non-clinical use; not validated in trials. There is no established cycle length for human tendon or muscle recovery. The recent human reports involved a procedure, occasional repeat procedures, or two consecutive infusion days. Their follow-up periods must not be mistaken for continuous treatment durations. The independent rat comparison used four weeks of treatment, while other animal studies used different schedules (PMIDs 34324435, 39325560, 40131143, 42542926). The reviewed studies do not establish tolerance, dependence, withdrawal effects, an effective break duration, or the consequences of repeated non-clinical cycles.

TITRATION

No validated human escalation, maintenance, or tapering schedule exists. The tendon experiments do not establish a therapeutic window or maximum tolerated human exposure. Positive animal findings across widely separated doses cannot prove a flat dose-response curve, equal efficacy, or a ceiling effect. Such conclusions require adequately powered comparisons between dose groups. The two-person intravenous pilot also cannot establish an escalation strategy because its sequential exposures were not randomized dose comparisons (PMIDs 14554208, 40131143). Perceived symptom improvement supplies no measurement of tissue peptide exposure or structural healing. Increasing an unvalidated dose therefore has an unknown relationship to both benefit and harm.

CONTEXT	DOSE	ROUTE	FREQUENCY	PROVENANCE
Approved product label	**No approved label dose was identified.**	Not applicable.	Not applicable.	The reviewed literature identifies no approved therapeutic formulation or validated clinical dosing regimen (PMID 42198317). · PMID 42198317
Human intravenous safety pilot, two previously exposed adults	**10 mg intravenously on day 1 and 20 mg intravenously on day 2, once daily, each in 250 mL normal saline over one hour (PMID 40131143).**	Intravenous infusion.	One infusion daily on two consecutive days.	Directly reported study exposure. Laboratory and symptom observations extended through day 3. This was not a dose-ranging trial and does not establish a suitable dose. · PMID 40131143
Human knee-pain retrospective series, BPC-157 alone	**4 mg by intra-articular injection, generally one procedure, using 2 mL at 2000 mcg/mL; two patients in the overall series received repeat injections after reinjury (PMID 34324435).**	Intra-articular injection into the knee.	Generally one procedure; repeat treatment occurred in two patients without a standardized repeat interval.	The primary paper explicitly reports the concentration and amount. [Primary knee-pain report](https://asipp.org/wp-content/uploads/Intra-Articular-Injection-of-BPC-157-for-Multiple-Types-of-Knee-Pain-2021-Alternative-Therapies-in-Health-and-Medicine.pdf). · PMID 34324435
Human interstitial-cystitis pilot, 12 women	**10 mg total by bladder-wall injections during one cystoscopic procedure (PMID 39325560).**	Intravesical bladder-wall injections during cystoscopy.	Single procedure.	Directly reported total exposure in an uncontrolled pilot. The symptom findings do not establish an effective regimen or justify extrapolation to other routes. · PMID 39325560
Rat Achilles tendon transection	**10 mcg/kg, 0.01 mcg/kg, or 0.00001 mcg/kg intraperitoneally once daily, starting 30 minutes after surgery (PMID 14554208).**	Intraperitoneal.	Once daily, with the last administration 24 hours before the assigned tissue assessment; assessments extended through day 14.	Direct animal-study doses, expressed consistently in mcg/kg. Positive results across widely separated doses do not establish a human dose or demonstrate dose equivalence. · PMID 14554208

CONTEXT	DOSE	ROUTE	FREQUENCY	PROVENANCE
Rat Achilles tendon transection and surgical repair, independent comparison	**10 mcg/kg BPC-157 intraperitoneally once daily for four postoperative weeks (PMID 42542926).**	Intraperitoneal.	Once daily for four weeks.	Directly reported experimental regimen. BPC-157 did not significantly improve maximum load to failure or total Bonar and Movin scores versus control. · PMID 42542926
Non-clinical subcutaneous descriptions	**250 to 500 mcg subcutaneously once or twice daily, commonly cited in non-clinical use; not validated in trials.**	Subcutaneous.	Once or twice daily in non-clinical descriptions.	Commonly cited in non-clinical use; not validated in trials. Retained as an explicitly unvalidated description, not a study-derived dose or recommendation. Vendor and forum usage, not evidence: listed so you can recognize it, not follow it; no trial has validated this regimen and it is not a recommendation.

STACKING

+ TB-500

No demonstrated human synergy. An exploratory rat comparison found no added benefit from the combination over the individual treatments (PMID 42542926). The paper describes its TB-500 material as synthetic thymosin beta-4, so its identity should not be assumed equivalent to every product using that name. Shared downstream pathways were proposed, not established as the explanation.

+ GHK-Cu

A wound-repair rationale is sometimes proposed, but a BPC-157 and GHK-Cu combination benefit is not established by the verified studies. Separate findings about angiogenesis or extracellular matrix remodeling cannot predict additive efficacy, optimal exposure, or adverse effects. This is a hypothesis rather than an evidence-supported combination.

+ KPV

The proposed rationale is overlapping interest in intestinal inflammation and mucosal injury. No verified combination trial supports additional benefit or a clinical regimen. Different mechanisms do not automatically produce complementary effects, and animal gastrointestinal findings cannot establish treatment of human inflammatory bowel disease.

+ Ipamorelin

The hypothesis extrapolates from increased growth hormone

– IGF-1 LR3

No verified clinical interaction or combination-safety evidence. Concern about overlapping growth and angiogenic signaling is theoretical. Neither benefit nor a quantified cancer risk can be assigned to the combination.

– Follistatin-344

No verified combination evidence establishes benefit, safety, or predictable tissue effects. Adding another investigational signaling intervention introduces uncertainty about exposure and adverse-event attribution. This caution reflects absent evidence, not a demonstrated pharmacological contraindication or proof that an interaction occurs.

receptor expression in cultured rat tendon fibroblasts (PMID 25415472). That experiment did not test ipamorelin, circulating hormone pulses, or a clinical combination. Greater receptor expression in a cell assay does not establish better healing or acceptable systemic effects.

SAFETY

COMMON EFFECTS

There is no reliable incidence table for BPC-157 adverse effects. The three recent human reports described no adverse events, but monitoring methods, populations, routes, and follow-up differed. The intravenous laboratory findings apply only to its two previously exposed participants (PMIDs 34324435, 39325560, 40131143). Headache, nausea, flushing, and local irritation appear in non-clinical accounts, but those accounts cannot establish frequency or causality. Symptoms may arise from the peptide, another ingredient, contaminants, the procedure, or an unrelated condition. Their absence in a small report is not evidence that they cannot occur. Preclinical toxicology provides information about particular experimental materials and exposures. It does not establish the safety of repeated human use or commercial preparations.

SERIOUS SIGNALS

Human adverse-event reports exist. FDA summarized injection-site reactions, shortness of breath requiring emergency evaluation, and pigmentation changes involving a combination product. Missing information and coexposures prevented attribution to BPC-157 itself. These reports establish surveillance signals, not incidence or causality. [FDA BPC-157 briefing document](https://www.fda.gov/media/193343/download). FDA also identifies potential immunogenicity, peptide-related impurities, and difficulties characterizing the active ingredient. These uncertainties concern both formulation quality and biological responses. [FDA safety-risk information](https://www.fda.gov/drugs/human-drug-compounding/certain-bulk-drug-substances-use-compounding-may-present-significant-safety-risks). Angiogenic signaling raises a theoretical concern in malignancy, but no reviewed human study establishes that BPC-157 causes or prevents cancer. Claims about neurodegenerative harm are likewise unproven. A mechanistic argument alone cannot quantify either risk. Nonsterile invasive administration can cause serious infection. Endotoxin contamination can cause systemic reactions even when a preparation contains the intended peptide. No comparative surveillance establishes which serious event is most likely in non-clinical use.

CONTRAINDICATIONS

There is no approved label defining formal BPC-157 contraindications. Relevant precautionary contexts include pregnancy, breastfeeding, childhood, active malignancy, and ongoing cancer treatment because adequate clinical evidence is lacking. A previous malignancy creates uncertainty requiring individual clinical assessment, not a proven universal contraindication. Known hypersensitivity to a preparation or its excipients is a separate concern. Active infection is particularly relevant to any proposed invasive procedure. The absence of interaction studies also leaves uncertainty with anticoagulants, immunosuppressants, and other prescription medicines. Anti-doping prohibition is a regulatory restriction, not a medical contraindication. Unverified identity, sterility, or endotoxin status is a product-quality problem that cannot be resolved by a favorable theoretical mechanism.

STOP RULES

Chest pain, breathing difficulty, facial or throat swelling, or collapse requires emergency medical evaluation. Fever with a hot, swollen joint or spreading redness after an invasive procedure requires urgent assessment for infection. Further exposure warrants suspension pending assessment when new systemic symptoms, unexplained bruising, progressive swelling, or worsening pain occurs. A new mass or persistent skin change also warrants clinical evaluation, although it does not establish peptide-related cancer. Pain relief does not demonstrate restoration of tendon strength or readiness for unrestricted loading. A worsening injury requires reassessment rather than interpretation as a reason to increase exposure. Cloudiness, discoloration, or visible particles raises a product-quality concern. Normal appearance cannot establish sterility, chemical identity, or retained potency.

RECONSTITUTION AND STORAGE

TYPICAL VIAL

There is no approved standard vial size or validated universal presentation. Labels describing lyophilized BPC-157 provide a nominal content claim, not proof of identity, potency, sterility, or formulation suitability. A nominal peptide mass also differs from the total mass of powder. Counterions, water, buffers, and other excipients can contribute to the material present. Distinguishing free peptide content from total product mass requires an appropriate quantitative assay. The biopharmaceutical review identifies major formulation-development gaps (PMID

42198317). Its broad statement that no pharmaceutical-grade formulation exists should not be treated as an assay of every preparation or a denial that experimental clinical formulations were manufactured.

SOLVENT

No approved BPC-157 label establishes a solvent, preservative, final concentration, mixing method, or multidose handling procedure. The intravenous pilot reports normal saline as its infusion vehicle, while the knee study describes a buffered preparation containing benzyl alcohol. Neither report validates home preparation or interchangeability of formulations (PMIDs 40131143, 34324435). Bacteriostatic water does not sterilize contaminated powder and does not remove endotoxin. Preservative presence alone does not establish compatibility, stability, or an acceptable period after opening. Preparation clarity is also not evidence of chemical integrity. Formulation behavior depends on the peptide form, concentration, excipients, container, and handling conditions.

STORAGE

No universal BPC-157 storage temperature, shipping tolerance, or post-reconstitution shelf life is established for all preparations. These depend on formulation, packaging, concentration, manufacturing controls, and validated stability testing. Chemical stability and microbiological acceptability are separate requirements. Refrigeration does not establish sterility, and a preservative does not prevent every contamination problem. Conversely, physical clarity cannot establish that intact peptide remains at the labeled concentration. Experimental storage conditions cannot automatically become instructions for commercial material.

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Study arithmetic only: the knee report used 4 mg intra-articularly in a generally single procedure, supplied as 2 mL at 2000 mcg/mL (PMID 34324435). 2000 mcg/mL multiplied by 2 mL equals 4000 mcg, which is 4 mg, matching the reported amount. This checks internal consistency; it does not establish efficacy or a suitable regimen. For any concentration calculation, mass divided by final solution volume gives concentration. Added solvent volume and final solution volume are not automatically identical. A calculation based on a label also inherits any error in that label. Syringe graduation units measure volume under a device-specific convention. They are not biological IU for BPC-157, and there is no approved BPC-157 biological-unit standard. A mass-to-volume conversion cannot supply missing information about formulation stability, sterility, absorption, or a clinically justified exposure.
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BUYING NOTES

Research-use labeling, a professional-looking certificate, and a high purity percentage do not establish a preparation suitable for human administration. A certificate of analysis describes a tested sample and the methods applied. Its usefulness depends on traceability to the material under discussion and on whether those methods answer the relevant questions. Chromatographic purity, peptide identity, quantitative content, sterility, and bacterial endotoxin are separate measurements. A high chromatographic area percentage does not prove the labeled amount of peptide or exclude every contaminant. Mass spectrometry can support identity, but interpreting a molecular mass requires accounting for the analytical method, charge state, counterions, and peptide form. The reported BPC-157 sequence is GEPPPGKPADDAGLV, with a free-peptide molecular weight around 1419 Da (PMID 14554208). A matching nominal mass alone cannot establish every structural detail, exclude related impurities, or demonstrate biological activity. Meaningful documentation identifies the batch, laboratory, sample, dates, analytical methods, acceptance criteria, and actual results. A generic certificate without a traceable batch relationship cannot establish the contents of a particular container. Independent testing can improve confidence in a measured property, but it does not turn an investigational preparation into an approved medicine. For invasive formulations, sterility and endotoxin assessments address different hazards. A chemical purity result supplies neither. Container compatibility, particulate testing, quantitative content, and stability are additional questions. Claims that one salt form has superior human absorption or clinical effectiveness require direct comparative evidence. Quality documentation also cannot compensate for the absence of a validated clinical regimen.

COMMON MISTAKES

- Converting rat doses directly into human regimens. Species, route, formulation, and measured exposure all affect interpretation. The rat and dog pharmacokinetic findings do not establish human subcutaneous bioavailability.
- Treating positive findings at several animal doses as proof that all doses are equivalent. A flat dose-response curve requires direct evidence, not the absence of an obvious difference in a small experiment.

- Repeating the claim that the knee paper omitted dosing. Its methods and results report administered amounts, while its outcome assessment remains uncontrolled and subjective.
- Counting three recent pilot reports as the entire history of human research. Older gastrointestinal studies exist, but limited reporting prevents confident conclusions about clinical effectiveness.
- Interpreting gastric stability as proof of oral absorption or delivery to injured tissue. Chemical survival in the stomach and systemic bioavailability are different questions.
- Assuming that BPC-157, thymosin beta-4, and products labeled TB-500 have interchangeable identities or evidence. The exact experimental material matters when interpreting a comparison or combination.
- Treating an advisory committee review, category removal, prescription, or certificate of analysis as drug approval. Each addresses a different question and provides different evidence.
- Inferring sterility, potency, or an acceptable storage period from a clear solution. Appearance cannot resolve those properties, and bacteriostatic water cannot correct contaminated starting material.
- Using reduced pain as evidence of structural healing or readiness for unrestricted training. The human reports do not establish repaired cartilage, restored tendon strength, or reduced reinjury risk.
- Equating no reported events with demonstrated safety. Small samples, selected participants, incomplete monitoring, and short follow-up leave uncommon and delayed harms unresolved.

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TB-500

Thymosin beta-4 fragment, Tβ4

Actin-binding peptide fragment | Module 3 · Shielding | Goals: Recovery | Route: SC | WADA prohibited

An acetylated thymosin beta-4 fragment with preclinical research, unresolved identity across marketed preparations, and no verified human trial establishing recovery benefits for Ac-LKKTETQ.

WHAT IT IS

In the analytical literature, TB-500 denotes Ac-LKKTETQ, the N-terminally acetylated seven-amino-acid fragment corresponding to residues 17-23 of thymosin beta-4. Researchers identified this ingredient in a marketed preparation using mass spectrometry and confirmed its identity through independent synthesis (PMID 22962027). Full-length thymosin beta-4 is a different molecule: a 43-amino-acid peptide with a molecular mass of approximately 4.9 kDa (PMID 9194528, PMID 17947592). The name TB-500 is not a reliable chemical specification. Some publications and marketed preparations use it interchangeably with synthetic thymosin beta-4. Consequently, a study mentioning TB-500 cannot automatically be assigned to Ac-LKKTETQ. Three related substances require separation: full-length thymosin beta-4, the unacetylated fragment LKKTETQ, and the acetylated fragment Ac-LKKTETQ. The aged-mouse wound study tested LKKTETQ and found activity comparable to the parent peptide in that model (PMID 12581423). It did not establish equivalence between unacetylated LKKTETQ and Ac-LKKTETQ in people. This distinction became more consequential in a later analytical study. Investigators evaluated Ac-LKKTETQ and its metabolites in experimental systems and found significant fibroblast wound-closure activity for one metabolite, Ac-LKKTE. The parent fragment did not demonstrate the same significant effect in that assay (PMID 38382158). Within the product's repair category, TB-500 represents an experimental tissue-repair concept. Human improvements in tendon healing, training capacity, joint function or body composition have not been established for chemically verified Ac-LKKTETQ. A study of the full-length peptide also failed to improve metabolic disturbances or muscle regeneration in its mouse models (PMID 34495765). Equine analytical research documents historical veterinary preparations containing the acetylated fragment (PMID 23084823). That history establishes a preparation and an analytical identity. It does not establish veterinary approval, human suitability, or a validated clinical development pathway.

MECHANISM

The strongest mechanistic evidence concerns full-length thymosin beta-4. It binds monomeric G-actin and buffers the actin pool available for filament assembly. This intracellular function supports changes in cell shape and movement. The parent peptide is largely unstructured in solution and adopts a more stable conformation when bound to actin (PMID 17468232, PMID 11311852).

LKKTETQ contains an actin-binding region, which motivated fragment research. However, containing that region does not establish that an isolated fragment reproduces the parent's binding properties, cellular distribution or downstream effects. Acetylation and enzymatic cleavage introduce additional differences that require direct testing (PMID 12581423, PMID 38382158).

Extracellular parent-peptide experiments support several repair-related actions. In cultured human endothelial cells, thymosin beta-4 increased directional migration, scratch closure and matrix metalloproteinase production (PMID 9194528). In rat skin wounds, topical or intraperitoneal treatment increased reepithelialization, collagen deposition and angiogenesis (PMID 10469335). These endpoints describe experimental repair processes, not demonstrated recovery of a human tendon.

Several signaling mechanisms have experimental support. In cardiac models, thymosin beta-4 formed a functional complex with PINCH and integrin-linked kinase, increasing Akt signaling. Treatment improved early cardiomyocyte survival and cardiac function after coronary ligation in mice (PMID 15565145). This is a signaling-complex observation, not proof of a single dedicated cell-surface receptor.

A separate endothelial study identified the beta subunit of cell-surface ATP synthase as a binding partner. Thymosin beta-4 increased extracellular ATP signaling, and P2X4 activity was required for the observed migration response (PMID 21106936). Corneal epithelial experiments found reduced NF-kappaB activation and nuclear translocation after inflammatory stimulation (PMID 17254567). These findings concern the parent molecule in specific experimental settings.

Domain mapping limits broad extrapolation. A study of 17 thymosin beta-4 domain combinations identified the C-terminal AGES region as important for cardiac protection in mice and pigs (PMID 26255251). The acetylated LKKTETQ fragment lacks that region. It also cannot generate the N-terminal metabolite Ac-SDKP, which has a separate body of biological research (PMID 17468232, PMID 41570941).

Developmental and injury studies further implicate endogenous thymosin beta-4 in vascular remodeling and myoblast migration (PMID 17495252, PMID 29202457, PMID 20880960). Endogenous gene expression, extracellular administration and administration of a shortened synthetic fragment are distinct experimental interventions.

For Ac-LKKTETQ specifically, metabolism may contribute substantially to activity. The study identifying Ac-LKKTE activity tested human serum outside the body, animal samples and cultured fibroblasts (PMID 38382158). It did not identify a clinically effective human exposure. The mechanism supporting an injected Ac-LKKTETQ preparation for human tendon repair therefore remains unestablished.

EVIDENCE · GRADE C

Grade C reflects a preclinical evidence base with substantial uncertainty about the exact molecule studied. No published human interventional trial of chemically verified Ac-LKKTETQ was identified in this PubMed review. Human trials of full-length or recombinant thymosin beta-4 cannot establish efficacy for the fragment.

The fragment literature includes analytical identification, animal metabolism and cell-based activity studies. Related unacetylated LKKTETQ has wound-repair evidence in aged mice (PMID 12581423, PMID 38382158). A recent rat tendon study reported benefits with material called TB-500, but did not establish its sequence or acetylation in the retrieved methods (PMID 42542926).

Current sports medicine reviews describe inadequate human evidence for musculoskeletal recovery and unresolved indications, dosing and treatment duration (PMID 41476424, PMID 41966639, PMID 42578445). These reviews summarize overlapping primary literature and should not be counted as independent demonstrations of efficacy.

The parent peptide has multiple human randomized studies, including cardiac research. Their results are mixed and indication-specific. The supplied grading scale classifies multiple human randomized trials as A, but that designation cannot be transferred between molecules or interpreted as proof of benefit. The Cochrane assessment of the small neurotrophic keratopathy trial rated its evidence as low certainty (PMID 41347649).

Human data. Ac-LKKTETQ: no qualifying human interventional trial was identified. Human serum metabolism experiments are laboratory studies, not human administration studies (PMID 38382158). Full-length synthetic thymosin beta-4: a randomized phase 1 study enrolled 40 healthy volunteers across four cohorts, including placebo recipients. Active treatment comprised 42, 140, 420 or 1260 mg intravenously once, followed after safety review by the same assigned dose daily for 14 days (PMID 20536472). Adverse events were infrequent and mild or moderate, with no reported serious adverse events or dose-limiting toxicity. This establishes limited short-term tolerability for that preparation. A separate recombinant thymosin beta-4 phase 1 study included 54 participants in its single-dose component and 30 in its repeated-dose component. Intravenous single doses ranged from 0.05 to 25 mcg/kg; repeated

Animal and mechanistic data. The rat Achilles tendon study randomized 32 male rats into control, BPC-157, TB-500 and combination groups. Material called TB-500 was administered at 60 mcg/kg intraperitoneally once daily for 30 postoperative days according to the full methods (PMID 42542926). The abstract summarizes the duration as four weeks. TB-500 treatment increased maximum load to failure and improved selected histological scores relative to control. Each group contained eight animals, but only four contributed to biomechanical testing and four to histological assessment. There was no prospective power calculation, and broader mechanical properties and functional recovery were not established. The retrieved methods identify a commercial preparation without reporting sequence confirmation or acetylation. This study therefore cannot be presented as confirmed Ac-LKKTETQ

doses were 0.5, 2 or 5 mcg/kg intravenously once daily for 10 days (PMID 34346165). No serious adverse events or dose-limiting toxicities were reported. The major difference from the earlier milligram-dose program does not justify a conversion between preparations. In venous ulcers, a randomized phase 2 study enrolled 73 patients. Topical thymosin beta-4 produced an exploratory healing signal, particularly among smaller or less severe ulcers, with tolerability comparable to placebo (PMID 20536470). The earlier publication described the ongoing protocol and is not a separate completed efficacy trial (PMID 17495250). A later program summary reported faster healing among patients who healed; that selected subgroup cannot establish benefit for every treated patient (PMID 23050815). A severe dry-eye trial enrolled nine patients. It used 0.1 percent ophthalmic thymosin beta-4 six times daily for 28 days, followed by observation through day 56 (PMID 25826322). The reported 12 treated and six control eyes came from nine people, not 18 independent participants. Another dry-eye trial enrolled 72 participants and missed both primary efficacy endpoints, despite favorable secondary findings (PMID 26056426). In neurotrophic keratopathy, complete healing at four weeks occurred in six of ten treated participants and one of eight placebo participants. The primary comparison was not statistically significant, with p = 0.0656; some secondary outcomes favored treatment (PMID 36613994). The small sample and imprecision remain central limitations (PMID 41347649). Cardiac development did not stop at phase 1. A 2025 publication reported a randomized, double-blind trial involving 96 patients with myocardial infarction after reperfusion. The overall infarct-area comparison was not significant. A subgroup receiving early treatment showed a favorable result, which requires confirmation (PMID 41229390). None of these studies establishes efficacy for subcutaneous Ac-LKKTETQ.

efficacy. The combination did not demonstrate additional benefit. This result does not prove pharmacological redundancy, equivalence, or the absence of benefit under every possible regimen. The experiment was small and assessed a single postoperative time point (PMID 42542926). Earlier skin studies support full-length thymosin beta-4 in rats and impaired-healing mouse models (PMID 10469335, PMID 12581423). The unacetylated LKKTETQ fragment reproduced parent-peptide activity in aged mice. That finding does not directly establish acetylated-fragment activity in diabetic mice or human tendons. Cardiac results vary by model. Positive mouse and pig findings coexist with a pig ischemia-reperfusion study that found no improvement in cardiac function or cell death (PMID 15565145, PMID 26255251, PMID 27199757). In dystrophin-deficient mice, full-length thymosin beta-4 at 150 mcg intraperitoneally twice weekly for six months increased regenerating muscle fibers without significantly improving strength, cardiac function or fibrosis (PMID 20126456). Another study found no improvement in mouse muscle regeneration or obesity-related metabolic disturbances (PMID 34495765). Increased repair markers therefore cannot substitute for demonstrated functional benefit.

REGULATORY STATUS AND SPORT

STATUS

TB-500 has no FDA-approved human therapeutic indication or approved dosing label. The FDA's safety information, current as of April 22, 2026, identifies potential immunogenicity concerns involving aggregation and peptide-related impurities. It also states that the agency has not identified human exposure data for drug products containing the thymosin beta-4 fragment. FDA approval, eligibility for pharmacy compounding, prescription scheduling and legality in another jurisdiction are different questions. A research-use label does not establish any of them. The parent peptide has clinical development programs in skin, ocular and cardiovascular conditions (PMID 20536470, PMID 25826322, PMID 36613994, PMID 34346165, PMID 41229390). A 2007 article described cardiac development plans, but it cannot establish the current absence of later trials (PMID 17947592). The 2025 cardiac randomized trial directly corrects that historical inference. The FDA source consulted was Certain Bulk Drug Substances for Use in Compounding that May Present Significant Safety Risks. Published clinical reviews also distinguish investigational peptides from approved treatments and describe major gaps in human safety evidence (PMID 41966639).

WADA

Prohibited at all times under S2.3, Growth Factors and Growth Factor Modulators. The 2026 list explicitly names thymosin beta-4 and derivatives including TB-500. This applies both in and out of competition. Source: [WADA 2026 Prohibited List](https://www.wada-

ama.org/sites/default/files/2025-09/2026list_en_final_clean_september_2025.pdf). The classification concerns the prohibited substance, not whether a preparation is called a fragment, research chemical or recovery aid. It also does not depend on proving improved athletic performance in humans. Published analytical studies establish that the fragment can be identified, but they do not predict an individual athlete's test result (PMID 22962027, PMID 23084823). Detection thresholds and timing strategies are not included.

RESEARCH USE · REPORTED, NOT RECOMMENDED

ROUTES

Human thymosin beta-4 research includes intravenous administration, topical wound treatment and ophthalmic delivery (PMID 20536472, PMID 34346165, PMID 20536470, PMID 25826322). These are preparation-specific routes for the parent or recombinant peptide. Related animal studies used topical or intraperitoneal administration. The rat tendon study used intraperitoneal administration of material called TB-500, with unresolved fragment identity (PMID 10469335, PMID 42542926). The chronic dystrophic-mouse study also used intraperitoneal administration, not subcutaneous administration (PMID 20126456). Subcutaneous and intramuscular fragment administration are described in non-clinical use, without a verified human efficacy or pharmacokinetic basis. Local placement near an injury has no demonstrated clinical advantage in the retrieved evidence. Oral bioavailability and effective oral dosing were not established.

HALF-LIFE

No human pharmacokinetic study of chemically verified Ac-LKKTETQ was identified. A half-life assigned to full-length or recombinant thymosin beta-4 does not establish the fragment's half-life after another route. The 2010 intravenous parent-peptide study reported dose-dependent exposure and increasing half-life with increasing dose (PMID 20536472). A separate 2021 recombinant-peptide study characterized intravenous pharmacokinetics and reported no obvious accumulation during its repeated-dose program (PMID 34346165). These are distinct datasets, not one universal thymosin beta-4 exposure profile. Equine and rat studies identify Ac-LKKTETQ metabolites, but animal detection results do not establish a human therapeutic half-life (PMID 23084823, PMID 38382158). Plasma elimination, metabolite persistence and duration of biological action are different measurements. None validates the intermittent schedules circulated for human fragment use.

TIMING

No clinical evidence establishes timing relative to exercise, meals, sleep or an injury for Ac-LKKTETQ. Repair-related mechanisms do not identify an optimal administration window. The rat tendon experiment began treatment on the first postoperative day (PMID 42542926). That is an experimental design choice, not evidence that earlier human administration improves outcomes. Likewise, the early-treatment subgroup in the parent-peptide cardiac trial concerns myocardial reperfusion, not musculoskeletal injuries (PMID 41229390). The retrieved literature does not establish that administration near an injured structure improves targeting. Evidence of systemic effects in animals also does not establish that every route produces equivalent exposure.

CYCLE LENGTH

No validated human cycle length exists for Ac-LKKTETQ. A four-to-six-week initial phase with optional maintenance is commonly cited in non-clinical use; not validated in trials. That convention is not evidence that finite use prevents harm or that maintenance preserves a benefit. The two retrieved systemic parent-peptide phase 1 programs used repeated-treatment periods of 14 and 10 days, respectively (PMID 20536472, PMID 34346165). These durations describe particular studies and do not establish a universal maximum duration for all human research. Follow-up after treatment is also different from continuous exposure. The six-month dystrophic-mouse experiment provides a long-duration animal observation, but did not establish functional efficacy or long-term human safety (PMID 20126456). Neither an animal treatment period nor short human tolerability studies define a validated fragment cycle.

TITRATION

No starting dose, titration schedule, target exposure or ceiling has been established for Ac-LKKTETQ in humans. Lack of adverse events at one exposure would not identify an effective exposure. The venous ulcer program evaluated different topical concentrations across research cohorts (PMID 17495250, PMID 20536470). The intravenous phase 1 programs likewise evaluated assigned dose cohorts under study monitoring (PMID 20536472, PMID 34346165). These designs are not instructions for individual dose escalation. The absence of dose-limiting toxicity in small, short studies does not establish a wide safety margin. Different molecules, formulations, routes and analytical assays further limit comparisons between programs.

CONTEXT	DOSE	ROUTE	FREQUENCY	PROVENANCE
Historical phase 1 study of full-length synthetic thymosin beta-4 in healthy volunteers	**42, 140, 420 or 1260 mg intravenously once, then the assigned dose intravenously once daily for 14 days after safety review (PMID 20536472).**	Intravenous.	Single-dose phase followed by daily administration for 14 days.	Randomized placebo-controlled study with 40 participants across four cohorts, including placebo recipients. These are reported parent-peptide exposures, not fragment doses. · PMID 20536472
Separate recombinant human thymosin beta-4 phase 1 study, single-dose component	**0.05, 0.25, 0.5, 2, 5, 12.5 or 25 mcg/kg intravenously as a single administration (PMID 34346165).**	Intravenous.	Once.	Randomized double-blind study with 54 participants in the single-dose component. Preparation-specific results cannot be converted into Ac-LKKTETQ dosing. · PMID 34346165
Separate recombinant human thymosin beta-4 phase 1 study, repeated-dose component	**0.5, 2 or 5 mcg/kg intravenously once daily for 10 days (PMID 34346165).**	Intravenous.	Once daily for 10 days.	Randomized double-blind study with 30 participants in the repeated-dose component. This is recombinant thymosin beta-4 research, not TB-500 fragment research. · PMID 34346165
Venous ulcer phase 2 study of topical full-length thymosin beta-4	**0.03 percent topical formulation was associated with an exploratory healing signal; application frequency was not established from the retrieved abstracts (PMID 20536470).**	Topical application to venous ulcers.	Not verified from the retrieved abstracts; the protocol described treatment over 84 days.	The concentration comes from PMID 20536470. The planned treatment duration comes from PMID 17495250. Concentration is not a complete administered mass dose. · PMID 20536470
Severe dry-eye phase 2 study of ophthalmic full-length thymosin beta-4	**0.1 percent ophthalmic solution administered six times daily for 28 days (PMID 25826322).**	Topical ophthalmic.	Six times daily for 28 days, followed by observation through day 56.	Small randomized trial involving nine patients. Day 56 was a follow-up assessment, not evidence of continuous treatment for 56 days. · PMID 25826322
Exploratory rat Achilles tendon repair study using material called TB-500	**60 mcg/kg intraperitoneally once daily for 30 postoperative days in the full methods (PMID 42542926).**	Intraperitoneal.	Once daily beginning on the first postoperative day, for 30 days; the abstract summarizes this as four weeks.	Randomized animal study. Sequence and acetylation were not established in the retrieved methods, so this is not a verified Ac-LKKTETQ regimen. · PMID 42542926
Long-duration full-length thymosin beta-4 study in dystrophin-deficient mice	**150 mcg intraperitoneally twice weekly for six months (PMID 20126456).**	Intraperitoneal.	Twice weekly for six months.	Primary animal study with increased regenerating fibers but no significant improvement in tested strength, cardiac function or fibrosis outcomes. · PMID 20126456

CONTEXT	DOSE	ROUTE	FREQUENCY	PROVENANCE
Reported non-clinical human fragment-use convention	**2 to 2.5 mg subcutaneously twice weekly during an initial period, followed by 2 to 2.5 mg subcutaneously every one to two weeks: commonly cited in non-clinical use; not validated in trials.**	Subcutaneous, as described in non-clinical use.	Twice weekly initially, then every one to two weeks; this is an unvalidated convention.	Commonly cited in non-clinical use; not validated in trials. No identified study establishes this loading pattern, maintenance interval, effective exposure or upper limit. Vendor and forum usage, not evidence: listed so you can recognize it, not follow it; no trial has validated this regimen and it is not a recommendation.

STACKING

+ BPC-157

Investigated pairing, without demonstrated synergy. The rat Achilles tendon study compared each agent, their combination and control. The combination did not show additional benefit on the measured outcomes (PMID 42542926). Small outcome-specific samples and unresolved TB-500 chemical identity limit interpretation. The result neither establishes human benefit nor proves that the agents share one mechanism. No validated human combination dose or duration was identified.

+ GHK-Cu

Hypothetical pairing only. Reviews discuss both agents within tissue-repair research, but discussion in the same review is not a combination experiment (PMID 41476424, PMID 42635865). Proposed matrix-remodeling and migration effects can overlap. No retrieved controlled study establishes an additive effect, compatible formulation or improved human outcome for this pairing.

+ CJC-1295

No demonstrated synergy. Growth hormone signaling and proposed thymosin-related repair mechanisms provide a conceptual rationale, but mechanistic difference does not establish a beneficial interaction (PMID 41966639). No verified human study of this pairing was identified. Additional systemic exposure adds interaction uncertainty and complicates attribution of benefits or adverse events.

+ Ipamorelin

No demonstrated synergy. The sports medicine literature reviews ipamorelin and thymosin-related compounds as separate interventions with major musculoskeletal evidence

– IGF-1 LR3

The concern is theoretical interaction between growth-promoting signaling and proposed migration or angiogenesis effects. Parent thymosin beta-4 cancer studies justify caution, but do not demonstrate a clinical cancer interaction with IGF-1 LR3 (PMID 21621326, PMID 34081824, PMID 36321670). No human combination safety study was identified.

– PEG-MGF

No retrieved evidence establishes benefit, compatibility or a predictable interaction with Ac-LKKTETQ. Combining experimental repair-related compounds adds uncertainty about exposure and adverse-event attribution. A shared marketing category does not establish biological redundancy or synergy. There is no validated human combination protocol in the reviewed evidence.

gaps (PMID 42578445). No retrieved trial validates their combined use. Claims about selectivity or complementary effects do not establish the safety or efficacy of the combination.

SAFETY

COMMON EFFECTS

The frequency and severity of adverse effects from human Ac-LKKTETQ administration are unknown. Injection-site reactions, flushing, fatigue and head-pressure sensations are anecdotal reports, not a reliable incidence dataset or a confirmed causal profile. Full-length synthetic and recombinant thymosin beta-4 phase 1 studies reported predominantly mild or moderate events and no serious adverse events in their limited samples (PMID 20536472, PMID 34346165). Topical and ophthalmic trials also reported generally favorable short-term tolerability within their studied populations (PMID 20536470, PMID 25826322, PMID 36613994). These observations cannot establish fragment tolerability after systemic administration. Both compound-related effects and preparation-related harms remain possible. Lack of symptoms does not establish chemical identity, sterility, absence of endotoxin or absence of delayed toxicity.

SERIOUS SIGNALS

Immunogenicity is a material unresolved concern. The FDA identifies potential risks involving peptide aggregation and peptide-related impurities in compounded thymosin beta-4 fragment preparations. Human studies are insufficient to estimate the likelihood or severity of these outcomes. Cancer-related findings require careful interpretation. Increased endogenous thymosin beta-4 expression promoted migration-related signaling in colon cancer experiments (PMID 21621326). Genetic and transplantation models implicated it in diffuse-type gastric cancer metastasis (PMID 34081824). Higher expression in human thyroid tumors correlated with more advanced disease characteristics (PMID 36321670). These are mechanistic, animal and observational findings. They do not establish that administered Ac-LKKTETQ initiates cancer or quantify a human recurrence risk. Conversely, endogenous occurrence does not establish that additional exposure is harmless. The relevant concern is unresolved activity in susceptible biological contexts. Fibrosis findings also vary by context. A liver review describes different effects of endogenous expression and exogenous parent-peptide treatment (PMID 27450733). A kidney review emphasizes model-dependent findings and unresolved translational issues (PMID 41570941). Neither supports a universal claim that TB-500 prevents scarring or causes fibrosis. A pig study found no cardiac protection in its ischemia-reperfusion model and identified experimental vascular and coagulation effects (PMID 27199757). These observations are not proven human adverse reactions, but further limit broad reassurance based on selected positive experiments.

CONTRAINDICATIONS

There is no approved Ac-LKKTETQ label defining formal contraindications. Active cancer, a cancer history, unexplained masses and proliferative vascular disease warrant particular caution because relevant human safety evidence is absent and parent-peptide mechanisms raise concerns. These are precautionary contexts, not proven fragment-specific contraindications. Pregnancy, breastfeeding and pediatric use lack an established clinical safety basis. Renal or hepatic impairment, immune disorders and concurrent treatments also have no validated fragment-specific dose adjustments or interaction guidance. Known hypersensitivity to a preparation or its ingredients is a reason to avoid re-exposure pending medical assessment. Anti-doping prohibition is a separate eligibility issue rather than a physiological contraindication. Contamination and administration-related infection are additional hazards; they do not replace uncertainty about the peptide itself.

STOP RULES

Breathing difficulty, facial swelling, fainting, chest pain or sudden visual symptoms require urgent medical assessment. Spreading redness, increasing warmth, discharge or fever after administration warrants prompt evaluation for infection or another adverse reaction. A new persistent mass, unexplained bleeding, sustained lymph-node enlargement or unexplained weight loss warrants assessment. These findings do not diagnose peptide-related cancer. Unexpected effects also do not prove adulteration, because allergy, infection, dose error, interactions and unrelated illness remain possible. Worsening pain, swelling, weakness or loss of function requires reassessment of the injury. Reduced pain alone does not establish restored tissue strength. Animal regeneration markers have increased without corresponding functional improvement (PMID 20126456). No validated Ac-LKKTETQ monitoring schedule or laboratory threshold can certify continued use as low risk.

RECONSTITUTION AND STORAGE

TYPICAL VIAL

There is no approved standard vial or validated human-use presentation for Ac-LKKTETQ. A label stating TB-500 does not resolve whether the contents are the acetylated fragment, unacetylated fragment or full-length thymosin beta-4. Chemical identity requires sequence and terminal-modification information supported by suitable analysis. The original analytical identification established Ac-LKKTETQ in the material examined, not in every subsequently marketed preparation (PMID 22962027). A stated vial mass describes nominal content, not a clinically validated dose.

SOLVENT

No universal human-use reconstitution solvent has been established for Ac-LKKTETQ in the retrieved literature. Compatibility depends on the actual peptide, excipients, concentration, container and intended experimental use. Bacteriostatic water does not sterilize contaminated powder, eliminate endotoxin or automatically validate repeated entry into a container. Its preservative also does not establish peptide stability or compatibility. A generic solvent recipe cannot substitute for formulation-specific data.

STORAGE

No independently verified shelf life or post-reconstitution storage period for generic Ac-LKKTETQ preparations was established in this review. Stability depends on formulation, concentration, pH, packaging and handling. A certificate of analysis reports specified test results; it does not automatically establish stability after opening or reconstitution. Cloudiness, particles or discoloration can indicate a problem, but a clear appearance does not establish sterility or chemical stability. Research storage claims require data for the actual preparation. The broader thymosin beta-4 literature identifies peptide stability and delivery as unresolved translational issues (PMID 41570941).

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Illustrative concentration arithmetic only, with no administration route or frequency: a
hypothetical analytical sample containing 5 mg in a final solution volume of 2 mL has a nominal
concentration of 2.5 mg/mL. These quantities are calculation assumptions, not a study dose, drug-
label instruction or human-use recipe.

The relationship is concentration = total mass divided by final solution volume. The word final
matters because added solvent volume and final solution volume are not always identical. A
calculation also assumes the stated mass is accurate and the material dissolves completely.

Syringe markings measure volume according to the device scale. They do not establish peptide
potency or biological activity, and an insulin syringe marking is not an IU of TB-500. There is no
validated TB-500 activity-unit conversion in the reviewed literature.

Correct arithmetic cannot establish chemical identity, delivered exposure, sterility, endotoxin
status or an effective human dose. No draw volume or injection instruction is derived from this
example.
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BUYING NOTES

Identity, purity, quantity, sterility and endotoxin are separate quality questions. Evidence answering one cannot be substituted for evidence answering the others. The original TB-500 identification required mass spectrometry and independent synthesis to establish the acetylated fragment's identity (PMID 22962027). An interpretable analytical report links the tested sample to a specific lot and identifies the sequence, terminal modifications and analytical methods. A chromatographic purity percentage alone does not establish that the dominant peak is Ac-LKKTETQ. It also does not establish the amount of peptide in a container or exclude every impurity. A mass consistent with the expected molecule strengthens identity assessment, but is not a complete evaluation of sequence, stereochemistry, contamination or clinical suitability. Nominal fill mass, peptide content and chromatographic purity can represent different measurements. Reports that do not define these measurements leave important uncertainty. Sterility and endotoxin require appropriate tests and sampling. A visible cake, clean film, sealed container or consistent appearance cannot verify those properties. Laboratory documentation also needs an identifiable sample, methods, dates and a credible connection to the material being described. A preparation supported by parent-peptide eye, skin or cardiac trials still requires evidence that its contents match those studies. Ac-LKKTETQ does not inherit the parent's trial results through a shared name. The rat tendon paper illustrates why published use of the term TB-500 is insufficient without chemical characterization (PMID 42542926). No certificate of analysis establishes human efficacy, an approved indication or an acceptable individual risk. Reviews of this market describe major gaps in clinical evidence and regulatory oversight (PMID 41966639, PMID 42635865). This section describes how documentation is interpreted; it does not identify or endorse a source.

COMMON MISTAKES

- Treating TB-500 as a standardized chemical name. Analytical literature identifies Ac-LKKTETQ, but other sources use the name for different thymosin-related materials. Sequence and terminal modifications determine whether a study applies (PMID 22962027, PMID 42542926).
- Treating unacetylated LKKTETQ, Ac-LKKTETQ and full-length thymosin beta-4 as interchangeable. The aged-mouse fragment study used LKKTETQ, while later acetylated-fragment research identified activity in a metabolite (PMID 12581423, PMID 38382158).
- Transferring ophthalmic or intravenous parent-peptide outcomes to subcutaneous fragment use. Different molecules, formulations, routes and indications require separate evidence. None of the cited parent-peptide trials establishes human tendon recovery with Ac-LKKTETQ.
- Describing the cardiac program as ending at phase 1. A 2025 randomized study included 96 myocardial infarction patients. Its overall infarct-area comparison was not significant, despite a favorable early-treatment subgroup (PMID 41229390).
- Calling a secondary endpoint or subgroup finding a confirmed clinical success. The larger dry-eye study missed its primary endpoints, and the small neurotrophic keratopathy trial had an inconclusive primary comparison (PMID 26056426, PMID 36613994).
- Reporting the dry-eye study as 56 days of treatment. The regimen was 0.1 percent ophthalmic solution six times daily for 28 days, followed by observation through day 56 (PMID 25826322).
- Describing the rat tendon experiment as definitive fragment evidence. Chemical identity was unresolved, each outcome used four animals per group, and assessment occurred at one postoperative time point (PMID 42542926).
- Assuming BPC-157 adds benefit. The small rat study did not demonstrate an additional combination effect. This is neither a validated human stack nor proof that the two agents are pharmacologically redundant (PMID 42542926).
- Quoting one universal half-life or translating between parent-peptide study doses. Separate synthetic and recombinant programs reported different exposures. Neither establishes Ac-LKKTETQ pharmacokinetics after subcutaneous administration (PMID 20536472, PMID 34346165).
- Equating increased regeneration markers with restored performance. Dystrophic mice had more regenerating fibers without significant strength or cardiac-function improvement. Pain relief or laboratory markers alone cannot establish tissue readiness (PMID 20126456).
- Claiming either proven cancer causation or absence of oncologic concern. Existing evidence concerns parent-peptide expression, experimental mechanisms and tumor associations, not measured cancer incidence after human Ac-LKKTETQ exposure (PMID 21621326, PMID 34081824, PMID 36321670).
- Treating a preservative, clear solution or purity percentage as proof of injectable quality. None establishes all of identity, potency, sterility, endotoxin status and stability. Correct concentration arithmetic does not resolve those gaps.
- Assuming endogenous occurrence establishes benefit from additional exposure. Exercise-related release of full-length thymosin beta-4 does not validate fragment administration or prove performance enhancement (PMID 34495765).
- Assuming out-of-competition use is permitted. The current prohibition applies at all times. Analytical detectability and anti-doping eligibility are separate questions from clinical efficacy.

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GHK-Cu (Copper Tripeptide-1)

Copper tripeptide-1

Copper-binding tripeptide | Module 3 · Shielding | Goals: Skin, Recovery | Route: Topical or SC

A copper-binding tripeptide with substantial preclinical research, mixed topical human results, and no established injectable regimen for recovery, muscle growth or skin rejuvenation.

WHAT IT IS

GHK is glycyl-L-histidyl-L-lysine, a naturally occurring tripeptide detected in human plasma, saliva and urine. Its copper(II) complex is GHK-Cu, commonly identified as Copper Tripeptide-1 in cosmetics. Copper-free GHK, GHK-Cu and other copper tripeptides are distinct experimental substances; their results cannot automatically be pooled.

GHK-Cu has been investigated in topical wound formulations and cosmetic products. Research powders marketed for systemic administration do not inherit the evidence supporting those formulations. Module 3, Shielding. Relevant research goals include skin repair, extracellular matrix remodeling and inflammatory signaling. These are research domains, not established indications for injectable treatment (PMID 26236730, PMID 41476424).

MECHANISM

GHK binds copper and influences extracellular matrix turnover in experimental systems. Copper supports enzymes involved in connective tissue biology, including lysyl oxidase. That biochemical role does not establish that additional GHK-Cu improves tissue function in copper-replete humans (PMID 26236730).

Cultured human fibroblasts increased collagen synthesis with GHK-Cu exposure, without a corresponding increase in cell number. The response peaked within the tested concentration range. The investigators also identified a GHK sequence within type I collagen, suggesting possible release during proteolysis. Release at human injury sites and its therapeutic importance remain hypotheses (PMID 3169264).

GHK-Cu increased sulfated glycosaminoglycan synthesis in fibroblast cultures. The response was biphasic, returning toward control levels at higher concentrations. Hyaluronic acid synthesis did not increase. These findings support selective matrix effects, not a general claim that more peptide produces more repair (PMID 1522753).

Rat wound experiments found lower TNF-alpha, MMP-2 and MMP-9 concentrations after topical treatment (PMID 14648529). Mouse lung studies reported changes in inflammatory, antioxidant and fibrosis-related pathways. These included NF-kB, p38 MAPK, Nrf2 and TGF-beta1/Smad2/3 signaling (PMID 27517151, PMID 31809714). A smoke-exposure study linked GHK-Cu effects on mouse muscle to SIRT1-dependent signaling. Its human component measured endogenous GHK associations, not treatment responses (PMID 36905132).

The frequently repeated gene-reset claim comes from computational and cell experiments. Connectivity Map analysis identified GHK as a candidate for reversing an emphysema-associated expression signature. Subsequent fibroblast experiments showed TGF-beta-like expression and matrix remodeling effects (PMID 22937864). This was not evidence that administering GHK-Cu rejuvenates human organs. Different experimental systems show different TGF-beta responses, preventing a simple universal mechanism from being assigned.

EVIDENCE · GRADE C

Grade C applies to systemic recovery, muscle and longevity claims: evidence remains preclinical or insufficient for clinical inference. Topical wound and cosmetic findings require separate assessment. Some topical contexts reach B because controlled human studies exist, but findings are limited, heterogeneous or

inconsistent. A 2026 systematic review included 18 preclinical studies and 2 randomized trials. It reported limited cosmetic benefits alongside substantial methodological limitations (PMID 42619529).

Human data. A randomized, evaluator-blinded diabetic ulcer study reported median percentage reduction in plantar ulcer area of 98.5 percent versus 60.8 percent with vehicle. These are area-reduction results, not percentages of patients achieving complete healing. Infection incidence was 7 percent versus 34 percent in the immediately treated subgroup. Treatment accompanied debridement, pressure-relieving footwear and standardized wound care (PMID 17147644). Among 86 evaluable participants in a venous ulcer trial, copper tripeptide cream did not outperform vehicle (PMID 1495150). A laser-resurfacing trial with 13 completers found no significant between-group differences in objective erythema, wrinkles or skin quality. Patient-reported satisfaction favored GHK-Cu (PMID 16847171). The 2026 aesthetic review also reports wrinkle-volume and wrinkle-depth improvements in included clinical research. Those findings should not be erased, but they do not validate arbitrary commercial formulations or injectable treatment (PMID 42619529). A separate hair study tested a combination of GHK and 5-aminolevulinic acid. It cannot establish GHK-Cu efficacy or isolate GHK's contribution (PMID 27489425). No therapeutic human injection trial supporting musculoskeletal recovery was identified (PMID 41476424).

Animal and mechanistic data. Rat ischemic wounds showed day-13 area reductions of 64.5 percent with active gel, 45.6 percent with vehicle and 28.2 percent untreated. Comparisons against untreated wounds therefore overstate the difference attributable to the active ingredient alone (PMID 14648529). After rat ACL reconstruction, treatment improved knee laxity at 6 weeks. Higher graft stiffness occurred in the lower-concentration group, without significant improvements in ultimate load, gait or histological scores. Between-group benefits were absent at 12 weeks (PMID 25731775). Mouse studies reported reduced inflammatory lung injury, pulmonary fibrosis, smoke-associated muscle dysfunction and Alzheimer-model pathology (PMID 27517151, PMID 31809714, PMID 36905132, PMID 40766919). These disease models do not establish benefits in healthy adults who train. Short experimental observation also cannot establish long-term systemic safety.

REGULATORY STATUS AND SPORT

STATUS

GHK-Cu is used in cosmetics, but cosmetic ingredient use is not approval as a therapeutic drug. No FDA-approved GHK-Cu drug or injectable dosing label was identified. The FDA identifies injectable GHK-Cu as a substance with potential significant safety concerns, including immunogenicity associated with aggregation and peptide-related impurities. Human safety information is limited. Compounding status and cosmetic marketing do not establish drug approval. Country-specific legal status requires separate verification. Source: [FDA safety assessment](https://www.fda.gov/drugs/human-drug-compounding/certain-bulk-drug-substances-use-compounding-may-present-significant-safety-risks).

WADA

GHK-Cu is not explicitly named in the 2026 Prohibited List. However, S0 prohibits pharmacological substances without governmental approval for human therapeutic use when other sections do not address them. Injectable GHK-Cu used as an unapproved pharmacological treatment therefore falls within the S0 prohibition on that reading. This is application of the general rule, not a compound-specific WADA ruling located during verification. Absence from the named examples does not establish permission, and cosmetic availability does not establish therapeutic approval. Source: [WADA 2026 Prohibited List, S0](https://www.wada-ama.org/sites/default/files/2025-09/2026list_en_final_clean_september_2025.pdf).

RESEARCH USE · REPORTED, NOT RECOMMENDED

ROUTES

Human interventional evidence concerns topical formulations. Rodent experiments include intra-articular, intraperitoneal and intranasal administration. No validated subcutaneous regimen for human recovery or cosmetic benefit was identified. In one laboratory study, almost no peptide or copper crossed intact human skin during the observation period. Microneedle pretreatment increased passage, but this does not establish clinical efficacy or justify extrapolation across formulations (PMID 25690343).

HALF-LIFE

Human GHK-Cu pharmacokinetics and an applicable elimination half-life are not established by the retrieved studies. An intravenous rat study found rapid degradation of GHK to His-Lys and rapid

metabolite elimination. It studied GHK and does not provide a human subcutaneous GHK-Cu half-life (PMID 9187381). Topical effects also depend on formulation, penetration and local stability.

TIMING

Immediate initiation after debridement mattered in the diabetic ulcer trial, alongside standardized wound care (PMID 17147644). This does not establish timing around exercise or injury for systemic administration. The disappearance of rat graft differences at later follow-up does not prove that continued treatment would preserve benefit (PMID 25731775).

CYCLE LENGTH

No validated human injection cycle or treatment break exists. Laser-resurfacing outcomes were assessed at 12 weeks (PMID 16847171). The distinct GHK combination hair trial lasted 6 months (PMID 27489425). Four to 8 weeks of subcutaneous daily use is commonly cited in non-clinical use; not validated in trials. Neither duration establishes an effective or tolerable systemic exposure.

TITRATION

No validated human titration scheme was identified. Biphasic fibroblast responses support caution when interpreting concentration-response relationships, but cannot define human dose ceilings (PMID 1522753). Cell-culture concentrations cannot be converted directly into subcutaneous doses. Dose escalation, maintenance dosing and biomarker targets remain unestablished.

CONTEXT	DOSE	ROUTE	FREQUENCY	PROVENANCE
Diabetic neuropathic ulcers with standardized wound care	**Metered topical gel quantity; concentration and mass per application were not provided in the retrieved abstract, PMID 17147644.**	Topical application to the debrided wound	Daily; treatment beginning immediately after initial debridement produced the reported optimal response	Human randomized trial, PMID 17147644. An exact dose cannot be reconstructed from the abstract. · PMID 17147644
Venous stasis ulcers; no advantage over vehicle	**0.4 percent copper tripeptide cream, equivalent to 4 mg/g if expressed by mass, PMID 1495150.**	Topical	Not specified in the retrieved abstract	Human randomized trial, PMID 1495150. Concentration is reported; application quantity and frequency were not verified. · PMID 1495150
Ischemic open wounds in rats	**2 percent copper tripeptide gel, equivalent to 20 mg/g if expressed by mass, PMID 14648529.**	Topical	Once daily for 13 days	Animal experiment, PMID 14648529. Concentration is not the mass delivered per wound. · PMID 14648529
Rat ACL reconstruction; transient improvements in selected mechanical outcomes	**0.3 mg/mL or 3 mg/mL GHK-Cu solution; injection volume was not provided in the retrieved abstract, PMID 25731775.**	Intra-articular	Once weekly for 4 weeks, beginning at postoperative week 2	Animal experiment, PMID 25731775. These are solution concentrations, not established human doses. · PMID 25731775
Pretreatment before experimentally induced mouse lung injury	**1 mg/kg or 10 mg/kg per administration, PMID 27517151.**	Intraperitoneal	Every 24 hours for 3 days before the inflammatory challenge	Animal experiment, PMID 27517151; dosing verified in the methods. Source: [Park study] (https://pmc.ncbi.nlm.nih.gov/articles/PMC5295439/). · PMID 27517151

CONTEXT	DOSE	ROUTE	FREQUENCY	PROVENANCE
Transgenic mouse model of Alzheimer's disease	**15 mg/kg per administration, PMID 40766919.**	Intranasal	Three times weekly for 3 months	Animal experiment, PMID 40766919. No human cognitive-treatment regimen is established. · PMID 40766919
See the references and the safety section for what is documented.	**1 to 2 mg subcutaneously once daily; commonly cited in non-clinical use; not validated in trials.**	Subcutaneous	Once daily; commonly cited in non-clinical use; not validated in trials	Commonly cited in non-clinical use; not validated in trials. Included as an unvalidated claim, not a recommended or independently established dosing standard. Vendor and forum usage, not evidence: listed so you can recognize it, not follow it; no trial has validated this regimen and it is not a recommendation.

STACKING

+ TB-500
No clinical synergy with GHK-Cu is established. Repair-related mechanisms discussed for these compounds do not demonstrate combined benefit. Evidence for full-length thymosin beta-4 also cannot automatically be assigned to TB-500 (PMID 41476424).

+ BPC-157
Separate preclinical repair findings do not establish an effective combination. GHK-Cu rat graft results cannot validate a human combination protocol. No controlled combination trial was identified (PMID 25731775, PMID 41476424).

+ Argireline
No controlled combination study was identified. Separate cosmetic rationales cannot establish additive benefit, skin penetration or formulation compatibility.

+ KPV
No controlled combination study was identified. GHK-Cu inflammatory-pathway findings in experimental models do not establish synergy with another peptide (PMID 27517151).

– IGF-1 LR3
Combined efficacy, exposure and safety are uncharacterized. Growth-signaling concerns are theoretical; there is no verified clinical interaction study establishing cancer promotion by this combination.

– PEG-MGF
No validated combination regimen or interaction evidence was identified. Uncertain biological activity and product quality prevent a reliable benefit-risk assessment.

SAFETY

COMMON EFFECTS
Topical irritation or sensitivity is plausible, including reactions to other formulation ingredients. The retrieved trials do not establish reliable adverse-event frequencies. Injection-site reactions are described in non-clinical use, but controlled human rates are unavailable. A small trial or brief animal experiment cannot exclude uncommon or delayed harms.

SERIOUS SIGNALS
Injectable concerns include immunogenicity, impurities, contamination and uncertain copper exposure. Copper accumulation risk depends on chemical composition, dose, route and clearance; an oral dietary upper limit cannot establish injectable tolerability. Copper-free GHK suppressed immune responses in a rodent experiment, which is not proof of clinical immunosuppression from GHK-Cu (PMID 12447473). Angiogenic and matrix-signaling effects warrant research attention in malignancy, but a human cancer-risk estimate is unavailable.

CONTRAINDICATIONS
No approved injectable label defines formal contraindications. Important precautionary contexts include Wilson disease or other copper-handling disorders, known hypersensitivity to ingredients, pregnancy and lactation. Severe liver disease and active malignancy require particular caution

	because systemic exposure is poorly characterized. Nickel allergy alone is not an established GHK-Cu contraindication. Anti-doping restrictions are separate from medical contraindications.
STOP RULES	Hives, blistering, progressive redness, painful swelling or nodules warrant discontinuation and clinical assessment. Breathing difficulty, facial swelling or systemic illness require urgent care. Jaundice or dark urine also warrant prompt assessment.

RECONSTITUTION AND STORAGE

TYPICAL VIAL	There is no approved standard injectable vial presentation. Research powder packaging does not establish identity, peptide content, copper stoichiometry, sterility or suitability for human administration. GHK-Cu salts and formulations may have different gross molecular masses. A universal copper mass fraction cannot be assumed from a product name.
SOLVENT	No validated human injectable formulation or reconstitution protocol was identified. Water solubility alone does not establish suitable pH, osmolality, preservative compatibility, sterility or stability. Chelators and reducing agents can alter copper coordination, but compatibility must be demonstrated for the complete formulation. Separate topical products are not equivalent to mixing ingredients in one container.
STORAGE	No universal storage temperature or beyond-use period for reconstituted injectable GHK-Cu was verified. Stability depends on formulation, container, light, temperature, preservatives and handling. A clear blue appearance cannot establish chemical stability or sterility. Color changes, cloudiness or particles indicate a quality concern but cannot identify the mechanism. Storage requirements need formulation-specific stability evidence.

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Concentration arithmetic can be illustrated using the topical cream reported in PMID 1495150. A 0.4 percent mass-based formulation corresponds to 0.4 g per 100 g, or 4 mg/g. This describes formulation strength, not an application dose. The retrieved abstract does not verify application quantity or frequency. Similarly, the rat solutions in PMID 25731775 were reported in mg/mL; without injection volume, delivered mass cannot be determined. No human injection calculation follows from either study. Body-surface-area scaling cannot validate an untested human regimen or establish equivalent tissue exposure.
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BUYING NOTES

A cosmetic ingredient list identifies declared ingredients, not necessarily their concentration, penetration or clinical performance. A certificate of analysis is meaningful only when its batch, laboratory, methods and tested sample are traceable. Mass spectrometry can support identity; chromatography assesses purity under specified conditions. Neither alone establishes net peptide content, copper content, sterility or endotoxin control. High chromatographic purity is not synonymous with injectable quality. Blue color does not verify identity, and a research-use label is not evidence of approval or suitability.

COMMON MISTAKES

- Treating all GHK, GHK-Cu and other copper-tripeptide studies as interchangeable.
- Reporting percentage ulcer-area reduction as the percentage of patients whose ulcers healed completely (PMID 17147644).
- Ignoring the vehicle response when quoting rat wound-healing results (PMID 14648529).
- Calling cosmetic evidence nonexistent despite limited randomized findings summarized in the 2026 review (PMID 42619529).
- Assuming topical wound findings establish human injection benefits or a systemic dose.
- Interpreting loss of a later between-group difference as proof that indefinite treatment is necessary or effective (PMID 25731775).
- Converting cell concentrations or animal doses into a self-administration protocol without human pharmacokinetic and safety data.
- Treating appearance, refrigeration or a purity certificate as proof of sterile, stable injectable material.

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KPV

Lys-Pro-Val, alpha-MSH 11-13

C-terminal alpha-MSH tripeptide | Module 3 · Shielding | Goals: Gut, Recovery | Route: Oral or SC

The three amino acid tail of alpha-MSH, studied for anti-inflammatory effects in cells and animals, with no published human treatment trial identified.

WHAT IT IS

KPV is the C-terminal tripeptide of alpha-melanocyte-stimulating hormone, corresponding to residues 11 to 13. Its sequence is lysine-proline-valine. The unmodified free tripeptide has a molecular weight of approximately 342.44 Da. Names in the literature include Lys-Pro-Val and alpha-MSH(11-13).

Researchers investigated this fragment because it retained anti-inflammatory activity in experimental systems without the pigmentary activity associated with the parent hormone. This rationale is described in the review by Brzoska and colleagues, PMID 18612139. It does not establish that KPV reproduces all beneficial effects of alpha-MSH, or that its human safety profile is better.

KPV lacks the His-Phe-Arg-Trp core associated with conventional melanocortin receptor activation. Experimental findings support mechanisms distinct from those of the parent hormone. However, the available experiments do not establish the absence of every possible receptor interaction in every tissue. Mechanistic conclusions belong to the tested cells and animal models.

Chemical identity matters. Unmodified KPV, Lys-D-Pro-Val, Lys-D-Pro-Thr, and terminally modified forms such as Ac-KPV-NH2 are distinct preparations. Lys-D-Pro-Val contains a different proline stereochemistry. Lys-D-Pro-Thr also changes the terminal amino acid. The review discusses KdPT in relation to an interleukin-1 beta sequence. Acetylation and amidation alter terminal chemistry, charge, molecular mass, and potentially biological behavior. Evidence for one preparation cannot automatically establish another preparation's effects.

Module 3. Research relevance: intestinal inflammation and local tissue repair. Neither exercise recovery nor body recomposition has an established human benefit. The strongest rationale concerns experimental intestinal inflammation, where uptake and delivery have been investigated directly.

MECHANISM

Melanocortin receptor independence is supported in specific experimental systems. In crystal-induced mouse peritonitis, KPV reduced neutrophil accumulation despite an MC3R/MC4R antagonist. Its anti-inflammatory activity also persisted in mice with nonfunctional MC1R. KPV did not increase macrophage cAMP in the tested assay, PMID 12750433.

That study also contains a limitation missing from broad summaries. KPV did not inhibit the measured macrophage activation responses under conditions where the comparator melanocortin peptides did. The findings therefore do not support universal suppression of activated macrophages. The authors proposed interference with interleukin-1 beta functions, but did not identify a single binding target explaining all KPV activity.

PepT1 provides a better characterized entry mechanism in intestinal models. This proton-coupled transporter carries dipeptides and tripeptides. It is expressed in the small intestine and can be upregulated in inflamed colonic tissue. Transport into a cell is different from demonstrated oral bioavailability throughout a living human body.

The intestinal study demonstrated uptake and anti-inflammatory activity in PepT1-expressing Caco2-BBE cells and Jurkat cells. HT29-Cl.19A cells initially lacked the relevant transporter and did not show the same response. Introducing PepT1 restored responsiveness. Competing transporter substrates reduced the effect. This distinction is central to interpreting the experiment, PMID 18061177. [Dalmasso study full text] (https://pmc.ncbi.nlm.nih.gov/articles/PMC2431115/)

Within those experimental conditions, KPV reduced activation of NF-kappaB and MAP kinase pathways and reduced inflammatory cytokine output. These are measurements in cultured cells. They do not establish a human anti-inflammatory dose, intestinal tissue concentration, or clinical response.

A separate mouse study strengthens the transporter hypothesis. In chemically induced colitis-associated cancer, KPV reduced tumorigenesis in wild-type mice. The corresponding inhibitory effect was absent in PepT1 knockout mice, PMID 27458604. This supports transporter dependence in that model. It does not prove that all KPV effects require luminal intestinal delivery, or that systemic administration cannot reach relevant cells.

An airway epithelial study investigated another part of the mechanism. KPV activity was associated with nuclear entry, stabilization of IkappaB-alpha, and reduced nuclear translocation of p65 RelA. Competition experiments implicated the interaction between p65 and importin-alpha 3, PMID 22837805. The proposed blockade of nuclear import is supported by that cell system, but has not been validated as a universal mechanism in humans.

Local repair may involve additional pathways. In rabbits with experimentally abraded corneas, a nitric oxide synthase inhibitor reduced KPV's wound-healing effect, PMID 16965771. This suggests nitric oxide involvement in that setting. It does not establish a general nitric oxide mechanism for intestinal disease, skin repair, or exercise recovery.

The defensible conclusion is that KPV has several experimentally supported anti-inflammatory actions. Their relative importance depends on tissue, stimulus, peptide preparation, and delivery. Human target engagement, exposure-response relationships, and clinically meaningful outcomes remain unestablished.

EVIDENCE · GRADE C

Grade C reflects positive animal findings without identified human treatment evidence. Human cell lines, blood samples, and excised skin provide mechanistic or delivery information, not clinical efficacy. The evidence is strongest for experimental intestinal inflammation and formulation-dependent local delivery. It does not establish treatment of inflammatory bowel disease, wound healing, training recovery, or longevity in people. Mechanistic detail increases biological plausibility but cannot determine whether a human dose produces benefit.

Human data. Searches included KPV, Lys-Pro-Val, and alpha-MSH(11-13), with additional clinical and pharmacokinetic terms. This is a search finding, not proof that every possible unpublished or unindexed exposure has been excluded. Human intestinal epithelial and Jurkat cell experiments investigated PepT1-dependent uptake and inflammatory signaling, PMID 18061177. Immortalized bronchial epithelial cells were used to investigate NF-kappaB nuclear import and chemokine secretion, PMID 22837805. Neither study administered KPV to patients. An older study exposed blood collected from people with HIV to melanocortin peptides, including alpha-MSH(11-13), and measured cytokine production. This was an experiment on blood samples, not treatment of the participants, PMID 9700761. Its separate experiments on normal peripheral blood mononuclear cells used the full alpha-MSH peptide. Those findings should not be silently reassigned to KPV. Excised human skin was used to examine delivery with microneedles and iontophoresis, PMID 28343991. The study measured peptide passage and retention under laboratory conditions. It did not establish symptom improvement, wound healing, or tolerability in living participants. The review by Brzoska and colleagues

Animal and mechanistic data. Intestinal inflammation is the most developed application in the verified literature. One study found improvements in DSS colitis and CD45RBhi transfer colitis in mice. Outcomes included body weight recovery, inflammatory histology, and colonic myeloperoxidase activity. KPV also improved survival in the study's MC1R-deficient DSS group, PMID 18092346. These findings concern particular experimental models and cannot establish outcomes in human inflammatory bowel disease. Another study administered KPV in drinking water and reported reduced inflammatory findings in DSS and TNBS mouse colitis, PMID 18061177. The result supports an oral experimental route, while leaving actual human absorption and dosing unresolved. In an AOM/DSS model of colitis-associated cancer, KPV reduced tumorigenesis in wild-type mice. Its inhibitory effect was absent in PepT1 knockout mice, PMID 27458604. These results support the role of PepT1 in that experimental system. They do not establish cancer prevention, treatment, or compatibility with cancer therapy in humans. Delivery studies provide a separate line of evidence. Colon-targeted nanoparticles achieved similar efficacy to free KPV at a reported 12,000-fold

discusses therapeutic development of KPV and related tripeptides, PMID 18612139. Its proposed indications remain development hypotheses rather than demonstrated human benefits. Evidence involving a dimer, a stereochemical analogue, or the parent hormone does not change the clinical evidence grade for KPV.

lower concentration in a mouse colitis model, PMID 19909746. Hyaluronic acid-functionalized nanoparticles improved targeting and reduced mucosal damage and inflammatory measures in another mouse study, PMID 28143741. These comparisons concern specific formulations and cannot be used as universal potency multipliers. Outside the gut, a single intraperitoneal administration reduced secondary brain lesion volume and neuronal apoptosis after controlled cortical impact in mice. Microglial morphology suggested reduced activation. TNF-alpha and IL-1 beta expression, and the total number of Iba-1-positive cells, were not reduced, PMID 23940690. This narrower description matters because the results do not show uniform suppression of brain inflammation. Topical KPV accelerated corneal epithelial repair after abrasion in rabbits, PMID 16965771. A rectally administered hydrogel improved TNBS colitis in rats, PMID 34547895. A mucoadhesive formulation improved experimental oral mucositis in rats, PMID 34846053. The mucositis formulation also contained an active antibacterial component, so its combined effects cannot all be assigned to KPV. Overall, the verified studies support further investigation of local delivery and inflammatory models. They do not validate a general-purpose recovery peptide or establish a human subcutaneous regimen.

REGULATORY STATUS AND SPORT

STATUS

KPV is an investigational substance without an identified approved human therapeutic indication. No FDA-approved KPV drug label was identified. FDA's July 2026 compounding advisory materials reported no identified clinical studies or human exposure data adequate to evaluate its clinical use. Discussion by a compounding advisory committee is not drug approval. [FDA July 2026 compounding evaluation](https://www.fda.gov/media/193773/download) Compounded preparations and research materials can appear in commerce without being approved drugs. Compounding eligibility is a separate legal question, dependent on jurisdiction and current rules. An advertisement, prescription, or certificate of analysis does not demonstrate marketing authorization or clinical efficacy. The available verification does not justify categorical claims about every regulator worldwide, every marketing application, or every country's supplement law. The supported description is unapproved investigational KPV, with no established human treatment regimen.

WADA

KPV falls under the S0 non-approved substances rule on the basis of its investigational pharmacological status and absence of identified human therapeutic approval. It should be treated as prohibited at all times, in and out of competition. This classification applies the S0 rule; it is not a claim that KPV is individually named in the list. The 2026 rule covers pharmacological substances without current governmental approval for human therapeutic use when they are not addressed by subsequent sections. Absence from the list by name does not establish permission. Research labeling and compounded availability do not themselves supply the therapeutic approval required by that rule. [WADA 2026 Prohibited List](https://www.wada-ama.org/sites/default/files/2025-09/2026list_en_final_clean_september_2025.pdf)

RESEARCH USE · REPORTED, NOT RECOMMENDED

ROUTES

Oral delivery has direct support in mouse colitis experiments, including drinking-water exposure and engineered colon-targeted systems, PMIDs 18061177, 19909746, and 28143741. These are different delivery formats. A free peptide solution, ordinary capsule, hydrogel, and nanoparticle preparation cannot be assumed to provide equivalent exposure. Rectal delivery has been studied using a stabilizing hydrogel in rat colitis, PMID 34547895. Topical ophthalmic delivery was studied

after corneal abrasion in rabbits, PMID 16965771. A mucoadhesive formulation was evaluated on oral mucosal wounds in rats, PMID 34846053. These findings involve different barriers, local conditions, and formulation components. Intraperitoneal administration appears in systemic animal experiments, including the mouse brain injury study, PMID 23940690. Intraperitoneal exposure is not equivalent to subcutaneous exposure. Its presence also means that the literature cannot accurately be described as exclusively local or exclusively oral. No validated human subcutaneous pharmacokinetic or outcome study was identified. Consequently, neither its effectiveness nor its inferiority to oral administration has been established in people. In excised human skin, passive permeation was below the assay's detection limit. Microneedles and iontophoresis increased delivery, PMID 28343991. That finding applies to the tested experimental conditions. It does not demonstrate that every cream is ineffective, or that enhanced transdermal delivery is clinically effective.

HALF-LIFE

No established human plasma half-life was identified. The verified literature also does not provide a validated animal plasma half-life that can support a human dosing interval. Molecular size, theoretical susceptibility to peptidases, and transporter uptake cannot substitute for a measured concentration-time profile. Three separate concepts are often conflated: chemical stability in a container, persistence in blood or tissue, and duration of a biological response. They require different experiments. A change in inflammatory signaling after exposure does not reveal how long intact KPV remains in circulation. The brain injury study used a single 1 mg/kg intraperitoneal dose in mice, administered 30 minutes after injury, PMID 23940690. Later histological findings demonstrate a biological consequence of that exposure. They do not establish peptide residence time or justify a human interval between doses. An analytical study identified degradation during acid, alkaline, and oxidative stress, PMID 25298219. This supports chemical instability under tested stress conditions. It cannot establish a universal refrigerated shelf life, a plasma half-life, or a reliable expiry period for a different formulation.

TIMING

No human timing study was identified. Animal administration followed each experimental model, including continuous drinking-water exposure and treatment after a defined injury. Those designs cannot establish a preferred time of day for human use. PepT1 also transports dietary peptides. Competition experiments therefore provide a mechanistic reason to investigate whether food changes KPV uptake. They do not establish that fasting improves outcomes, or define an interval separating KPV from protein-containing meals. No validated fed-versus-fasted human regimen was identified. Local exposure introduces additional timing questions. Contact time, release rate, tissue injury, and clearance may affect delivery independently of the clock. A formulation designed to remain on a mucosal wound cannot be equated with a rapidly cleared solution. The available studies support investigation of these variables, not a general timing rule.

CYCLE LENGTH

No human treatment cycle is established. Animal experiments followed the duration of their disease or injury models, and the brain injury experiment used a single administration. These designs do not determine the duration needed for chronic human symptoms. Descriptions of 2 to 4 week courses are commonly cited in non-clinical use; not validated in trials. There is no established evidence that such a course improves benefit, reduces harm, prevents tolerance, or permits a particular interval before repeated exposure. No validated taper, maintenance schedule, receptor-reset interval, or treatment-free period was identified. The absence of documented tolerance does not demonstrate that repeated exposure preserves benefit or avoids adverse effects.

TITRATION

No clinical dose-response relationship, maximum tolerated dose, or validated titration schedule exists for KPV. Animal efficacy and cell concentration-response experiments cannot define a human starting dose or escalation rule. The nanoparticle result shows that formulation can substantially change experimental performance, PMID 19909746. It does not demonstrate that delivery always matters more than mass, or that the reported relative concentration difference applies to other formulations. Both administered quantity and delivery characteristics matter, but neither is characterized sufficiently for human titration. Symptoms alone also provide a weak basis for interpreting exposure. Fluctuating gastrointestinal symptoms can reflect disease activity, diet, infection, other medicines, or expectation. Without a controlled study and verified preparation, improvement cannot establish a dose-response relationship. Worsening symptoms cannot distinguish ineffective treatment from an adverse effect without clinical evaluation.

CONTEXT	DOSE	ROUTE	FREQUENCY	PROVENANCE
Mouse DSS colitis, drinking-water experiment	**100 micromolar KPV in drinking water, approximately 34.2 mcg/mL when calculated using the unmodified free tripeptide molecular weight. Oral exposure was continuous for 8 days in the DSS experiment, PMID 18061177.**	Oral, through drinking water	Continuous access for 8 days in the DSS experiment	Dalmasso G, Gastroenterology, 2008, PMID 18061177. The full text reports the molar concentration. The mass concentration is an arithmetic conversion, not a measured daily intake. · PMID 18061177
Mouse controlled cortical impact traumatic brain injury	**1 mg/kg by intraperitoneal injection, once, 30 minutes after injury, PMID 23940690.**	Intraperitoneal	Single administration 30 minutes after injury	Schaible EV, PloS one, 2013, PMID 23940690. This is an animal study dose, not a human recommendation. · PMID 23940690
Rabbit corneal epithelial wound healing after mechanical abrasion	**KPV solutions of 1, 5, or 10 mg/mL, administered topically to the eyes as two drops four times daily for 4 days, PMID 16965771. The abstract also specifies a volume of 0.03 mL, without unambiguously defining whether it applies to each drop or the complete instillation.**	Topical ophthalmic	Two drops four times daily for 4 days, starting immediately after abrasion	Bonfiglio V, Experimental eye research, 2006, PMID 16965771. Concentrations and schedule are directly reported. Total mass per instillation is not assigned because the abstract's volume wording is ambiguous. · PMID 16965771
Mouse DSS colitis with colon-targeted nanoparticle delivery	**The study reports comparable efficacy at a KPV concentration 12,000-fold lower than free solution. This is a formulation comparison, not an absolute administered dose, PMID 19909746.**	Oral, using nanoparticles incorporated into an alginate-chitosan hydrogel	The exact administration schedule was not verified from the retrieved abstract	Laroui H, Gastroenterology, 2010, PMID 19909746. The abstract verifies the relative concentration comparison but does not establish an independently reproducible dosing schedule. · PMID 19909746
Non-clinical dosing range retained for recognition of circulating claims	**200 to 500 mcg by subcutaneous administration once daily, commonly cited in non-clinical use; not validated in trials.**	Subcutaneous	Once daily in the cited non-clinical convention	commonly cited in non-clinical use; not validated in trials. No PubMed study validating this human range, frequency, or route was identified. Vendor and forum usage, not evidence: listed so you can recognize it, not follow it; no trial has validated this regimen and it is not a recommendation.

STACKING

+ BPC-157

Proposed overlap concerns intestinal inflammation and tissue repair. No verified study establishes additive or synergistic benefit from KPV combined with BPC-157. Separate experiments involving either compound cannot determine the combination's exposure, effectiveness, or adverse effects. A shared target organ does not establish that the compounds improve the

– LL-37

No direct interaction study was verified. Labeling the pair a proven directional conflict overstates what can be inferred from separate immune-signaling experiments. This is an uncharacterized combination, with no established benefit or compatibility. A change in symptoms during simultaneous exposure would not reliably identify which compound, preparation, or underlying disease process caused it.

	same outcome or complement one another.
+ TB-500	No verified evidence supports combining KPV with TB-500 for injury recovery. Claims about complementary inflammation and repair pathways are insufficient to establish synergy. Evidence involving full-length thymosin beta-4 cannot automatically be assigned to preparations described as TB-500. Peptide identity, formulation, and measured outcomes would need to match before even the individual evidence could support a combination hypothesis.
+ GHK-Cu	A topical combination with GHK-Cu is a proposed formulation concept, not a clinically established synergy. No verified KPV and GHK-Cu combination study supports improved skin repair. Mixing compounds can change stability, penetration, and local tolerability. The excised-skin study of KPV does not validate a combined cream, and the rabbit corneal findings do not establish effectiveness on intact human skin.
+ ARA-290	Different proposed anti-inflammatory pathways do not establish useful complementarity. No verified evidence supports KPV combined with ARA-290 for inflammatory or neuropathic symptoms. Different molecular targets can still produce overlapping downstream effects or unanticipated interactions. Neither additive benefit nor excessive immune suppression has been demonstrated for this pair. The combination remains a research question.
– Thymosin Alpha-1	No verified study establishes antagonism or compatibility between KPV and thymosin alpha 1. Classifying one as an immune activator and the other as an immune suppressor is too coarse to predict clinical effects. Their combination cannot be described as balancing immunity. Its consequences for infection, inflammatory disease, and concurrent immune-directed treatment remain unknown.
– Melanotan II	A relationship to alpha-MSH does not establish a shared mechanism or justify a combination. KPV's experimental activity differs from conventional melanocortin receptor agonism. No verified study demonstrates added benefit or characterizes interactions with melanotan II. This is a lack-of-evidence warning, not a demonstrated drug interaction or proof that adverse effects would be impossible to attribute.

SAFETY

COMMON EFFECTS

Common adverse effects cannot be established because controlled human safety data are lacking. No reliable incidence is available for headache, nausea, diarrhea, skin irritation, or injection-site reactions attributable specifically to KPV. Unverified reports cannot distinguish the peptide from formulation ingredients, contamination, other exposures, or the underlying illness. The reviewed animal efficacy experiments do not establish a human safety margin. Normal appearance, preserved body weight, or favorable cell viability in an experiment is not equivalent to systematic toxicology. Route, exposure duration, tissue distribution, and formulation can change risk. Lack of pigmentary activity is part of KPV's experimental rationale, PMID 18612139. It does not demonstrate that every preparation has identical effects, or that a product labeled KPV cannot cause pigmentary changes through misidentification or other ingredients. It also does not establish the absence of unrelated adverse effects.

SERIOUS SIGNALS

No reliable human incidence or well-characterized KPV-specific serious adverse event pattern was identified. Limited exposure documentation and surveillance prevent meaningful reassurance from an absence of reports. The effects of sustained inflammatory-pathway modulation on infection control, wound responses, and immune function remain unknown. NF-kappaB participates in these processes, but cell-level inhibition does not establish clinically important immunosuppression at an unmeasured human exposure. Infection risk is therefore an unresolved concern, not a quantified adverse effect. Antibacterial activity has been reported for terminally modified KPV-related peptides in laboratory assays, PMID 18355945. Such findings do not establish treatment of infection or offset potential immune-related risks. The verified mucositis hydrogel also contained an antibacterial component, further limiting attribution of its antimicrobial effect to KPV, PMID 34846053. Separate risks arise from preparation quality and administration. Nonsterile material, endotoxin, residual chemicals, incorrect identity, and concentration errors can cause harm independently of the intended molecule. Injectable preparations introduce risks of abscess, cellulitis, and systemic infection. The available evidence does not quantify which risk is largest for KPV. Potential allergic or immune reactions are also uncharacterized. A small peptide size or familiar amino acid sequence does not establish that a specific preparation cannot trigger a reaction.

CONTRAINDICATIONS

There is no approved KPV label establishing formal contraindications. Pregnancy, breastfeeding, use in children, significant organ impairment, and prolonged exposure lack adequate safety evidence. These are populations or circumstances with unresolved risk, rather than trial-defined contraindications. Active or suspected infection requires particular caution because KPV's effects on human host defense are unknown. Concurrent immunosuppressive or other immune-directed therapy introduces unstudied interactions. A mechanistic hypothesis does not establish either a contraindication or compatibility with a particular medicine. Active cancer or a cancer history requires disease-specific clinical assessment. Reduced tumorigenesis in an inflammation-driven mouse model does not establish cancer protection or permission for use during oncology treatment, PMID 27458604. Known hypersensitivity to a preparation or its ingredients is relevant. A preservative allergy applies to formulations containing that preservative, not automatically to the KPV molecule. Anti-doping prohibition is an additional eligibility restriction for tested athletes, separate from medical contraindications.

STOP RULES

Breathing difficulty, throat tightness, fainting, or swelling of the lips, tongue, or face requires emergency care and no further exposure. A new generalized rash also warrants stopping exposure and prompt assessment. Fever, chills, or spreading redness, warmth, pain, swelling, or discharge after an injection requires urgent medical evaluation. These symptoms can indicate infection or another serious reaction and should not be assumed to represent ordinary local irritation. New or worsening gastrointestinal symptoms require assessment rather than dose escalation. Blood in the stool, unexplained weight loss, persistent nighttime symptoms, dehydration, or fever can indicate disease requiring diagnosis and treatment. A symptom tracker can document when changes occurred, but cannot establish whether KPV caused them. The product identity, route, timing, other medicines, and accompanying symptoms are useful clinical information. Improvement after stopping exposure may help assessment but does not by itself prove causation.

RECONSTITUTION AND STORAGE

TYPICAL VIAL

No approved KPV vial presentation or standardized clinical package exists. Research packaging varies, and package mass is not a dose. A nominal amount on a container does not establish the amount of intact peptide, its salt content, or its suitability for human administration. For the unmodified free tripeptide, the approximate molecular weight is 342.44 Da. Acetylated or amidated forms require different mass calculations. Counterions and water content can also affect the relationship between weighed material and actual peptide content. KPV and Lys-D-Pro-Val have the same nominal elemental composition despite differing in stereochemistry. An expected molecular mass alone therefore cannot distinguish them. A short sequence is easier to describe chemically, but that does not remove the need for identity testing. The amount supplied should be interpreted as inventory information. It does not establish a validated reconstitution volume, concentration, route, schedule, or treatment duration. No clinical inference follows from one package containing more material than another.

SOLVENT

No validated human KPV reconstitution solvent was identified. Animal and analytical studies used preparations suited to their experimental purpose. Those methods do not establish that a particular diluent is appropriate for an injectable, oral, topical, or ophthalmic human preparation. Bacteriostatic water is not a sterilization process. A preservative does not remove endotoxin, synthesis residues, particles, or an incorrect peptide. It also does not convert research-grade material into a validated multidose medicine. Compatibility and microbiological control require evidence for the actual formulation and container. Solubility alone is insufficient. A clear solution can still have inappropriate pH, osmolarity, concentration, contamination, or degradation.

Conversely, adding a solvent without visible precipitation does not establish chemical stability or retained biological activity. The rabbit ophthalmic experiment used a controlled topical preparation and a phosphate-buffered saline vehicle control, PMID 16965771. That experiment does not authorize substituting an injectable diluent for an eye preparation. Route-specific formulation requirements remain separate from elementary concentration arithmetic.

STORAGE

No universal KPV storage temperature, refrigerated shelf life, or post-reconstitution expiry was established by the verified references. Stability depends on peptide form, solvent, pH, concentration, container, and environmental exposure. A storage statement for one preparation cannot automatically be applied to another. The stability-indicating HPLC study separated KPV from degradation products in aqueous solutions and skin homogenates. Under acid, alkaline, and hydrogen peroxide stress, it identified lys-pro-diketopiperazine as a major degradation product, PMID 25298219. Forced degradation supports analytical method development and identifies vulnerabilities. It does not reproduce every ordinary storage condition or define an expiry period. A rectal hydrogel study reported improved stability and retained experimental activity compared with solution under its tested conditions, PMID 34547895. That supports the formulation's research rationale. It does not validate storage claims for a different solution or package. Visible cloudiness, discoloration, or particles can identify a failed preparation, but visual clarity cannot demonstrate acceptable potency or microbiological quality. Chemical degradation, microbial contamination, and endotoxin are different problems. A single appearance check cannot exclude them. Validated storage and expiry information would need to come from testing of the actual preparation.

This is a hypothetical laboratory concentration calculation, not a preparation or administration procedure. A sample containing 10 mg of actual peptide in a final total solution volume of 5 mL has a concentration of 2 mg/mL. That equals 2,000 mcg/mL. The example assumes verified peptide content and complete dissolution.

Final volume matters. The calculation uses the total solution volume, not an assumption that any stated added volume necessarily equals the final volume. It also assumes the mass refers to peptide content rather than a mixture of peptide, counterion, water, and other material.

A second hypothetical sample containing 5 mg in a final total volume of 5 mL has a concentration of 1 mg/mL. The concentration is half that of the first example. These numbers illustrate dilution arithmetic only. They are not study doses, human exposure targets, or evidence that either preparation is suitable for any route.

The mouse drinking-water experiment provides a different kind of quantity. It reported 100 micromolar KPV with continuous oral access for 8 days in the DSS experiment, PMID 18061177. Using the unmodified free tripeptide molecular weight gives approximately 34.2 mcg/mL. This is a calculated solution concentration. Actual daily intake would also require the amount consumed by each animal and the relevant body weight.

The corneal study reported topical solutions of 1, 5, or 10 mg/mL, administered as two drops four times daily for 4 days, PMID 16965771. Concentration alone does not identify the mass administered. The abstract's accompanying 0.03 mL volume is not sufficiently explicit to assign a definitive mass per complete instillation.

These examples distinguish package mass, solution concentration, administered volume, and actual exposure. Each answers a different question. A calculator can check arithmetic when the inputs are correct. It cannot verify identity, sterility, stability, absorption, tissue delivery, or whether an exposure benefits a human.

No syringe marking conversion or self-administration procedure is established by these examples. There is no validated human KPV regimen to which such a procedure could be anchored.

BUYING NOTES

Quality assessment begins with the precise substance being described. A name such as KPV does not disclose terminal modifications, stereochemistry, counterion, water content, or the amount of intact peptide. These details can change how analytical results and published studies should be interpreted.

A useful certificate of analysis identifies the batch, tested sample, sequence, chemical form, methods, dates, and responsible laboratory. The sample identifier must connect the analytical report to the material being evaluated. A document describing another batch does not establish the characteristics of the current one.

Mass spectrometry supports identity by examining molecular ions and, where performed, fragmentation. The neutral molecular mass and an instrument's measured mass-to-charge value are not interchangeable. The

report should specify the ion assignment rather than merely display a number near the expected molecular weight.

Mass alone cannot distinguish every relevant alternative. KPV and its D-proline stereoisomer require methods capable of addressing stereochemistry. Similarly, a sequence claim may require information beyond a single intact-mass peak. Analytical identity is strongest when complementary methods address different possible errors.

HPLC area percent describes the relative detector response of resolved peaks under the stated method. It is not automatically peptide content by weight, and it does not establish sterility or acceptable endotoxin. An actual chromatogram, method description, integration information, and suitable standards make the result more interpretable.

Counterion testing, residual solvent testing, water determination, peptide content, microbial quality, and endotoxin address different questions. Passing one does not imply passing the others. An endotoxin result does not establish sterility, and a sterility result does not exclude endotoxin.

Independent testing can reduce reliance on unsupported paperwork, but it is not absolute verification. Its value depends on chain of custody, representative sampling, validated methods, laboratory competence, and access to the original results. Independence alone does not make an incomplete assay conclusive.

No analytical certificate establishes clinical efficacy or a human dosing schedule. Low manufacturing cost also does not establish that adulteration is unlikely. Identity, potency, contamination, formulation performance, and clinical evidence remain separate uncertainties.

COMMON MISTAKES

- Treating KPV as an established melanocortin receptor agonist because it is a fragment of alpha-MSH. The peritonitis and cell experiments support distinct mechanisms in the tested systems, PMID 12750433. They do not establish tanning, appetite suppression, or another conventional melanocortin-mediated clinical effect. Structural ancestry does not substitute for receptor pharmacology.
- Combining evidence for unmodified KPV, terminally modified KPV, Lys-D-Pro-Val, KdPT, or a dimer as if they were one preparation. Chemical modifications can change properties without changing the informal name used in a summary. Molecular mass alone cannot distinguish KPV from its D-proline stereoisomer. Exact identity is necessary before a study can support a claim.
- Describing all human-origin research as human clinical evidence. Cultured cells, blood exposed outside the body, and excised skin answer mechanistic or delivery questions. They do not show that treated people improve. The blood-sample study, PMID 9700761, is especially easy to misread because its title refers to patients even though the experiment treated their collected blood.
- Claiming subcutaneous administration necessarily bypasses every relevant mechanism. PepT1 dependence supports a cellular uptake pathway, while the intestinal literature provides a rationale for local delivery. Neither establishes the fate of subcutaneously administered KPV in humans. The supported conclusion is that human subcutaneous exposure and outcomes remain uncharacterized.
- Quoting a precise half-life or choosing a repeated dosing interval from the timing of an animal outcome. Chemical stability, pharmacokinetics, and biological response duration are separate measurements. A later difference in lesion size does not show that the peptide remained in circulation until that assessment.
- Applying the nanoparticle study's 12,000-fold concentration comparison to ordinary capsules, creams, or injectable preparations. The result belongs to a specific formulation and mouse model, PMID 19909746. It does not establish a universal potency conversion, and concentration is not the same as total administered mass or exposure at the target tissue.
- Assuming antimicrobial benefit offsets unknown infection risk. Laboratory antibacterial findings for modified peptides do not establish treatment of infection in humans, PMID 18355945. Formulations containing other active ingredients also require careful attribution. Antimicrobial activity, immune modulation, and clinical infection outcomes cannot be treated as interchangeable endpoints.
- Reading absence from the WADA list by name as permission. The S0 rule addresses unapproved pharmacological substances without requiring individual naming. A research label, prescription, or

compounding discussion does not itself establish governmental approval for human therapeutic use. Anti-doping eligibility remains separate from the quality of a preparation.

- Treating clear appearance, refrigeration, or a high HPLC area percentage as a complete quality assessment. These observations cannot establish identity, concentration, sterility, endotoxin, or a validated expiry. The stability study identifies stress-related degradation but does not supply a universal home-storage rule, PMID 25298219.
- Using a plausible mechanism to explain away persistent or worsening symptoms. Blood in the stool, unexplained weight loss, nighttime symptoms, fever, or dehydration require clinical assessment. A tracker may help document the course, but neither the tracker nor an unapproved peptide establishes the diagnosis.

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LL-37

Cathelicidin

Human antimicrobial peptide | Module 3 · Shielding | Goals: Immune, Recovery | Route: SC (research)

A human cathelicidin peptide with formulation-specific clinical trials, mixed wound-healing results, and no established subcutaneous protocol for immunity, training recovery or performance.

WHAT IT IS

LL-37 is the active 37 amino acid fragment of hCAP18, the precursor protein encoded by the human CAMP gene. Humans have one cathelicidin gene, but the precursor and its processed peptides are not interchangeable terms. LL-37 starts with two leucines and contains 37 residues. Its sequence is LLGDFFRKSKEKIGKEFKRIVQRIKDFLRNLVPRTES, with a molecular mass of approximately 4.5 kDa.

The peptide is cationic and amphipathic. Its positive charge and distribution of water-attracting and water-repelling regions influence membrane binding, molecular association and biological activity. These properties contribute to antimicrobial effects, but also to damage in mammalian cells under experimental conditions. Endogenous origin does not establish the tolerability of an administered preparation (PMID 10417311).

Neutrophils and epithelial cells produce hCAP18. Proteolytic processing releases LL-37, which participates in host defense and inflammatory signaling. Experiments demonstrate recruitment of immune cells, endothelial activation and keratinocyte migration. These functions make the description antimicrobial peptide accurate but incomplete (PMID 11015447, PMID 12782669, PMID 16177113).

Human wound research provides an important biological foundation. In sampled healing wounds, hCAP18 expression peaked approximately 48 hours after injury and declined with closure. Chronic ulcer edge epithelium lacked detectable hCAP18/LL-37 immunoreactivity in that study. Antibodies against LL-37 also inhibited re-epithelialization in an organ-cultured human skin model. These findings support involvement in wound repair, without proving that administered peptide improves every type of wound (PMID 12603850).

Names require care when reading references. CAMP identifies the gene, hCAP18 identifies the precursor, and LL-37 identifies a processed peptide. CRAMP is the murine counterpart with a different sequence. A mouse deficiency experiment does not directly test human LL-37 treatment.

Formulation matters equally. A topical wound preparation, an intratumoral investigational preparation and engineered bacteria producing LL-37 represent different exposures. Their results cannot be transferred automatically to research powder or subcutaneous administration.

MECHANISM

LL-37 has overlapping membrane, receptor and nucleic-acid interactions. Their relative importance depends on concentration, cell type, surrounding proteins and experimental conditions. The evidence does not establish a universal concentration boundary separating beneficial signaling from tissue injury.

Direct membrane effects are well documented experimentally. LL-37 interacts with negatively charged membranes and can disrupt their organization. Oren and colleagues also demonstrated cytotoxicity toward normal eukaryotic cells and hemolytic activity in vitro. Their membrane measurements supported a detergent-like mechanism rather than a conventional channel-forming model. The N-terminal region contributed to hemolysis and proteolytic resistance, without being essential for antimicrobial activity in their comparisons (PMID 10417311).

That study also described equilibrium between monomers and oligomers at low concentrations, together with resistance to proteolysis under the tested conditions. These observations explain aspects of laboratory behavior. They do not establish an injectable therapeutic window, a human plasma half-life or irreversible aggregation after routine handling (PMID 10417311).

Immune-cell recruitment involves receptor signaling. LL-37 induced chemotaxis and calcium mobilization in human monocytes and cells expressing FPRL1, now commonly called FPR2. Cross-desensitization experiments supported receptor involvement. Human neutrophils and T lymphocytes also migrated toward the peptide. Recruitment of immune cells demonstrates biological activity, not a general improvement in immune function (PMID 11015447).

Endothelial experiments linked FPR2 signaling to proliferation and vessel-like structures. Related work demonstrated neovascularization in a chorioallantoic membrane assay and a rabbit hind-limb ischemia model. Reduced wound vascularization in CRAMP-deficient mice supported a physiological contribution from cathelicidins. These findings establish an experimental angiogenic role, without demonstrating exercise recovery benefits (PMID 12782669).

Keratinocyte migration involves another pathway. LL-37 activated heparin-binding EGF-dependent EGFR transactivation and downstream STAT3 signaling in cultured cells. Inhibitors and dominant-negative constructs interrupted the response. This is mechanistic support for re-epithelialization, rather than proof that every administered formulation produces the same effect (PMID 16177113).

Mast-cell recruitment and degranulation are distinct processes. An experimental chemotaxis study implicated a Gi protein and phospholipase C pathway, with findings arguing against FPRL1 as the relevant mast-cell receptor. Separate work demonstrated LL-37 activation of MRGPRX2-associated calcium signaling and mast-cell degranulation. These mechanisms make inflammatory and allergic-type reactions plausible, but do not establish their frequency after subcutaneous exposure (PMID 11972628, PMID 33101278).

LL-37 also binds self-DNA and forms complexes that reach endosomal compartments in plasmacytoid dendritic cells. These complexes can activate TLR9 and stimulate type I interferon production. Lande and colleagues identified this pathway in psoriasis research. It is an important contributor to disease biology, not a complete explanation of psoriasis or proof that every exposure triggers disease (PMID 17873860).

In lipopolysaccharide-primed macrophages, LL-37 promoted P2X7-associated internalization, lysosomal destabilization and NLRP3 inflammasome activation. Intradermal exposure produced rosacea-like inflammation in mice, with marked attenuation in NLRP3-deficient animals. The priming conditions and species matter when interpreting these results (PMID 33745908).

Another endothelial pathway involves COX-1, prostaglandin E2 and EP3 signaling. Experimental inhibition reduced angiogenic responses. This creates concern about context-dependent effects in tumor biology, but angiogenesis alone does not prove that administered LL-37 causes cancer (PMID 23766266).

None of these mechanisms establishes an effective subcutaneous dose for healthy adults seeking recovery, body recomposition or fewer infections.

EVIDENCE · GRADE A

Grade A reflects the supplied scale's criterion of multiple human randomized trials. It describes the existence of clinical study designs, not regulatory approval or consistently demonstrated benefit. Human results are formulation-specific and mixed. The larger venous ulcer trial did not demonstrate an overall healing benefit, while smaller wound studies reported favorable signals. Subcutaneous use for immunity, training recovery or performance has no supporting human trial identified in this review. Those application claims remain unsupported, with at most grade C preclinical rationale. An overall A must not be displayed as proof of efficacy for those goals.

Human data. The human literature extends beyond the two venous ulcer trials. At least three randomized topical wound studies and a randomized study of an engineered oral bacterial formulation were identified. Their populations, formulations and endpoints differ substantially. The initial venous ulcer study enrolled 34 patients. Topical LL-37 at 0.5, 1.6 or 3.2 mg/mL was applied twice weekly for 4 weeks after a placebo run-in (PMID 25041740). The lowest concentration produced a healing rate constant approximately six

Animal and mechanistic data. Animal studies provide evidence of activity in particular disease models. They do not establish benefits in healthy people or validate a human regimen. Cirioni and colleagues studied three rat models of gram-negative sepsis. LL-37 was administered intravenously at 1 mg/kg as a single treatment under each experimental schedule (PMID 16641434). Treatment reduced lethality and bacterial growth relative to controls. Endotoxin and TNF-alpha measurements were lower

times the placebo estimate. The intermediate concentration produced an approximately threefold estimate, but its comparison with placebo was not conventionally significant, with p = 0.088. The highest concentration did not improve healing relative to placebo. Reported mean ulcer-area reductions were 68 percent and 50 percent in the two lower-concentration groups. These were healing predictors in a small trial, not proof of complete wound closure or systemic benefit. The phase IIb study reported 148 treated participants. Topical LL-37 at 0.5 or 1.6 mg/mL was applied twice weekly for up to 13 weeks alongside compression therapy (PMID 34687253). The overall analysis did not demonstrate significant improvement in healing compared with placebo. A post hoc subgroup with wounds of at least 10 cm2 showed favorable results across related healing measures. Because this analysis followed the main comparison, it requires prospective confirmation. Calling the study pivotal or treating the subgroup as confirmed efficacy overstates the evidence. A 2023 diabetic foot ulcer study randomized 25 participants to LL-37 cream or placebo. The methods reported a topical cream concentration of 0.5 mg/g, applied twice weekly for 4 weeks (PMID 37480520). Granulation index improved more with LL-37 at measured visits. Differences in inflammatory markers and aerobic bacterial colonization did not establish the proposed anti-inflammatory or antimicrobial benefits. This was a small study of mildly infected diabetic ulcers, with a different formulation and disease context from venous ulcers. A separate 2023 randomized, open-label, single-center study enrolled 238 hospitalized adults with an Omicron SARS-CoV-2 infection. Its oral intervention contained recombinant Lactococcus lactis producing LL-37. Earlier treatment was associated with faster viral RNA negative conversion, and no severe adverse events were reported during the assessed period. This formulation-specific result does not demonstrate absorption or effectiveness of swallowed purified LL-37. Viral RNA conversion also does not establish improved exercise recovery or broad infection prevention (PMID 37605995). Intratumoral human exposure is documented in a melanoma phase 1 case report. A patient received eight weekly injections, with shrinkage of injected lesions followed by a widespread skin eruption. Previous immunotherapy and chemotherapy complicate causal interpretation. The report provides a clinically relevant toxicity signal, but cannot estimate incidence or establish melanoma efficacy (PMID 29665030). No human trial identified here tested subcutaneous LL-37 for body composition, performance, routine immune support or recovery after training. Studies measuring endogenous LL-37 during other than with some antibiotic comparators. Antimicrobial and antiendotoxin effects did not differ significantly from polymyxin B in the reported comparisons. These findings concern severe experimentally induced infection, not preventive immune enhancement. Angiogenesis experiments demonstrated activity in rabbit ischemia and other vascular models. CRAMP-deficient mice also showed reduced wound vascularization. These observations support a role in repair biology, but replacement of a missing endogenous function differs from adding peptide to an intact system (PMID 12782669). In a vaccinia study, pox lesions developed in four of six CRAMP-deficient mice and one of fifteen controls. Cell-based experiments also supported antiviral activity. The knockout comparison concerns susceptibility associated with cathelicidin deficiency, without establishing an LL-37 treatment protocol for people (PMID 14734759). Adverse biological effects appear in animal research as well. Intradermal LL-37 produced rosacea-like inflammation involving NLRP3, while separate work demonstrated prostaglandin-dependent angiogenesis (PMID 33745908, PMID 23766266). The direction of an effect therefore depends on the disease model, tissue and exposure. A biologically active peptide can support repair in one setting and amplify inflammation in another.

interventions do not constitute trials of administered LL-37.

REGULATORY STATUS AND SPORT

STATUS

LL-37 remains investigational in the clinical sources reviewed. No approved human LL-37 drug label was identified for the applications described here. Trial participation and publication do not establish marketing authorization, an approved indication or a labeled dose. The FDA identifies cathelicidin LL-37 on its page covering bulk substances used in compounding that may present significant safety risks. Its concerns include potential immunogenicity, peptide-related impurities and difficulties characterizing the active pharmaceutical ingredient. The agency states that safety information is insufficient. It also notes nonclinical findings involving male reproduction and protumorigenic effects in some tissues. These are regulatory concerns, not quantified human risks. The venous ulcer phase IIb result does not establish that all LL-37 development stopped or that every possible application lacks benefit. Later topical and oral formulation studies demonstrate why that inference would be incorrect (PMID 34687253, PMID 37480520, PMID 37605995). Research use only labeling does not establish suitability for administration to people. Conversely, the wording alone cannot prove exactly how a particular batch was manufactured or tested. Legal status depends on jurisdiction, intended use and applicable drug rules. Blanket claims about every country's approval system or all possible sales circumstances are not supported by this review.

WADA

LL-37 is prohibited at all times as a non-approved pharmacological substance under the S0 framework. The 2026 List applies S0 to substances without governmental approval for human therapeutic use when another prohibited class does not already address them. Source: [2026 WADA Prohibited List, S0](https://www.wada-ama.org/sites/default/files/2025-09/2026list_en_final_clean_september_2025.pdf). LL-37 is not named individually in the List. This classification applies the published category to its investigational status; it is not a compound-specific WADA ruling retrieved in this review. Absence from the examples does not indicate permission. Nor does an endogenous sequence, a research label or a route of administration establish an exception. The earlier blanket exclusion of S2 was unjustified because that section includes broad biological categories. The practical status remains prohibited, without offering any testing or clearance guidance.

RESEARCH USE · REPORTED, NOT RECOMMENDED

ROUTES

Documented human research includes topical wound formulations, intratumoral administration and an oral formulation using recombinant bacteria that produce LL-37. These exposures should be described separately (PMID 25041740, PMID 34687253, PMID 37480520, PMID 29665030, PMID 37605995). Intravenous administration appears in rat sepsis research. Intradermal administration appears in mouse inflammation models (PMID 16641434, PMID 33745908). Neither establishes a human route for routine immune or recovery goals. No relevant human subcutaneous trial was identified. Human efficacy for ordinary purified LL-37 administered intranasally or by nebulization was also not established by the retrieved studies. Oral delivery cannot be dismissed categorically, because an engineered bacterial formulation has human trial data. That finding does not establish systemic bioavailability of unformulated peptide powder.

HALF-LIFE

No validated human pharmacokinetic half-life for subcutaneous LL-37 was identified in the searches performed. The available clinical reports do not establish a concentration-time profile that supports an injection interval for fitness applications. Laboratory resistance to proteolysis and monomer-oligomer equilibrium were documented under specific experimental conditions. These findings cannot supply a human elimination half-life or a duration of action (PMID 10417311). Endogenous peptide measurements, disappearance from an experimental solution and terminal elimination after an administered drug are different measurements. A numerical half-life needs a named preparation, route, species, assay and study. Without those details, a circulation-time claim cannot support a dosing schedule. The absence of a retrieved measurement is not proof that every published pharmacokinetic experiment is nonexistent.

TIMING

Twice-weekly application in the venous ulcer studies reflected the wound-care schedule. The phase IIb protocol coordinated applications with dressing changes and compression therapy (PMID 25041740, PMID 34687253). No retrieved evidence supports a fasting requirement, a preferred time of day or a relationship to exercise for subcutaneous LL-37. Earlier treatment relative to infection onset mattered in the oral bacterial formulation study, but that is a different clinical question. It cannot establish meal timing or training timing for purified peptide (PMID 37605995).

CYCLE LENGTH

Clinical treatment duration depends on the indication and formulation. The initial topical venous ulcer study treated for 4 weeks, with 4 weeks of follow-up. The phase IIb topical study treated for up to 13 weeks and included a subsequent observation period (PMID 25041740, PMID 34687253). The diabetic ulcer cream study treated for 4 weeks (PMID 37480520). The melanoma case involved

eight weekly intratumoral administrations, with an eruption beginning approximately 45 days after initiation (PMID 29665030). These durations describe studies. They do not establish a subcutaneous cycle, a maximum tolerated duration or a period during which adverse effects cannot occur. The timing of one case cannot define a general toxicity threshold.

TITRATION

No validated subcutaneous titration scheme was identified. In the initial venous ulcer trial, topical concentrations of 0.5, 1.6 and 3.2 mg/mL were each administered twice weekly for 4 weeks (PMID 25041740). The lowest concentration produced the strongest healing-rate signal, and the highest did not outperform placebo. This finding argues against assuming a simple linear dose-response relationship. It does not prove that increasing concentration caused membrane toxicity in those participants. The larger trial also failed to confirm an overall benefit at the lower concentrations (PMID 34687253). Receptor signaling, membrane effects and tissue exposure provide possible explanations for nonlinear responses. They do not establish an escalation algorithm, an optimal systemic exposure or a rescue strategy after a poor response.

CONTEXT	DOSE	ROUTE	FREQUENCY	PROVENANCE
Phase I/IIa randomized placebo-controlled study in 34 adults with hard-to-heal venous leg ulcers.	**0.5, 1.6 or 3.2 mg/mL, applied topically to ulcers twice weekly for 4 weeks, study concentrations reported in PMID 25041740.**	Topical application to the wound bed.	Twice weekly for 4 weeks, after a 3-week placebo run-in, followed by 4 weeks of observation.	Grönberg 2014, PMID 25041740. Concentrations describe the studied preparation, not a fixed amount per person. The lowest concentration produced the strongest healing-rate signal; the highest did not improve healing relative to placebo. · PMID 25041740
Phase IIb randomized placebo-controlled venous ulcer study with 148 treated participants and compression therapy.	**0.5 or 1.6 mg/mL, applied topically twice weekly at 0.025 mL/cm2, corresponding to 12.5 or 40 mcg/cm2 per application, PMID 34687253.**	Topical polyvinyl alcohol formulation applied to the wound bed.	Twice weekly, approximately every 3 days with protocol flexibility of 1 day, for up to 13 weeks.	Mahlapuu 2021, PMID 34687253, full-text treatment protocol. Amount depended on wound area. The full population did not show significant healing improvement compared with placebo. · PMID 34687253
Randomized double-blind study in 25 adults with mildly infected diabetic foot ulcers.	**The methods report 0.5 mg/g cream, applied topically twice weekly for 4 weeks at 0.025 mL/cm2 of wound area, PMID 37480520.**	Topical cream applied to the ulcer.	Twice weekly for 4 weeks.	Miranda 2023, PMID 37480520, full-text formulation and intervention sections. Concentration is reported by cream mass, while application volume is reported by wound area. Conversion to peptide mass per application would require formulation density. The paper also contains inconsistent concentration units elsewhere, so these reported quantities are not silently harmonized. · PMID 37480520
Published toxicity case from an intratumoral phase 1 melanoma study.	**The retrieved abstract does not provide an amount per injection. No numerical dose is assigned.**	Intratumoral injection.	Weekly, eight injections reported.	Dolkar 2018, PMID 29665030. Injected lesions shrank, followed by a widespread eruption with atypical squamous proliferation. Lesions resolved within approximately 2 months after treatment cessation. · PMID 29665030

CONTEXT	DOSE	ROUTE	FREQUENCY	PROVENANCE
Randomized study of an oral recombinant bacterial formulation in hospitalized adults with SARS-CoV-2 infection.	**The retrieved abstract does not provide a reproducible dose or peptide output. No mcg or mg equivalent is inferred.**	Oral recombinant Lactococcus lactis producing LL-37.	Administration frequency was not established from the retrieved abstract.	Zhao 2023, PMID 37605995. This was a formulation-specific intervention. Its dose cannot be translated into an amount of purified LL-37 from the available abstract. · PMID 37605995
Adult male Wistar rats in three experimental gram-negative sepsis models.	**1 mg/kg intravenously as a single treatment under the relevant experimental schedule, animal study dose reported in PMID 16641434.**	Intravenous.	Single administration immediately after challenge or surgery; an additional surgical-model experiment evaluated a single administration delayed by 6 hours.	Cirioni 2006, PMID 16641434, full-text methods. The study does not establish a human-equivalent regimen or a repeated treatment schedule. · PMID 16641434
Mouse model of LL-37-induced rosacea-like inflammation.	**The retrieved abstract does not state an amount per administration. No numerical dose is inferred.**	Intradermal.	Not established from the retrieved abstract.	Yoon 2021, PMID 33745908. Included to document inflammatory effects of local experimental exposure, not therapeutic dosing. · PMID 33745908
Non-clinical subcutaneous use for immune support, training recovery or performance.	**No validated dose or independently verified numerical range was identified.**	Subcutaneous, discussed in non-clinical use without a supporting human protocol identified here.	No validated administration frequency or treatment duration.	No regulatory label or relevant human trial identified. Unreferenced circulating schedules do not establish exposure, efficacy or tolerability.

STACKING

+ GHK-Cu

No verified LL-37 plus GHK-Cu combination study was identified. LL-37 wound and cell-migration findings do not establish additive effects from another topical peptide. Different mechanisms are insufficient to predict compatibility, efficacy or tolerability.

+ BPC-157

No clinical evidence identified here supports combined use for wound, tendon or gut recovery. Separate repair-related hypotheses cannot establish the outcome of simultaneous exposure. The absence of a known shared receptor also cannot establish the absence of an interaction. There is no supported combined dose, route or schedule.

+ TB-500

No verified LL-37 combination evidence supports improved tissue repair. Mechanisms attributed to full-length thymosin beta-4 cannot automatically be assigned to every preparation

– IGF-1 LR3

There is no documented clinical interaction established here. LL-37 has experimental angiogenic activity, creating a theoretical concern around additional growth-promoting exposures. This is a precautionary rationale in people with malignancy concerns, not evidence that the combination causes cancer (PMID 12782669, PMID 23766266).

– Melanotan II

No direct interaction study was identified. Concurrent exposures associated with skin changes could complicate assessment of a new lesion. The LL-37 melanoma case supports attention to widespread eruptions and atypical squamous proliferation, without proving an interaction with MT-2 (PMID 29665030).

– PT-141

No verified pharmacokinetic or clinical interaction was identified. Multiple simultaneous exposures can complicate

	described as TB-500. This proposed pairing has no established clinical benefit or interaction profile in the retrieved evidence.
+ KPV	The claim that KPV counterbalances LL-37 inflammation is untested. LL-37-related inflammasome and mast-cell findings do not show that another peptide prevents those effects. Symptom suppression would not establish control of underlying tissue injury. No verified combination experiment supports this protective rationale (PMID 33745908, PMID 33101278).
+ Thymosin Alpha-1	Evidence for thymosin alpha-1 in separate indications cannot establish a benefit from adding LL-37. No verified combination study was identified for routine immune support or fitness recovery. An immune-related mechanism is too broad to establish complementary clinical effects.

	attribution of flushing or allergic-type symptoms. LL-37 mast-cell activation provides a mechanistic concern, but does not establish the incidence or severity of a combined reaction (PMID 33101278).

SAFETY

COMMON EFFECTS

The frequency of adverse effects after subcutaneous LL-37 is unknown. Redness, itching, wheals, burning and flushing are mechanistically plausible, but cannot be presented as measured common effects from a clinical injection cohort. Experimental mast-cell chemotaxis and MRGPRX2 activation support plausibility, not incidence estimates (PMID 11972628, PMID 33101278). The initial venous ulcer trial did not identify local or systemic safety concerns during its limited follow-up. The phase IIb trial described acceptable tolerability for its topical preparations (PMID 25041740, PMID 34687253). Those observations apply to selected participants, wound-care formulations and monitored treatment schedules. Small studies cannot reliably exclude uncommon events. Topical tolerability also cannot establish tolerability after subcutaneous or intravenous administration. Formulation, excipients, impurities and route may change the adverse-effect profile. No severe adverse events in the oral bacterial study likewise cannot establish the safety of purified peptide administered by another route (PMID 37605995).

SERIOUS SIGNALS

The clearest retrieved human injection signal is a widespread eruption during intratumoral melanoma treatment. Approximately 45 days after initiation, the patient developed verrucous papules and a vesiculobullous lesion. Eleven of twelve biopsies showed lichenoid inflammation with atypical squamous epithelial proliferation. Lesions had features resembling keratoacanthoma or squamous malignancy clinically. They resolved within approximately 2 months after treatment stopped (PMID 29665030). This was one patient with advanced melanoma and previous systemic cancer treatments. The temporal relationship and resolution support concern, but do not prove a general cancer-causing effect or establish reaction frequency. The pathology should not be summarized as confirmed skin cancer caused by LL-37. Autoimmune and inflammatory mechanisms provide additional concerns. LL-37 can deliver self-DNA to TLR9-containing compartments and promote interferon responses relevant to psoriasis (PMID 17873860). It also produces NLRP3-dependent inflammatory responses in experimental rosacea models (PMID 33745908). These findings support caution in susceptible populations, without quantifying the probability of a human flare after administration. Direct membrane toxicity and hemolysis were demonstrated in laboratory experiments. They identify potential hazards, rather than a documented frequency of hemolysis in treated people (PMID 10417311). No retrieved study maps an effective systemic exposure against those hazards for subcutaneous use. The FDA additionally identifies potential immunogenicity and peptide-characterization concerns. Its assessment cites nonclinical reproductive and tissue-specific tumor concerns. These regulatory signals reinforce uncertainty; they do not provide a numerical human risk estimate.

CONTRAINDICATIONS

There is no approved LL-37 label establishing formal contraindications. The following are precautionary clinical concerns, not validated prescribing criteria. Psoriasis and rosacea warrant particular concern because LL-37 participates in relevant inflammatory pathways. Other interferon-associated autoimmune conditions, including lupus, also require individualized assessment rather than extrapolation from wound trials. The magnitude of any additional risk remains unmeasured (PMID 17873860, PMID 33745908). Active malignancy, suspicious skin lesions and a history of skin cancer require specialist assessment. The peptide's experimental angiogenic activity and the reported eruption justify caution, but do not establish universal tumor-promoting effects (PMID 12782669, PMID 23766266, PMID 29665030). Mast-cell disorders, recurrent urticaria and previous severe allergic-type drug reactions are additional concerns given the experimental activation pathways (PMID 33101278). Pregnancy, breastfeeding, pediatric exposure and effects on fertility lack adequate clinical evidence for the uses described here. Active infection requires established clinical evaluation and treatment. LL-37 research does not establish a substitute for antimicrobial treatment, wound management or urgent assessment of suspected sepsis.

STOP RULES

A new widespread eruption, warty or crusted papules, blistering, or a changing skin lesion warrants stopping the investigational exposure and prompt clinical assessment. The reported melanoma case demonstrates why examination and sometimes biopsy may be needed (PMID 29665030). New scaly plaques, persistent facial inflammation or worsening inflammatory skin disease also warrant assessment. These symptoms cannot be diagnosed from the peptide's proposed mechanism alone. Persistent pain, expanding redness, warmth, drainage or fever may indicate infection rather than a harmless local reaction. Breathing difficulty, throat or tongue swelling, fainting or rapidly spreading hives require emergency care. Unexplained systemic illness also warrants medical evaluation. These are precautionary response rules, not a validated LL-37 monitoring protocol. Lack of symptoms during early exposure does not establish longer-term tolerability. Reducing an amount or adding another peptide has not been shown to control an emerging adverse reaction.

RECONSTITUTION AND STORAGE

TYPICAL VIAL

No approved vial strength or standardized human injectable presentation was identified. Research packaging varies, and the physical appearance of a powder cannot verify its identity or amount. A stated powder mass may refer to peptide content or material that includes counterions, water and other components. The reporting basis must be explicit. It is incorrect to assume that every preparation contains a fixed percentage of active peptide or that all labels report gross rather than net mass. The clinical wound formulations were prepared for specific research protocols. A vial bearing the same sequence name does not establish equivalence in formulation, stability, sterility or release testing.

SOLVENT

No validated diluent or home preparation method for human subcutaneous LL-37 was identified. Bacteriostatic water cannot be designated the appropriate solvent merely because it contains a preservative. Compatibility, peptide integrity, container interactions and microbial control require formulation-specific evidence. The phase IIb venous ulcer study used a polyvinyl alcohol formulation. The diabetic ulcer study used a cream. Neither provides a preparation protocol for a human injectable solution (PMID 34687253, PMID 37480520). Preservatives do not sterilize contaminated starting material or remove endotoxin. Claims that routine agitation necessarily causes irreversible LL-37 aggregation were not established by the cited structural study. That paper examined molecular association under experimental conditions, not a validated preparation process (PMID 10417311).

STORAGE

No universal storage temperature, refrigerated lifetime or post-reconstitution use period can be assigned from the retrieved evidence. Storage depends on the actual formulation, container, concentration, analytical stability data and microbiological controls. The structural study's observations about oligomers and proteolytic resistance do not establish a shelf life (PMID 10417311). Stability testing of a particular cream cannot establish stability of an aqueous injectable preparation (PMID 37480520). Visible cloudiness, particles or discoloration indicate a preparation requiring investigation. They do not identify the underlying cause. Conversely, a clear solution does not establish sterility, purity or retained biological activity. A validated laboratory protocol would define handling limits and acceptance criteria for its own material. Generic peptide-storage advice cannot replace that evidence, and a preservative does not establish a multiweek usable lifetime.

The phase IIb wound protocol illustrates the distinction between concentration and delivered amount without requiring an injection example. It applied topical LL-37 at 0.5 mg/mL twice weekly using 0.025 mL/cm2 of wound area, equivalent to 12.5 mcg/cm2 per application (PMID 34687253).

The same study applied topical LL-37 at 1.6 mg/mL twice weekly using the same 0.025 mL/cm2 application volume, equivalent to 40 mcg/cm2 per application (PMID 34687253). These are documented

wound-area doses from the trial, not recommended doses for another route.

The calculation multiplies solution concentration by application volume per unit wound area. A concentration alone does not specify total administered peptide, because total amount also depends on the treated area. Neither value provides a systemic dose or establishes how much peptide reaches circulation.

The diabetic ulcer paper reports cream concentration by mass and application quantity by volume. Those units cannot be converted into a reliable peptide amount without additional formulation information. Treating mg/g and mg/mL as interchangeable would introduce an unsupported assumption (PMID 37480520).

No syringe-unit conversion or research-vial preparation is supplied because no validated human subcutaneous protocol was identified.

BUYING NOTES

A certificate of analysis can characterize a batch, but it cannot establish clinical suitability or efficacy. Relevant distinctions include identity, purity, peptide content, formulation and microbial quality. These are separate questions requiring appropriate methods.

Identity testing should establish that the material corresponds to LL-37 rather than merely another peptide with a similar label. Mass spectrometry supports molecular identification, while additional characterization may be needed to distinguish related impurities. Appearance and dissolution behavior are not identity tests.

Chromatographic purity is the proportion of measured signal assigned to selected components under a particular method. It is not automatically the percentage of the container's mass represented by intact peptide. Counterions, residual water and components not detected by the method can affect interpretation. A report needs a clear reporting basis and traceability to the actual lot.

Net peptide content, when reported, requires its own measurement or justified calculation. A generic correction factor cannot establish the active amount. The assumption that all LL-37 preparations contain approximately the same net fraction was not supported by the retrieved evidence.

Endotoxin, sterility and chemical purity are also distinct. A favorable purity chromatogram does not establish microbiological quality. LL-37's interactions with bacterial products make interpretation of biological assays especially dependent on appropriate controls. Endotoxin methods require validation for the tested preparation, including assessment of interference.

The FDA specifically identifies peptide impurities, active-ingredient characterization and immunogenicity as concerns for compounded LL-37. Documentation does not eliminate uncertainty about those issues or establish a suitable human administration route.

The clinical studies evaluated particular preparations in defined settings. Matching their peptide sequence does not reproduce their manufacturing controls or exposure conditions. A batch report answers limited analytical questions. It cannot convert mixed clinical results into a proven recovery treatment or supply the missing subcutaneous evidence.

COMMON MISTAKES

- Treating the evidence grade as an efficacy verdict. Multiple randomized trials meet the supplied A criterion, but their outcomes remain mixed and formulation-specific. None identified here establishes subcutaneous benefit for training recovery, body composition or routine immune support.
- Saying only two human randomized trials exist. The literature also includes a diabetic ulcer cream trial and an oral recombinant bacterial formulation trial. Their findings need separate interpretation rather than omission or automatic generalization (PMID 37480520, PMID 37605995).
- Citing the small positive venous ulcer study without the larger negative study. The phase IIb trial did not establish overall healing improvement, and its favorable subgroup analysis requires prospective confirmation (PMID 25041740, PMID 34687253).
- Calling every favorable healing measure complete healing. Changes in wound area, modeled healing rates and granulation index are different endpoints. A statistically significant intermediate measure does not automatically establish durable closure, infection control or functional recovery.

- Assuming a higher concentration must work better. The initial wound trial showed a nonlinear response. It did not establish the mechanism of that response or a systemic titration rule. Its highest concentration's lack of benefit is not proof of clinical membrane toxicity (PMID 25041740).
- Describing oral delivery as universally ineffective. The oral trial used engineered Lactococcus lactis producing LL-37. That finding contradicts a categorical dismissal, but does not establish the effectiveness or absorption of swallowed purified peptide (PMID 37605995).
- Using animal sepsis findings as a human immune protocol. The rat study administered LL-37 intravenously at 1 mg/kg as a single experimental treatment, PMID 16641434. Species, severe infection models and route prevent direct transfer to routine human use.
- Turning disease mechanisms into certain clinical outcomes. LL-37 participates in psoriasis-related interferon signaling and experimental rosacea inflammation. These findings justify concern, but do not quantify an individual's risk of a flare after exposure (PMID 17873860, PMID 33745908).
- Calling the melanoma eruption confirmed LL-37-induced skin cancer. The case described atypical squamous proliferation, previous cancer treatments and resolution after cessation. It supports a toxicity signal, without establishing malignancy causation or incidence (PMID 29665030).
- Treating a theoretical stack as a tested combination. Different proposed mechanisms do not establish additive benefit, compatibility or protection against adverse effects. No verified evidence supports the listed pairings as clinical LL-37 regimens.
- Equating oligomers with visible contamination or irreversible damage. Molecular association in laboratory experiments does not diagnose the cause of haze or establish a universal handling rule. Clear appearance also cannot establish purity or sterility (PMID 10417311).
- Confusing concentration with dose. A topical solution's concentration requires application volume and treated area to determine delivered amount. Cream mass and solution volume are not interchangeable. Neither quantity determines systemic exposure (PMID 34687253, PMID 37480520).
- Assuming absence from WADA's named examples means permission. The List uses classes that extend beyond individual names. Non-approved pharmacological status can establish prohibition under S0 even when a compound has no separate entry.
- Treating research labeling or a favorable certificate as clinical authorization. Analytical identity, regulatory status and evidence of benefit are separate questions. None supplies the missing human subcutaneous protocol.

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Thymosin Alpha-1

Thymalfasin, Zadaxin

Thymic immunomodulatory peptide | Module 3 · Shielding | Goals: Immune | Route: SC

An immunomodulatory peptide with substantial clinical research, no demonstrated mortality benefit in the largest verified sepsis trial, and no established training or infection-prevention benefit in healthy athletes.

WHAT IT IS

Thymosin alpha-1, also called thymalfasin, is a synthetic, N-terminally acetylated peptide containing 28 amino acids. It was originally isolated from thymosin fraction 5, a bovine thymus extract containing multiple peptides. The purified synthetic peptide and mixed thymic extracts are different preparations (PMID 15482167). Its principal research role is immunomodulation. It influences dendritic cells, T cells, cytokine responses, and other components of immune function. These activities do not establish an anabolic effect, improved recovery from training, or general protection against infection (PMID 27450734). The clinical literature includes chronic viral hepatitis, sepsis, cancer-related treatment settings, vaccine responses, and pharmacokinetic studies. A crossover pharmacokinetic study administered thymosin alpha-1 to nine healthy volunteers (PMID 10027483). That distinction matters. A study can establish absorption and elimination without establishing clinical benefit. Healthy-volunteer exposure does not demonstrate fewer respiratory infections, improved exercise performance, better body composition, or faster recovery. No trial establishing those outcomes in healthy trained adults was identified during this verification. Thymalfasin has a history of medicinal use and reported authorization outside the United States. The specific product, indication, jurisdiction, and current authorization require separate verification. Neither a research publication nor a certificate of analysis establishes marketing authorization.

MECHANISM

Thymosin alpha-1 has multiple reported immune effects. The retrieved evidence does not establish one exclusive, clinically validated receptor mechanism that explains every indication. Toll-like receptor signaling in dendritic cells is a central experimental finding, but pathway involvement does not necessarily establish direct receptor binding (PMID 27450734).

Dendritic cells help determine how the immune system responds to antigens. They influence T-cell activation and the balance between inflammatory responses and tolerance. Experimental thymosin alpha-1 effects therefore depend on cell type, stimulation conditions, and the surrounding immune environment.

In human and murine dendritic-cell experiments, thymosin alpha-1 affected T-helper priming and tolerance. In murine cells, it induced indoleamine 2,3-dioxygenase, usually abbreviated IDO. This enzyme participates in tryptophan metabolism and immune regulation. IDO induction required TLR9 and type I interferon receptor signaling. The experiments also demonstrated interleukin-10 production and regulatory T-cell generation (PMID 16741252).

Those findings support a more specific description than simply boosting immunity. In the studied models, thymosin alpha-1 could support antifungal T-helper type 1 responses while promoting regulatory mechanisms. They do not show that the peptide automatically corrects any immune imbalance in a person.

A separate study examined human monocyte-derived dendritic cells exposed to different infectious stimuli. With viral TLR3 and TLR7/8 agonists, thymosin alpha-1 increased antigen-presentation markers and several inflammatory cytokines. During pandemic H1N1 infection, it increased maturation markers and interferon responses. With bacterial TLR2 and TLR4 stimulation, several measured responses decreased instead (PMID 26096650).

This is evidence of context-dependent activity in cultured cells. It does not establish that treatment improves viral infections while suppressing bacterial inflammation in clinical practice. The experimental conditions and

measured endpoints differ substantially from infection outcomes in patients.

Reviews also describe effects on T-cell maturation, natural killer cell activity, and cytokines involved in cellular immunity. These are proposed contributors to its pharmacology, rather than validated predictors of individual response. A laboratory change cannot substitute for a patient-important outcome such as survival or infection frequency (PMIDs 27450734 and 15482167).

A 2026 study proposed an additional microRNA chaperone mechanism. Circulating thymosin alpha-1 decreased after chemotherapy in patients with several cancers and in tumor-bearing mice. Experimental work showed peptide binding to tumor apoptotic bodies and interaction with their microRNA cargo. Protection of miR-146a-5p from degradation enabled TLR7-dependent dendritic-cell activation. Treatment enhanced chemotherapy-associated tumor control in selected mouse models (PMID 42295795).

The human component involved measurements associated with chemotherapy. It was not a randomized demonstration that this mechanism improves cancer outcomes in patients. The therapeutic findings remain preclinical and require independent confirmation and clinical testing.

The supported mechanistic conclusion is immune modulation across several experimental systems. The unsupported extrapolation is that these effects reliably translate into improved immune resilience, longevity, or training outcomes in otherwise healthy adults.

EVIDENCE · GRADE A

Grade A reflects the presence of multiple human randomized trials under this product's evidence scale. It describes the level of clinical investigation, not a blanket conclusion of efficacy. The evidence must remain specific to the indication, formulation, schedule, comparator, and endpoint.

Older hepatitis B studies reported sustained virological responses, but their results and designs were heterogeneous. The large TESTS trial did not demonstrate lower sepsis mortality. COVID-19 evidence remains inconsistent and substantially vulnerable to confounding. Healthy-volunteer pharmacokinetics and vaccine-response studies do not establish clinical benefit in healthy trained adults.

For fewer infections, improved training recovery, body recomposition, or longevity in healthy athletes, the claim-specific grade is D. No directly applicable efficacy trial was identified. Mechanistic plausibility cannot fill that clinical evidence gap.

Human data. Chronic hepatitis B: a 2004 review summarized seven randomized studies of thymosin alpha-1 monotherapy. The reported regimen was 1.6 mg subcutaneously twice weekly for six months (PMID 15482167). The review described higher sustained response rates than untreated controls, with responses sometimes accumulating after treatment ended. It does not establish superiority to contemporary treatment options or a reduction in cirrhosis, liver cancer, or mortality. An earlier pharmacology review summarized four hepatitis B trials involving 195 patients and described mixed results. One randomized trial reported HBV DNA clearance of 40.6 percent after a six-month treatment course, compared with 9.4 percent among untreated controls. Different designs, follow-up periods, and response definitions limit comparisons across these studies (PMID 11381492). Sepsis: ETASS followed 361 patients after post-randomization withdrawals. It was a multicenter, single-blind randomized trial. Mortality at 28 days was 26.0 percent with thymosin alpha-1 and 35.0 percent with control. The relative risk was 0.74, with a 95 percent confidence interval of 0.54 to 1.02. The reported P value for this

Animal and mechanistic data. The most directly relevant retained animal evidence concerns immune mechanisms rather than training outcomes. Romani and colleagues studied dendritic-cell priming, tryptophan metabolism, and tolerance in murine systems, alongside human cell experiments. TLR9 and type I interferon receptor signaling were required for IDO induction in the murine cells. Transfer experiments supported coordinated antifungal responses and regulation of reactions to alloantigens (PMID 16741252). The 2026 microRNA study demonstrated chemotherapy-associated antitumor activity in selected mouse models. The proposed effect depended on TLR7 signaling and sufficient miR-146a-5p expression. That conditional result argues against treating the mechanism as a universal immune-enhancing effect. It also does not establish cancer prevention or treatment efficacy in humans (PMID 42295795). These findings support preclinical hypotheses, generally grade C for animal efficacy and grade D for isolated cellular mechanisms. They do not elevate unrelated clinical claims to grade A merely because the compound also has randomized trials for other diseases. That paper primarily concerns

comparison was 0.062. Monocyte HLA-DR improved at measured follow-up points, but the mortality comparison did not establish a statistically significant benefit (PMID 23327199). TESTS randomized 1106 adults with sepsis across 22 centers. Its modified intention-to-treat analysis included 1089 patients, with 542 receiving thymosin alpha-1 and 547 receiving placebo. The trial reported 1.6 mg subcutaneously every 12 hours for up to seven days (PMID 39814420). Mortality at 28 days was 23.4 percent with thymosin alpha-1 and 24.1 percent with placebo. The corrected hazard ratio was 0.97, with a 95 percent confidence interval of 0.76 to 1.24. No secondary clinical or safety outcome differed significantly between groups. The published correction changed numerical hazard-ratio estimates without changing the overall conclusion (PMIDs 39814420 and 40447307). TESTS provides stronger evidence than the earlier small trials against a large, broadly applicable mortality benefit in sepsis. Its confidence interval still includes potentially meaningful benefit and harm. A nonsignificant result does not prove exact equivalence or rule out every possible subgroup effect. COVID-19: a meta-analysis of eight studies reported a mortality risk ratio of 0.59, with a 95 percent confidence interval of 0.37 to 0.93. Heterogeneity was substantial, with I-squared of 84 percent. Mechanical ventilation requirements and hospital length of stay did not differ significantly. The authors called for randomized trials to verify the findings (PMID 37845598). A separate multicenter cohort included 306 treated and 1976 untreated patients. Thymosin alpha-1 exposure was associated with higher non-recovery after adjustment, with an odds ratio of 1.5 and a 95 percent confidence interval of 1.1 to 2.1. Confounding by indication and residual differences in illness severity prevent a causal conclusion (PMID 34408744). Another COVID-19 report included 78 treated patients and 49 controls. It described itself as a retrospective analysis despite also using random-allocation language. That inconsistency limits confidence in treating it as a rigorously randomized efficacy trial. It primarily explored differences in immune and inflammatory measurements (PMID 33160854). Healthy-volunteer evidence exists. A randomized crossover study in nine volunteers compared three formulations and assessed single-dose and short multiple-dose pharmacokinetics. It demonstrated absorption and formulation-related differences in exposure, without establishing infection prevention or performance benefits (PMID 10027483). A double-blind vaccine-adjuvant study randomized 90 elderly men, with sera from 85 available for analysis. It examined antibody responses to influenza vaccination. This establishes research outside acute hospital treatment, but albumin-thymosin fusion proteins with altered pharmacokinetics. No animal dose is supplied here because a relevant native-peptide regimen was not verified from the retained sources. Animal exposure cannot be converted into a human training protocol using a simple body-weight calculation.

antibody responses in elderly men cannot establish fewer infections in healthy athletes (PMID 2642497).

REGULATORY STATUS AND SPORT

STATUS

Thymosin alpha-1 is not FDA-approved for any indication. FDA advisory materials describe reported medicinal authorizations outside the United States, principally for hepatitis-related and immune-adjuvant uses. Those materials also state that FDA could not independently verify the full set of foreign-approval claims. This card therefore does not assert a current worldwide country count or a universal licensed indication. [FDA advisory committee briefing] (https://www.fda.gov/media/183820/download). FDA also identifies potential immunogenicity, peptide-impurity, and active-ingredient characterization concerns for compounded thymosin alpha-1. Its assessment states that available safety information is insufficient to characterize the proposed compounded preparations adequately. [FDA compounding safety assessment] (https://www.fda.gov/drugs/human-drug-compounding/certain-bulk-drug-substances-use-compounding-may-present-significant-safety-risks). Approval, prescribing status, import rules, and compounding eligibility are separate regulatory questions. A clinical publication or foreign authorization does not establish authorization in another jurisdiction. Unapproved does not mean exempt from regulation. Safety findings from a controlled pharmaceutical supply chain cannot establish the quality of an unrelated research-labeled preparation.

WADA

As reviewed on September 5, 2026, thymosin alpha-1 is not explicitly named on the 2026 WADA Prohibited List. Thymosin beta-4 and its derivatives, including TB-500, are explicitly prohibited at all times under S2. These substances are different from thymosin alpha-1. [2026 WADA Prohibited List](https://www.wada-ama.org/sites/default/files/2025-09/2026list_en_final_clean_september_2025.pdf). Absence from the named examples is not an unconditional clearance, because several categories are open-ended. S0 concerns substances without current approval for human therapeutic use by any governmental health authority. Lack of FDA approval alone does not establish S0 prohibition when a qualifying authorization exists elsewhere. This card does not substitute for an authoritative determination covering the exact substance and current rules. Misidentification or contamination with a prohibited substance creates a separate anti-doping risk. No testing-avoidance methods or clearance periods are provided.

RESEARCH USE · REPORTED, NOT RECOMMENDED

ROUTES

Subcutaneous administration is documented in the hepatitis literature, both major sepsis trials, the vaccine-adjuvant study, and the healthy-volunteer pharmacokinetic study. These sources do not establish equivalent exposure or efficacy for oral, nasal, or topical preparations (PMIDs 11381492, 23327199, 39814420, 2642497, and 10027483). A marketed formulation claim and validated human bioavailability are different questions. The retrieved evidence supports describing the studied route, without claiming that every possible formulation has been excluded.

HALF-LIFE

The pharmacology review reports an approximately two-hour serum half-life, peak concentrations within two hours, and return toward baseline within 24 hours (PMID 11381492). The healthy-volunteer study reported an elimination half-life below three hours and peak concentrations after approximately one to two hours. Exposure differed between formulations (PMID 10027483). These values describe circulating peptide under the studied conditions. They do not directly measure how long downstream immune changes persist. Conversely, a proposed persistent cellular effect does not prove that a particular interval is effective. The short plasma half-life does not justify escalating frequency or importing an intensive-care schedule into preventive use.

TIMING

The retained trials describe scheduled administration linked to treatment protocols. They do not establish an optimal relationship to meals, sleep, or exercise. Fixed timing within a clinical protocol is different from a randomized comparison of timing strategies. No evidence-based pre-workout, post-workout, or bedtime window was identified. The absence of a reported timing effect does not prove that timing is biologically irrelevant. It means that the available studies do not answer that question for the intended fitness population.

CYCLE LENGTH

The literature spans several durations. Historical hepatitis B studies commonly used six-month courses, while the pharmacology review also describes longer treatment periods. ETASS and TESTS used approximately one-week treatment periods. The influenza vaccine study used eight administrations over approximately four weeks (PMIDs 15482167, 11381492, 23327199, 39814420, and 2642497). These durations reflect different diseases and endpoints, not interchangeable cycles. No validated course length, repeat-course interval, or continuous-use schedule for healthy trained adults was identified. A delayed hepatitis response also cannot establish the duration of a hypothetical preventive effect.

TITRATION

The retained hepatitis and sepsis regimens used fixed schedules rather than response-guided escalation. Some studies expressed exposure by body surface area. No validated titration scheme

for infection prevention or training outcomes in healthy adults was identified. The TESTS authors discussed earlier dosing rationales, but TESTS was not a randomized dose-ranging trial. Its negative primary result cannot establish that a higher or lower schedule would work. Short plasma persistence, subjective sensations, and isolated immune markers are not validated titration targets for this purpose.

CONTEXT	DOSE	ROUTE	FREQUENCY	PROVENANCE
Historical chronic hepatitis B monotherapy studies summarized in a clinical review	**1.6 mg per administration, reported in PMID 15482167**	Subcutaneous, supported by the pharmacology review, PMID 11381492	Twice weekly for six months	PMID 15482167 summarizes seven randomized studies using 1.6 mg twice weekly for six months. PMID 11381492 documents the subcutaneous route. This is a historical study regimen, not a recommendation or a universal current label. · PMID 15482167
Body-surface-area expression of the historical hepatitis regimen	**900 mcg/m2 per administration, reported in PMID 11381492**	Subcutaneous	Twice weekly	The pharmacology review reports 1.6 mg and 900 mcg/m2 as corresponding descriptions of subcutaneous twice-weekly dosing. Their equivalence depends on body surface area and is not exact for every adult (PMID 11381492). · PMID 11381492
Severe sepsis, ETASS randomized trial, 181 patients in the analyzed treatment group	**1.6 mg per administration, reported in PMID 23327199**	Subcutaneous	Twice daily for five days, then once daily for two days	The ETASS methods specify this fixed regimen alongside standard sepsis care. The trial did not establish a statistically significant difference in its reported 28-day mortality comparison (PMID 23327199). · PMID 23327199
Sepsis, TESTS phase 3 trial, 542 patients in the modified intention-to-treat treatment group	**1.6 mg per administration, reported in PMID 39814420**	Subcutaneous	Every 12 hours for up to seven days	The TESTS methods specify this regimen, with earlier discontinuation for ICU discharge, death, or withdrawal of consent. Treatment did not demonstrate lower 28-day mortality than placebo (PMID 39814420). · PMID 39814420
Influenza vaccine-adjuvant study in elderly men	**900 mcg/m2 per administration, reported in PMID 2642497**	Subcutaneous	Twice weekly for eight administrations	The double-blind placebo-controlled study reports this schedule alongside influenza vaccination. It examined antibody responses, rather than exercise performance or infection prevention in healthy trained adults (PMID 2642497). · PMID 2642497

STACKING

No combination is documented for this compound in the sources cited. Use the avoid list and the protocol that includes it as the guide.

– TB-500

Identity and anti-doping caution, not a demonstrated drug interaction. Thymosin alpha-1 and thymosin beta-4 are distinct molecules. TB-500 terminology can refer to beta-4-related material and does not identify thymalfasin. WADA explicitly prohibits thymosin beta-4 and its derivatives. No verified human evidence establishes benefit from combining them. Similar names do not establish

	interchangeable mechanisms, formulations, or regulatory status.
– Thymalin	Evidence-gap caution, not an established contraindication. Thymalin is a different thymic preparation and cannot inherit thymalfasin's clinical evidence. No controlled human combination study was identified in the verification sources. Simultaneous exposure would complicate attribution of benefits, adverse events, and laboratory changes. Claims of either useful complementarity or definite harmful redundancy remain unsupported.
– LL-37	Uncertain immune interaction. Both substances have experimental effects relevant to innate immunity, but that observation does not establish a clinically predictable interaction. No verified human combination evidence supports efficacy, tolerability, or a dosing schedule. The concern is uncertainty in an already context-dependent immune system, rather than proof that the combination necessarily causes excessive inflammation.

SAFETY

COMMON EFFECTS

Local injection-site irritation is a recurring treatment-associated finding in the older clinical literature. The pharmacology review describes generally favorable short-term tolerability, but this does not establish the absence of uncommon reactions or long-term effects (PMID 11381492). ETASS reported no drug-related serious adverse events or discontinuations for intolerance. Its population, duration, and sample size limit what that observation can establish about rare outcomes (PMID 23327199). In TESTS, adverse events occurred in 66.4 percent of treated patients and 67.6 percent of placebo patients. Serious adverse events occurred in 26.8 percent and 29.3 percent, respectively. Neither comparison was statistically significant, and investigators reported no unexpected serious adverse events related to thymosin alpha-1 (PMID 39814420). These were patients with sepsis, in whom anemia, fever, coagulation abnormalities, and other complications can arise from critical illness. Such events cannot automatically be attributed to the peptide. Equally, similar group rates do not establish that every event was unrelated or exclude rare treatment harms. The controlled-trial record describes specific pharmaceutical preparations used under clinical supervision. It does not establish the tolerability of unrelated compounded or research-labeled material, prolonged preventive use, or experimental combinations.

SERIOUS SIGNALS

TESTS reported a prespecified age-subgroup signal requiring caution. Among patients younger than 60, the hazard ratio for 28-day mortality was 1.67, with a 95 percent confidence interval of 1.04 to 2.67. The interaction P value was 0.01. This did not meet the study's stricter threshold for multiple subgroup comparisons (PMID 39814420). The overall trial was negative, and baseline differences and multiple testing complicate interpretation. The finding is hypothesis-generating. It does not prove that thymosin alpha-1 increases mortality in younger people generally, nor that older people benefit. It also prevents a simple claim that immune modulation has no possible downside. The large COVID-19 cohort associated treatment with higher non-recovery after adjustment. Sicker patients may have been more likely to receive treatment, and adjustment cannot eliminate all confounding. This signal is observational rather than proof of causation (PMID 34408744). Potential allergic reactions and immunogenicity remain relevant, particularly when formulation quality or peptide characterization is uncertain. The frequency and clinical importance of these risks cannot be inferred reliably for an unspecified preparation from the available trials.

CONTRAINDICATIONS

Known hypersensitivity to thymosin alpha-1 or formulation components is a clinically relevant contraindication. Current product-specific labeling, where a medicinal product is authorized, determines the formal contraindication list. TESTS excluded pregnancy, lactation, hematological malignancy, organ or bone-marrow transplantation, acute autoimmune disease or glomerulonephritis, and recent specified immunosuppressive or anticancer treatments (PMID 39814420). These exclusions limit generalizability. They are not interchangeable with proof that each condition is an absolute contraindication in every therapeutic setting. Transplantation, deliberate immunosuppression, and active autoimmune disease require specialist assessment because changing immune function may conflict with treatment goals. Pregnancy and breastfeeding lack an adequate evidence base in the retained studies. A trial exclusion should neither be dismissed nor presented as direct evidence of a particular harm.

STOP RULES

Airway swelling, breathing difficulty, fainting, or rapidly progressing systemic allergic symptoms require emergency assessment and no further exposure pending evaluation. A spreading painful injection-site reaction, drainage, persistent fever, or systemic deterioration requires prompt clinical review. New inflammatory symptoms, unexplained rash, joint swelling, or worsening of a known autoimmune condition warrant assessment before further exposure. These are general clinical escalation criteria, not a validated thymosin alpha-1 monitoring algorithm. Changes to prescribed immunosuppression or transplant therapy require the treating specialist. A subjective feeling of benefit, a change in one immune marker, or lack of local irritation does not establish clinical efficacy.

RECONSTITUTION AND STORAGE

TYPICAL VIAL

The ETASS and TESTS methods describe lyophilized preparations containing 1.6 mg for reconstitution. These are verified trial presentation amounts, not a universal vial standard or a recommended personal dose (PMIDs 23327199 and 39814420). A different labeled amount, counterion, excipient composition, or container does not establish equivalence to the trial preparation. The amount printed on a vial and the measured amount of active peptide are separate quality questions. No unsupported prevalence claim about underfilled research vials is made here.

SOLVENT

ETASS reports reconstitution with 1 mL of the supplied sterile water for injection. TESTS reports dissolving the lyophilized trial preparation in 1 mL of sterile water before subcutaneous administration (PMIDs 23327199 and 39814420). These descriptions document trial preparation. They do not validate substitution with bacteriostatic water, repeated withdrawals, or a prolonged storage period. Adding a preservative does not establish compatibility, chemical stability, or a validated multidose presentation. The retrieved trials do not establish universal instructions about mixing force, shaking, foam, or container technique. Product-specific validated instructions are necessary to resolve those questions.

STORAGE

Storage requirements depend on the exact authorized formulation, container, diluent, and validated product instructions. The clinical papers do not establish a universal shelf life for arbitrary thymosin alpha-1 preparations. No validated post-reconstitution storage interval for substitution with bacteriostatic water was established from the retrieved studies. A general multidose-vial discard convention cannot be transferred automatically to a peptide preparation that lacks corresponding validation. Preservative content also does not establish peptide potency over time. Discoloration, particles, or cloudiness can indicate a quality problem, but normal appearance does not establish sterility or identity. Trial tolerability results cannot resolve storage uncertainty for a different preparation. Product labeling and pharmacy stability data answer different questions from clinical efficacy studies.

The ETASS preparation contained 1.6 mg in a reported final concentration of 1.6 mg/mL after reconstitution with 1 mL of supplied diluent (PMID 23327199). This illustrates concentration arithmetic, not a recommendation for self-administration. For that documented preparation, dividing the reported peptide mass by the reported volume gives 1.6 mg/mL. Expressed in another mass unit, this is 1600 mcg/mL. The conversion changes the unit, not the amount of active ingredient or the evidence supporting the trial regimen. A calculator needs verified peptide content and the actual final solution volume. A nominal vial label cannot correct an inaccurate assay, uncertain identity, or inappropriate formulation. The calculation also assumes that the material has dissolved and that the preparation matches its validated specifications. Syringe graduations describe volume calibration. They are not biological IU of thymosin alpha-1. Device markings, peptide mass, and clinical dosing are different quantities. No fractional-dose or repeated-withdrawal schedule is inferred from this example. They extended beyond the documented preparation and could imply that mathematical accuracy alone validates a regimen. Concentration arithmetic does not establish sterility, stability, route suitability, or treatment benefit.

BUYING NOTES

Quality documentation concerns identity, content, impurities, and manufacturing controls. It cannot establish that a proposed use is effective. A research-use label is not marketing authorization, and a certificate of analysis is not a clinical safety study.

A useful certificate identifies the tested batch, laboratory, sampling date, methods, and specifications. The reported batch must correspond to the actual material. A generic certificate without traceability cannot establish the contents of an individual container.

Chromatographic purity, peptide identity, and net peptide content are distinct measurements. A high HPLC area percentage does not establish the mass of peptide present. It also does not independently establish sterility, endotoxin control, residual solvent levels, or absence of every relevant impurity.

Identity testing should be consistent with the intended acetylated sequence and molecular form. Mass spectrometry provides important evidence, but interpretation requires attention to charge states, adducts, salts, and the analytical method. One reported mass is not complete structural confirmation, and a mass discrepancy alone does not prove a specific manufacturing shortcut.

For material represented as suitable for parenteral use, sterility and bacterial-endotoxin testing address different hazards. Neither can be inferred from a purity chromatogram. Water content, counterions, residual processing chemicals, and degradation products can also affect interpretation of the labeled amount.

Independent testing is useful when sampling, methods, laboratory competence, and chain of custody are credible. Independence alone does not guarantee that the tested sample represents every vial. A document's appearance or claimed purity percentage cannot substitute for those details.

No supplier is endorsed. These criteria explain the limits of analytical evidence; they do not convert unapproved material into an authorized medicine or transfer the trial preparation's safety record to another product.

COMMON MISTAKES

- Confusing thymosin alpha-1 with thymosin beta-4 or TB-500. Similar terminology does not establish chemical identity. The 2026 WADA list explicitly prohibits thymosin beta-4 and its derivatives, while thymosin alpha-1 is not explicitly named. Exact identity and authoritative status assessment matter.
- Claiming that no healthy person has ever received thymosin alpha-1 in a study. Healthy-volunteer pharmacokinetic research exists (PMID 10027483). The actual evidence gap concerns demonstrated clinical benefits, including fewer infections or better training outcomes, in healthy trained adults.
- Reading grade A as proof that every proposed use works. The grade reflects multiple human randomized trials. Historical hepatitis responses, a negative sepsis trial, and mechanistic findings answer different questions. Evidence quality and direction of effect must be assessed separately.
- Presenting ETASS as definitive evidence of reduced sepsis mortality. Its reported mortality confidence interval crossed the null. The larger TESTS trial did not demonstrate benefit, and its corrected hazard ratio remains consistent with that conclusion (PMIDs 23327199, 39814420, and 40447307).
- Treating a nonsignificant trial as proof of exactly zero effect. TESTS provides evidence against a large general benefit under its studied conditions. Its confidence interval still contains possible benefit and harm. Subgroup findings require confirmation rather than selective adoption.
- Importing an intensive-care schedule into preventive use. Hepatitis, sepsis, vaccine-response, and pharmacokinetic studies used schedules chosen for different questions. Their existence does not create a validated cycle or titration plan for a healthy person.
- Assuming different receptors establish compatible combinations. No verified clinical synergy was identified for thymosin alpha-1 with BPC-157, KPV, ARA-290, or NAD. Mechanistic descriptions do not establish independent effects, low interaction risk, or additive benefit.
- Equating tolerability with efficacy or comprehensive safety. Similar adverse-event rates in TESTS are informative for its preparation and clinical setting. They do not establish preventive benefit, exclude rare harms, or validate prolonged exposure and experimental combinations.
- Treating trial exclusions as a universal contraindication list. Exclusions identify populations to which the findings may not apply. Formal contraindications require product-specific labeling, while transplantation,

active autoimmunity, and immunosuppression require specialist assessment.

- Assuming bacteriostatic water validates repeated use or a standard storage interval. Preservative substitution, multidose handling, and post-reconstitution stability need formulation-specific evidence. The trial descriptions do not supply that evidence.
- Assuming a correct concentration calculation establishes product quality. Arithmetic depends on accurate content and volume inputs. It cannot verify identity, sterility, endotoxin control, or manufacturing consistency, and it cannot establish that the calculated regimen is clinically useful.

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Thymalin

Thymic polypeptide extract

Thymic peptide complex | Module 3 · Shielding | Goals: Immune, Longevity | Route: IM (research)

Bovine thymus polypeptide extract with Russian medical approval, limited human immune-marker findings, and insufficient evidence for longevity or training benefits.

WHAT IT IS

Thymalin is a mixture of polypeptides extracted from calf thymus, rather than a single defined peptide. The clinical literature describes components up to 10 kDa and Russian medical approval dating to 1982, registration 82/1108/8 (PMID 33575961). An earlier paper describes mild acid extraction and isolation of Glu-Trp from the mixture (PMID 9637345).

Reported constituents include Glu-Trp, Lys-Glu and Glu-Asp-Pro, but their individual contributions to clinical effects remain incompletely established. A synthetic constituent is not automatically equivalent to the complete extract. Names encountered in the literature include Thymalin, thymaline, Timalin and thymus-derived polypeptide factor. Historical preparations require formulation-specific interpretation.

Class: thymic polypeptide extract. Module 3, Shielding. Research themes: immune dysfunction and aging. It differs from thymosin alpha 1 and thymosin beta 4. Composition, manufacturing controls and biological activity matter when comparing batches or interpreting published results.

MECHANISM

Cell differentiation hypothesis: cultured human hematopoietic cells showed reduced CD44 and CD117 expression and increased CD28 expression after Thymalin exposure (PMID 33237528). The reported changes were approximately twofold to threefold decreases and a 6.8-fold increase, respectively. These markers indirectly support altered differentiation. They do not establish functional immune restoration or identify a receptor. Earlier research describes effects on T-cell differentiation, peptide-MHC recognition, cyclic nucleotides and cytokine release (PMID 9637345).

Inflammatory signaling is context-dependent. A THP-1 cell study reported ERK1/2 phosphorylation, cytokine changes and reduced adhesion to activated endothelial cells (PMID 35408963). Its monocyte experiments used a single overnight culture exposure to 0.1 mcg/mL, with separate macrophage time-course experiments. This was laboratory exposure, not a human administration regimen. Findings across the different tested peptides cannot all be attributed specifically to Thymalin.

In another study, human peripheral blood mononuclear cells received a single 18-hour culture exposure to 1 mg/mL Thymalin (PMID 37686182). In stimulated cells, TNF-alpha and IL-1beta release decreased approximately 2.2-fold and 2.7-fold. However, IL-6 release increased approximately fourfold in unstimulated cells. The extract therefore cannot be described as uniformly suppressing inflammatory cytokines. Experiments involved samples from four donors and do not establish clinical exposure-response relationships.

DNA binding remains proposed. Molecular docking nominated DNA sequences and possible AKT1/AKT2-related pathways for constituent dipeptides (PMID 37686182). Docking does not demonstrate target engagement in patients. Mouse findings also suggest age-dependent thymus-pineal signaling, without proving human rejuvenation (PMID 17333624). No validated human receptor model or established mechanism linking Thymalin to longer life emerged from these records.

EVIDENCE · GRADE A

A applies only through this catalog's approved-drug criterion, because the literature documents Russian medical approval. It does not represent high-certainty evidence for every proposed use. The small human immune-marker studies fit B. Human longevity claims fit C because reporting and replication are insufficient.

Cellular mechanism findings fit D. No verified evidence establishes improved muscle gain, fat loss or athletic recovery.

Human data. The 2003 report followed 266 older adults for six to eight years after courses of thymic or pineal extracts (PMID 14523363). It reported lower mortality with Thymalin, with larger differences in certain combined-treatment groups. PubMed indexes the paper as a randomized controlled trial. However, the abstract does not explain allocation, blinding, group-level denominators or detailed dosing. It cannot support a reliable personal estimate of mortality reduction. Independent confirmation of the longevity finding was not established in this review. The 2021 COVID-19 study was single-center, prospective, open-label and randomized using an envelope method (PMID 33575961). It compared 42 patients receiving standard treatment plus Thymalin with 50 controls. The study regimen was 10 mg IM once daily for five days, added to standard therapy. Participants had moderate or severe disease and lymphopenia, with mean ages around 60. The treated group showed increases in lymphocytes, CD3 cells and CD4 cells. CD4 increased approximately 88.9 percent from baseline. IL-6, CRP and D-dimer declined approximately 5.5-fold, 9.7-fold and 5.7-fold within that group. These are before-after changes, not equivalent reductions in clinical risk. Controls also improved on several markers, and concomitant treatments complicate interpretation. Neither group had deaths. The study therefore cannot establish a mortality benefit or thrombosis prevention. The 2022 severe COVID-19 comparison reported hematologic changes and hospital mortality (PMID 36169363). Its English and Russian abstracts contain conflicting mortality percentages for treated groups. Exact mortality estimates are omitted pending reconciliation with the original study data. The abstract also leaves allocation methods and group sizes unclear. Older reports described 32 burn patients and 30 patients with periodontal disease (PMIDs 11188814 and 6546722). These provide limited clinical observations, not evidence for use in healthy adults. Overall, short follow-up, incomplete safety reporting and overlapping investigator networks constrain confidence.

Animal and mechanistic data. A 1982 study reported improved immune responses and longer lifespan with thymus-derived factors in mice (PMID 6752596). A 1989 study administered 0.1 mg per mouse SC daily during five-day courses repeated monthly (PMID 2682058). Lifespan increased when treatment began at 3.5 months, but not when it began at 12 months. Reduced mammary tumor incidence was also limited to the younger-start group. These findings cannot define a human dose or predict human lifespan. A rat sarcoma study reported tumor growth inhibition using modulated, comparatively low doses (PMID 29797130). It does not establish a cancer treatment or support a simple lower-is-better rule. A separate mouse study found age-dependent effects on pineal melatonin production (PMID 17333624). That result concerns a specific endocrine response, not all effects in older animals. A 48-rat mandibular-defect experiment examined local Thymalin exposure, a bone substitute and their combination (PMID 38642352). Changes in immune-cell populations accompanied the repair model. This is not evidence for systemic athletic injury recovery or combination benefits with other catalog peptides. Animal findings remain grade C.

REGULATORY STATUS AND SPORT

STATUS

PMID 33575961 documents Russian medical approval since 1982. The retrieved Russian prescribing information describes a prescription medicine for immune-deficiency-related conditions. Historical registration details alone do not verify every currently marketed preparation. Thymalin has no FDA-approved therapeutic indication; FDA has identified marketed Thymalin as an unapproved drug. Source: [FDA enforcement record](https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/us-chem-labs-669074-02072024). No EMA authorization was established in this review. Research-use labeling does not establish authorization for human treatment or import.

WADA

Thymalin is not named in the reviewed 2026 prohibited-substance listing. This does not establish permission for a particular extract or preparation. S0 addresses substances without current

governmental approval for human therapeutic use, while other prohibited categories can apply independently of approval. Russian approval therefore does not justify a blanket permitted classification. No Thymalin-specific determination was established in this review. Thymosin beta 4 and its derivatives, including TB-500, are prohibited at all times under S2.3. Product-specific interpretation belongs with the relevant anti-doping organization. Source: [FINCIS 2026 prohibited-substance listing](https://kamu.suek.fi/en/dopingsubstances/).

RESEARCH USE · REPORTED, NOT RECOMMENDED

ROUTES

IM is the route in the retrieved Russian prescribing information and the verified 2021 COVID-19 trial (PMID 33575961). Historical human literature also describes electrophoresis within a multifactorial diabetic-foot treatment program (PMID 15584605). That study cannot isolate Thymalin's contribution or establish systemic bioavailability. Mouse experiments used SC administration, and a rat bone-repair experiment used local soft-tissue administration (PMIDs 2682058 and 38642352). Human SC-to-IM equivalence and oral efficacy were not established.

HALF-LIFE

No validated human elimination half-life for the complete extract was identified in the retrieved literature. A mixture may have component-specific kinetics rather than one meaningful plasma half-life. Peptide length alone cannot establish clearance within minutes. Repeated biological effects also do not identify plasma persistence. Numeric half-life claims require a formulation-specific pharmacokinetic study.

TIMING

The verified COVID-19 trial used daily administration without establishing an optimal time of day (PMID 33575961). No human evidence retrieved supports morning administration or timing around exercise. A daily study schedule does not imply a particular elimination half-life.

CYCLE LENGTH

The Russian prescribing information describes short courses, and the COVID-19 trial used five days (PMID 33575961). The geriatric report describes courses during the initial observation years and a separate annually treated combination group (PMID 14523363). Its abstract does not provide a reproducible longevity protocol. Monthly animal courses and non-clinical annual schedules are different evidence categories.

TITRATION

The verified COVID-19 trial used a fixed regimen rather than titration (PMID 33575961). The label contains dose ranges, which are not evidence of a validated escalation strategy. The rat sarcoma study modulated dosing during treatment (PMID 29797130). That model cannot establish an optimal human dose or justify adjusting treatment from subjective effects.

CONTEXT	DOSE	ROUTE	FREQUENCY	PROVENANCE
Adults with the immune-deficiency-related conditions described in Russian prescribing information	**5 to 20 mg per administration, with 30 to 100 mg per course, according to the Russian Thymalin prescribing information**	IM	Once daily for 3 to 10 days; the label describes repeat courses after 1 to 6 months when indicated	Russian Thymalin prescribing information for lyophilisate for intramuscular administration, reproduced in the retrieved drug monograph. This is a label regimen, not a recommendation for healthy adults. Source: [Thymalin prescribing information](https://medvisor.ru/medicine/drug/timalin_40588/).
Open-label randomized trial in hospitalized COVID-19 patients with lymphopenia, 42 treated and 50 controls	**10 mg per administration, as reported in PMID 33575961**	IM	Once daily for five days, added to standard therapy	Regimen verified in the full-text methods of PMID 33575961. The study population and concomitant treatments limit extrapolation to healthy adults. · PMID 33575961
Female SHR mice, lifespan and spontaneous tumor study	**0.1 mg per mouse per administration, as reported in PMID 2682058**	SC	Daily during five-day courses repeated monthly, starting at 3.5 or 12 months of age	Regimen reported in the abstract of PMID 2682058. Lifespan benefit was limited to the younger-start group. No human-equivalent dose is inferred. · PMID 2682058

CONTEXT	DOSE	ROUTE	FREQUENCY	PROVENANCE
Non-clinical adult immune or longevity use described in the submitted draft	**5 to 10 mg per administration, commonly cited in non-clinical use; not validated in trials**	SC or IM, as claimed in non-clinical descriptions	Once daily for ten days, sometimes repeated once or twice yearly	Commonly cited in non-clinical use; not validated in trials. Frequency of actual use was not independently verified. This complete regimen, indication and route cannot inherit validation from an IM hospital trial. Vendor and forum usage, not evidence: listed so you can recognize it, not follow it; no trial has validated this regimen and it is not a recommendation.

STACKING

No combination is documented for this compound in the sources cited. Use the avoid list and the protocol that includes it as the guide.

– Epitalon	The human combination study used Epithalamin, a pineal extract, rather than synthetic Epitalon (PMID 14523363). It cannot validate a Thymalin-Epitalon combination.
– BPC-157	No direct combination evidence was identified. The Thymalin bone-repair experiment did not test BPC-157 (PMID 38642352). Different proposed mechanisms do not demonstrate additive benefit, compatibility or acceptable combined risk.
– Thymosin Alpha-1	Thymosin alpha 1 is a different intervention. No direct evidence was identified for combining it with Thymalin. Overlapping immune effects create uncertainty, but a specific harmful interaction has not been established.
– TB-500	The names describe different interventions. No direct combination evidence was identified, and TB-500 is prohibited at all times under WADA S2.3. Thymalin's separate regulatory history does not alter that prohibition.

SAFETY

COMMON EFFECTS

The retrieved Russian prescribing information lists allergic reactions. Reliable incidence estimates were not provided. Injection-site pain and redness are possible with parenteral administration, but their frequency was not established in the retrieved Thymalin studies. The COVID-19 paper reports no deaths, not a comprehensive demonstration of tolerability (PMID 33575961).

SERIOUS SIGNALS

Serious hypersensitivity is a plausible concern with a parenteral animal-derived preparation, but a Thymalin-specific anaphylaxis rate was not established. Tissue sourcing, manufacturing and contamination controls matter for bovine extracts. Transmissible spongiform encephalopathy risk cannot be quantified from a peptide purity percentage. No product-specific transmission event was verified here. Effects in autoimmune disease, transplantation and lymphoid malignancy remain insufficiently characterized. These are mechanistic precautions, not proven adverse outcomes from the cited studies. Hemostatic findings do not establish an anticoagulant effect or define drug interactions. The COVID-19 trial included anticoagulant treatment, which prevents attributing clotting-related findings to Thymalin alone (PMID 33575961).

CONTRAINDICATIONS

Known hypersensitivity to the preparation or its components is a relevant exclusion. Pregnancy and breastfeeding lack adequate clinical safety evidence; product-specific contraindications require the applicable authorized insert. Active autoimmune disease, transplant immunosuppression and lymphoproliferative disorders warrant specialist assessment because immune effects are uncertain. They are not presented here as universally established label contraindications.

STOP RULES

Wheeze, facial or throat swelling, faintness or rapidly progressing hives after exposure require immediate discontinuation and emergency assessment. Persistent fever, new lymph-node enlargement, unexpected bleeding or worsening inflammatory symptoms warrant prompt clinical review. These are precautionary clinical triggers, not validated Thymalin-specific stopping thresholds. An unexplained product identity or batch discrepancy also prevents meaningful assessment of further exposure.

RECONSTITUTION AND STORAGE

TYPICAL VIAL

The retrieved Russian Thymalin prescribing information describes 10 mg of active extract per vial. This is a formulation strength, not a personal dose. The mass does not identify the amount of every constituent peptide or establish equivalence with an uncharacterized preparation.

SOLVENT

The retrieved Russian prescribing information specifies isotonic sodium chloride, 1 to 2 mL, for preparation before IM administration. Bacteriostatic water and repeated withdrawal from a stored solution were not validated in the retrieved sources.

STORAGE

The retrieved Russian prescribing information specifies protection from light and storage at no more than 20 C. Storage conditions are formulation-specific. No validated refrigerated multidose shelf life or freeze-thaw stability was established for reconstituted Thymalin. Adding a preservative does not establish chemical stability or justify storing the solution for weeks.

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Descriptive concentration arithmetic: a labeled 10 mg extract vial in a final volume of 2.0 mL
would contain 5 mg/mL, equivalent to 5000 mcg/mL. The vial strength and preparation-volume range
come from the Russian Thymalin prescribing information. This calculation assumes the stated final
volume and complete dissolution; it does not measure potency or peptide composition.

The 10 mg IM once-daily regimen studied for five days in PMID 33575961 would mathematically
correspond to 2.0 mL at that concentration. This does not establish the trial's actual
reconstitution volume, which the retrieved methods do not specify. It also does not validate SC
administration, a particular device or a different solvent. Syringe-unit conversions are omitted
because volume markings do not express Thymalin biological activity.
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BUYING NOTES

The relevant distinction is a traceable pharmaceutical extract versus material whose composition and manufacturing controls are unknown. A certificate of analysis can support identity and quality assessment, but cannot establish clinical efficacy or authorization.

For an extract, a percentage labeled purity is uninterpretable without the assay method, reference standard, integration rules and definition of the measured material. A single chromatographic peak does not automatically prove fraud, and multiple peaks do not prove authenticity. Useful documentation identifies the tested batch, peptide content, molecular profile, source tissue and relevant microbial controls. Sterility, endotoxin and tissue-sourcing documentation answer different questions. No single certificate establishes all of them. Evidence from the pharmaceutical preparation does not automatically transfer to another mixture sold under the same name.

COMMON MISTAKES

- Treating Russian approval as high-certainty evidence for longevity, muscle gain or recovery. Approval and claim-specific evidence must be interpreted separately.
- Reading before-after biomarker changes as equivalent reductions in infection, thrombosis or mortality risk.
- Quoting the 2022 mortality percentages without addressing the discrepancy between its English and Russian abstracts.
- Calling Thymalin uniformly anti-inflammatory while omitting increased IL-6 in unstimulated cells reported in PMID 37686182.
- Substituting synthetic Epitalon for the pineal extract used in the human combination study.
- Assuming that SC, IM, oral and electrophoretic administration produce equivalent exposure or clinical effects.
- Assigning one half-life to an incompletely characterized mixture or inferring clearance from peptide length.
- Treating an HPLC purity percentage as proof of identity, sterility, biological potency or pharmaceutical equivalence.

- Converting a short hospital trial into a recurring wellness schedule without evidence for that population, route or duration.
- Presenting theoretical immune risks as established contraindications, or treating incomplete adverse-event reporting as evidence that harms do not occur.

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ARA-290 (Cibinetide)

Cibinetide

Erythropoietin-derived innate repair receptor agonist | Module 3 · Shielding | Goals: Recovery | Route: SC

An investigational, nonerythropoietic EPO-derived peptide with preliminary human neuropathy findings, uncertain clinical benefit, and no established application to exercise recovery.

WHAT IT IS

ARA-290, also called cibinetide or pyroglutamate helix B surface peptide, is a synthetic peptide containing 11 amino acids. Its design reproduces features of the three-dimensional surface of erythropoietin's helix B region. Calling it simply a fragment copied from EPO obscures this structure-based design. The N-terminal residue is pyroglutamate (PMID 25728128).

The development goal was to separate EPO's tissue-protective signaling from its stimulation of red blood cell production. Experimental studies describe anti-inflammatory and cytoprotective effects without corresponding erythropoietic activity. That distinction does not establish freedom from cardiovascular, immune, or other adverse effects in humans (PMID 25728128, PMID 29570934).

Cibinetide remains investigational. Published patient studies concentrate on sarcoidosis-associated small fiber neuropathy, diabetic neuropathy, and diabetic macular edema. A separate randomized experiment assessed emotional processing in healthy volunteers without demonstrating improved mood (PMID 26431906).

Within a recovery module, this compound belongs under experimental nerve and inflammatory disease research. No controlled human evidence identified here establishes faster recovery from resistance training, tendon injury, muscle damage, or joint injury. Human muscle samples have been examined for receptor expression, but those experiments were not clinical treatment trials (PMID 24055514).

MECHANISM

The principal model distinguishes erythropoietic signaling through the EPOR homodimer from tissue-protective signaling involving EPOR and CD131. The latter complex is commonly called the innate repair receptor. Cibinetide was designed to preferentially engage this protective pathway without reproducing EPO's erythropoietic effects (PMID 25728128).

CD131 also participates in receptors for several immune cytokines. Its involvement does not mean cibinetide activates or blocks every receptor containing that subunit. The receptor's composition, cellular context, and downstream signaling remain relevant to interpretation. A shared subunit alone cannot predict a clinical drug interaction.

Human skeletal muscle from patients with critical limb ischemia showed increased EPOR and CD131 expression. Both proteins also colocalized in control muscle. Colocalization supports biological plausibility but does not independently demonstrate direct peptide binding or establish receptor stoichiometry. The therapeutic experiments in that paper involved ischemic myotubes in vitro, not treated patients (PMID 24055514).

Functional receptor evidence comes from animal perturbation experiments. Cibinetide's antiallodynic effect disappeared in mice lacking CD131. The relevant paper's title emphasizes ketamine, but its experiments also directly tested ARA-290, so the citation is relevant (PMID 23936499). In experimental cerebral ischemia, CD131 knockdown suppressed ARA290-associated neuroprotection (PMID 38488446). These findings support receptor involvement in those models rather than proving one exclusive mechanism across all tissues.

In experimental colitis, cibinetide reduced inflammatory cell infiltration and inflammatory mediator production. Macrophage experiments implicated functional CD131 and JAK2, with reduced NF-kappaB p65 activity (PMID 29026145). In autoimmune neuritis, treatment shifted helper T-cell populations, reduced inflammatory

activation, and improved nerve repair measures (PMID 24603865). Islet transplantation experiments also found reduced dendritic cell maturation and allogeneic T-cell responses (PMID 32345869).

Other studies describe tissue-survival pathways rather than a general growth effect. Diabetic mouse wounds showed changes in VEGF, phosphorylated Akt, and phosphorylated eNOS alongside improved healing (PMID 29223734). Kidney cell experiments found reduced cisplatin-associated injury and apoptosis, but these were cell-line findings rather than clinical renal protection (PMID 36085231).

A separate study reported inhibition of TRPV1 activity and reduced capsaicin-associated hypersensitivity (PMID 26774587). This suggests another possible mechanism. It does not establish clinically meaningful TRPV1 antagonism or prove independence from the repair-receptor pathway in patients.

The frequently cited molecular-switch explanation addresses the mismatch between brief circulating exposure and longer biological effects. A pharmacology review reports a plasma half-life of approximately two minutes and proposes persistent downstream signaling (PMID 25728128). This remains a mechanistic explanation, not a validated method for predicting treatment duration, redosing intervals, or reversibility of adverse effects.

EVIDENCE · GRADE B

B for preliminary human neuropathy findings under the scale's small, short-trial category. Several randomized studies exist, but their size, duration, endpoints, and mixed results limit clinical certainty. Their existence does not establish an effective treatment for neuropathy or justify an exercise-recovery claim. Corneal nerve measurements are promising surrogate outcomes, while pain and functional benefits require confirmation. Exercise recovery remains unsupported, with only mechanistic extrapolation relevant to that intended use.

Human data. The reviewed clinical literature includes five patient treatment studies and a randomized experiment in healthy volunteers. These should not be described as four trials or treated as one homogeneous body of evidence. The initial sarcoidosis pilot enrolled 22 patients. It reported improved small fiber neuropathy screening scores versus placebo. Brief Pain Inventory and fatigue scores improved similarly in both groups, limiting claims of a specific analgesic or antifatigue effect (PMID 23168581). A subsequent blinded sarcoidosis study used daily subcutaneous administration for 28 days. It reported changes in neuropathic symptoms, corneal nerve fiber density, temperature sensitivity, and six-minute walking distance (PMID 24136731). Walking performance in patients with sarcoidosis is not evidence of enhanced athletic performance in healthy adults. The phase 2b sarcoidosis study randomized 64 participants. The middle-dose group showed a significant placebo-corrected increase in corneal nerve fiber area and a signal in regenerating skin nerve fibers. The lower and higher groups did not reach significance on the primary comparison. The reported pain comparison in the moderate-to-severe subgroup was not statistically significant, with P = 0.157 (PMID 28475703). A difference in significance between dose groups does not establish a significant difference between those groups. The diabetic neuropathy study reported changes in PainDetect scores, HbA1c, and lipid measures. Its corneal nerve finding concerned participants with sufficiently reduced baseline nerve density, not an unequivocal effect across all participants (PMID 25387363). These exploratory findings require independent replication

Animal and mechanistic data. Animal findings support biological activity across several disease models, but they do not form a validated human recovery protocol. Disease induction, species, timing, and outcome selection differ substantially between experiments. In rats with spared nerve injury, short-course treatment reduced allodynia for extended observation periods and altered spinal microglial responses. The reported behavioral effects extended to 20 weeks in that model (PMID 24529189). CD131-deficient mice lacked the corresponding antiallodynic response, supporting receptor involvement (PMID 23936499). Experimental autoimmune neuritis showed improved nerve regeneration and remyelination alongside altered inflammatory and T-cell responses (PMID 24603865). Mouse colitis experiments reported less inflammatory injury and improved disease measures (PMID 29026145). These findings cannot establish treatment of human autoimmune disease or inflammatory bowel disease. Islet studies found reduced inflammatory injury and improved engraftment in mice (PMID 26683514). An allogeneic transplantation experiment reported improved graft survival with a concomitant immunosuppressant, which is a specific experimental combination rather than evidence for general peptide stacking (PMID 32345869). Experiments using isolated human islets and transplantation into mice remain preclinical, despite the human origin of the cells (PMID 34498509). Other findings include improved diabetic wound healing, reduced injury after experimental cerebral ischemia, and reduced autoimmune abnormalities in lupus models (PMID 29223734, PMID 38488446, PMID 29570934). Retinal

and do not establish diabetes treatment or prevention of neuropathy complications. The uncontrolled retinal study recruited nine patients, with eight completing treatment. Mean visual acuity, retinal thickness, retinal sensitivity, and tear production did not improve. A questionnaire signal and individual responses cannot establish efficacy without a comparator (PMID 32674280). The healthy-volunteer experiment randomized 36 participants. It found some changes in emotional processing but no improvement in mood or affective symptoms. The authors did not consider the overall pattern clearly antidepressant-like (PMID 26431906). A methodological analysis supports corneal nerve area as a measure of morphological change. It does not validate every change as a predictor of durable symptom relief (PMID 29549285). A systematic review of sarcoidosis fatigue treatments likewise found limited trial evidence (PMID 27507833). Safety reporting must include observed adverse events rather than relying exclusively on reassuring abstract conclusions.

experiments examined enhancement of transplanted endothelial cell repair in an ischemic mouse model, not established treatment of human retinal edema (PMID 30876881). In an Alzheimer-like mouse model, early treatment affected amyloid pathology and cognition, but benefits were compromised in older animals with advanced pathology (PMID 34343617). A later diabetic mouse study improved insulin sensitivity and changed monocyte populations without rescuing executive cognitive flexibility (PMID 41933665). These negative or conditional findings limit broad neuroprotection claims. A 15-month study in aging rats reported cardiovascular and frailty-related changes, not demonstrated human longevity benefits (PMID 36741836). Another mouse study increased bone mineral density and inhibited osteoclast development (PMID 35008482). These results show additional biological effects that require human investigation rather than supporting claims of universal tissue repair.

REGULATORY STATUS AND SPORT

STATUS

Investigational, with no approved therapeutic indication identified in this review. Published human development includes phase 2 studies; no phase 3 efficacy publication was identified. This does not establish that development has permanently stopped or verify the status of every jurisdiction worldwide. A 2026 review discusses cibinetide within a field still limited by inadequate clinical evidence and regulatory uncertainty (PMID 42635865). Trial registration, an investigational authorization, a substance identifier, and orphan designation are different from marketing approval. None independently establishes an approved prescription product, an approved dose, or a label-supported preparation procedure. The relevant patient programs include sarcoidosis-associated neuropathy, diabetic neuropathy, and diabetic macular edema. The retinal study was registered as EudraCT 2015-001940-12 and ISRCTN16962255 (PMID 32674280). Claims that pharmaceutical-quality investigational material cannot exist because a drug lacks approval are incorrect. Clinical-trial manufacturing quality and marketing authorization are separate questions.

WADA

Prohibited at all times under the 2026 framework. S2.1.5 covers innate repair receptor agonists, the pharmacological category applicable to cibinetide. This classification is based on the listed class, although cibinetide is not named among its examples. S0 applies to unapproved substances not already addressed by subsequent sections, so S0 is not the appropriate primary explanation here. Source: [WADA 2026 Prohibited List, S2.1.5](https://ita.sport/uploads/2025/09/2026list_en_final_clean_september_2025.pdf). Published anti-doping research also explicitly treats ARA-290 as prohibited (PMID 28941172, PMID 25382550). Its nonerythropoietic design and short plasma half-life do not make it permitted.

RESEARCH USE · REPORTED, NOT RECOMMENDED

ROUTES

Published patient trials used intravenous or subcutaneous administration. The initial sarcoidosis pilot used repeated intravenous administration (PMID 23168581). Later neuropathy and retinal studies used subcutaneous administration (PMID 24136731, PMID 25387363, PMID 32674280). The phase 2b registry explicitly confirms the subcutaneous route, resolving the omission from its abstract (PMID 28475703; NCT02039687). A healthy-volunteer experiment used a single intravenous administration (PMID 26431906; NCT02070783). No clinically validated oral or intranasal regimen was identified. Absence of an identified formulation is not proof that no experimental formulation has ever been studied.

HALF-LIFE

Approximately two minutes in plasma is reported in the pharmacology review, but it should not be presented as a universally established human subcutaneous terminal half-life (PMID 25728128). Absorption, sampling, assay methods, and administration route affect pharmacokinetic estimates. In vitro blood experiments documented rapid enzymatic breakdown, providing separate metabolic evidence rather than a clinical dosing schedule (PMID 28941172). A later review discusses short exposure as a development limitation and describes a cyclized derivative as a separate research

approach (PMID 38943972). Short circulating exposure does not establish the duration of benefit, justify repeated daily administration, or determine solution shelf life.

TIMING

No identified trial compared dosing around meals, bedtime, or exercise. The clinical schedules varied between repeated intravenous administration, daily subcutaneous administration, and a single experimental administration. Therefore, the statement that every human trial used daily dosing was incorrect. A short plasma half-life does not establish that the peptide is completely absent by a particular activity or that circulating concentrations are irrelevant. There is no clinical evidence supporting workout-specific timing (PMID 23168581, PMID 25387363, PMID 26431906).

CYCLE LENGTH

Several neuropathy trials used approximately four weeks of treatment, followed in some cases by observation without treatment. The longest repeated human course identified here was the 12-week retinal pilot (PMID 32674280). These are study durations, not validated cycling schedules. They do not establish a treatment-free interval, a maximum number of courses, or the consequences of repeated courses. The diabetic neuropathy study included a month of post-treatment observation. Persistence of selected measurements does not demonstrate permanent nerve repair or define the duration of an individual response (PMID 25387363). The 15-month aging-rat experiment supplies long-duration animal exposure, not evidence supporting chronic human administration (PMID 36741836).

TITRATION

No clinically validated titration protocol was identified. The principal dose-ranging trial assigned fixed regimens rather than escalating participants according to response. Its middle-dose group met the placebo comparison on the primary endpoint, while the other groups did not (PMID 28475703). This pattern neither establishes a bell-shaped dose-response curve nor proves that escalation reduces efficacy. Those conclusions would require adequate direct comparisons and replication. Published fixed-dose experiments do not supply a validated response-based escalation or tapering algorithm.

CONTEXT	DOSE	ROUTE	FREQUENCY	PROVENANCE
Phase 2b randomized sarcoidosis-associated small fiber neuropathy trial, 64 randomized participants.	**1 mg, 4 mg, or 8 mg per administration, subcutaneously once daily for 28 days, reported in PMID 28475703 and registry NCT02039687.**	Subcutaneous, confirmed in NCT02039687.	Once daily for 28 days.	Human trial, PMID 28475703. Only the middle-dose group reached statistical significance versus placebo on corneal nerve fiber area. This does not prove superiority over the higher-dose group or establish an optimal clinical dose. Registry methods: [NCT02039687] (https://clinicaltrials.gov/study/NCT02039687). · PMID 28475703
Randomized phase 2 study in type 2 diabetes with painful neuropathy.	**4 mg per administration, subcutaneously once daily for 28 days, reported in PMID 25387363.**	Subcutaneous.	Once daily for 28 days, followed by 28 days without study treatment.	Human trial, PMID 25387363. Reported metabolic and symptom signals were exploratory. The corneal nerve finding concerned a subgroup with reduced baseline density. This is a study regimen, not an established treatment recommendation. · PMID 25387363
Initial randomized sarcoidosis pilot, 22 participants.	**2 mg per administration, intravenously three times weekly for four weeks, reported in PMID 23168581.**	Intravenous.	Three times weekly for four weeks.	Human trial, PMID 23168581. Small fiber neuropathy screening scores improved versus placebo. Pain inventory and fatigue scores improved similarly in both groups. · PMID 23168581
Open-label diabetic macular edema pilot.	**4 mg per administration, subcutaneously once daily for 12 weeks, reported in PMID 32674280.**	Subcutaneous.	Once daily for up to 12 weeks.	Human trial, PMID 32674280. The study did not demonstrate improvement in its principal mean visual or retinal outcomes. Its uncontrolled design cannot establish efficacy. · PMID 32674280

CONTEXT	DOSE	ROUTE	FREQUENCY	PROVENANCE
Diabetic mouse incisional wound-healing experiment.	**30 mcg/kg per administration, subcutaneously once daily, with assessments through 14 days, reported in PMID 29223734.**	Subcutaneous.	Once daily; animals were assessed at different time points after injury.	Animal study, PMID 29223734. Reported changes included wound healing, angiogenesis, and biochemical markers. This weight-based animal dose does not establish a human equivalent. · PMID 29223734
Mouse pancreatic islet transplantation experiment.	**120 mcg/kg per administration, intraperitoneally before transplantation and at 0, 6, and 24 hours afterward, reported in PMID 26683514.**	Intraperitoneal.	Periprocedural administrations before transplantation and at the specified postoperative time points.	Animal study, PMID 26683514. The regimen addressed transplantation-associated inflammation. It is not a daily human maintenance schedule and does not translate through simple body-weight multiplication. · PMID 26683514
Randomized emotional-processing experiment in 36 healthy volunteers.	**2 mg intravenously as a single administration, reported in PMID 26431906, with route confirmed in NCT02070783.**	Intravenous.	One administration; neuropsychological assessment occurred one week later.	Human experimental study, PMID 26431906, registry NCT02070783. Some emotional-processing measures changed, but mood and affective symptoms did not improve. · PMID 26431906

STACKING

+ BPC-157

No demonstrated combination benefit. Cibinetide's diabetic wound findings include angiogenic and survival-signaling changes, but pathway overlap does not establish additivity or redundancy with BPC-157 (PMID 29223734). No identified combination trial supports this pairing or a musculoskeletal recovery claim.

+ TB-500

No demonstrated combination benefit or established interaction profile. Mechanisms attributed to full-length thymosin beta-4 cannot automatically be assigned to every material described as TB-500. A proposed difference in targets does not establish complementary clinical effects with cibinetide.

+ GHK-Cu

No demonstrated synergy. Different routes or intended tissue compartments do not prove that two agents cannot interact. No identified clinical study establishes the efficacy, systemic exposure, or tolerability of this combination.

– FOXO4-DRI

An unstudied combination, not an established pharmacological contraindication. Cibinetide reduced apoptosis in specific cell experiments, but this does not prove that it blocks FOXO4-DRI-mediated senolysis (PMID 36085231). Effects depend on cell state, exposure, and pathway engagement.

– Thymosin Alpha-1

An unstudied immune-modulating combination. Cibinetide affected T-cell differentiation and dendritic cell responses in experimental systems (PMID 24603865, PMID 32345869). These observations do not establish an opposite clinical effect to thymosin alpha-1 or predict the net response.

– LL-37

An unstudied combination with uncertain immune effects. Cibinetide's inhibition of selected inflammatory responses does not prove that LL-37 and cibinetide cancel one another (PMID 29026145). A simple immune-amplifier versus immune-suppressor model is insufficient.

+ KPV	No demonstrated synergy. Cibinetide has experimental colitis evidence, but that does not validate a combination with KPV or establish a distinct receptor mechanism for the pair (PMID 29026145). The proposed gut-inflammation application remains untested.

SAFETY

COMMON EFFECTS

In the retinal pilot, all nine participants experienced at least one adverse event. Reported events included headache, cold symptoms, nausea, and laboratory changes. Investigators considered headache, cold symptoms, and nausea potentially treatment-related. Elevated glucose and triglycerides were difficult to interpret because fasting was not confirmed (PMID 32674280). Source: [Retinal trial safety results](https://pmc.ncbi.nlm.nih.gov/articles/PMC7408632/). The phase 2b registry also contains systematic adverse-event tables, including events in placebo recipients. These are events observed during the study, not automatically adverse reactions caused by cibinetide. The available studies cannot reliably define population-level frequencies or long-term tolerability. Dose amount alone does not establish injection volume or discomfort; concentration and formulation also matter.

SERIOUS SIGNALS

The phase 2b registry reports serious adverse events in active-treatment recipients. Recorded terms include syncope, headache, chest tightness, shortness of breath, enteritis, and suicidal ideation. The registry does not establish that cibinetide caused these events. Nevertheless, their presence makes an unqualified claim of no serious human signals inappropriate. Source: [NCT02039687 adverse-event results](https://clinicaltrials.gov/study/NCT02039687?tab=results). The compound's nonerythropoietic design does not prove absence of thrombosis or cardiovascular risk. A review contrasting EPO with nonerythropoietic derivatives primarily discusses experimental protection and the problems encountered with EPO, not definitive human cardiovascular safety for ARA-290 (PMID 23964738). Cancer, infection, and immune effects remain insufficiently characterized. Anti-apoptotic effects in cultured cells and immune changes in animals provide reasons for investigation, not evidence that specific clinical harms necessarily occur. Bone metabolism also changed in mice, without corresponding human outcome data (PMID 35008482).

CONTRAINDICATIONS

There is no approved label defining formal contraindications. Pregnancy, breastfeeding, pediatric treatment, and long-term administration lack adequate clinical safety evidence. A history of hypersensitivity to the compound or formulation would be a clinical exclusion concern. Active malignancy, serious infection, significant immunosuppression, severe organ disease, and psychiatric instability require separate clinical assessment because evidence is insufficient. Trial exclusion criteria should not be presented as proven drug contraindications. Conversely, the absence of a formal contraindication does not establish suitability. Animal immunomodulation does not establish universal immune suppression in humans (PMID 24603865, PMID 32345869). Existing neuropathy, diabetes, retinal disease, and psychiatric care are relevant to interpreting symptoms and laboratory changes during any investigational exposure. WADA prohibition is a sporting restriction, not a medical contraindication.

STOP RULES

Breathing difficulty, facial or throat swelling, chest pain, fainting, or new suicidal thoughts require urgent medical assessment and interruption of further investigational exposure pending review. Fever with spreading injection-site redness, new neurological deficits, or deteriorating vision also warrants prompt assessment. These are general clinical response rules, not a validated cibinetide monitoring algorithm. A predefined trial duration is not proof that continuing until that endpoint is appropriate when symptoms worsen. Conversely, completing a published duration does not establish the effectiveness or safety of another course. No evidence-based self-management schedule for extension, retreatment, or tapering was identified.

RECONSTITUTION AND STORAGE

TYPICAL VIAL

No approved commercial vial strength or standardized consumer presentation exists. Research-market package sizes are not clinical specifications, and none is endorsed here as typical. Investigational trial material should not be assumed equivalent to a powder bearing the same compound name. A stated vial mass may refer to nominal content, measured peptide content, or total material containing counterions and residual water. These measurements are not interchangeable. Identity, assay, impurity profile, sterility, and endotoxin testing answer different questions.

SOLVENT

No general reconstitution solvent is established by the cited clinical evidence for arbitrary research material. A trial's formulation cannot be reconstructed from its dose and administration route alone. Benzyl alcohol compatibility, pH, osmolality, adsorption, container interactions, and peptide stability require formulation-specific data. Bacteriostatic water does not sterilize a contaminated powder and does not establish suitability for repeated access. Plain sterile water does not resolve those limitations either. The observed enzymatic breakdown in blood concerns metabolism, not compatibility with a particular solvent or storage container (PMID 28941172).

STORAGE

No universal temperature, freezing rule, or post-reconstitution expiry can be assigned from the cited literature to unspecified research material. Valid storage conditions depend on formulation, container, manufacturing controls, and stability testing. Blood half-life cannot supply a refrigerated shelf life. Cloudiness, visible particles, discoloration, or damaged packaging indicate a quality problem, but a clear solution does not demonstrate sterility or chemical stability. A proposed expiry measured in days is still an unsupported expiry when no relevant data exist. Trial-specific handling instructions apply to that investigational preparation and should not be generalized to other material.

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Illustrative concentration arithmetic only, not a preparation or administration protocol: a hypothetical solution containing 5 mg of peptide in a final volume of 1.0 mL has a concentration of 5 mg/mL. This equals 5000 mcg/mL. These hypothetical quantities describe solution content, not a studied dose or validated formulation. If that same hypothetical peptide mass were present in a final volume of 2.0 mL, the concentration would be 2.5 mg/mL. Doubling final volume halves concentration. The relevant denominator is final solution volume, which should not automatically be assumed identical to added solvent volume. The governing relationships are concentration equals peptide mass divided by final volume, and represented mass equals concentration multiplied by measured volume. Milligrams, micrograms, and milliliters describe different quantities. A device marking does not independently state peptide mass, and a mass calculation does not establish bioactivity or sterility. No injection-device conversion or preferred dilution follows from this example. Actual tolerability depends on the complete formulation and administration conditions. Arithmetic also cannot establish peptide identity, assay accuracy, solution stability, or whether material matches that used in a trial.
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BUYING NOTES

There is no established consumer supply equivalent to the investigational preparations used in these studies. A certificate of analysis can support particular analytical claims but cannot establish therapeutic suitability. Marketing descriptions such as pharmaceutical grade are not substitutes for documented manufacturing and release standards.

An interpretable analytical package identifies the sampled lot, laboratory, methods, dates, specifications, and measured results. Mass spectrometry can support molecular identity, while chromatographic methods can characterize detectable impurities. A chromatographic purity percentage is not a measurement of the peptide mass in a vial, and neither result independently establishes biological potency.

For cibinetide, identity characterization needs to distinguish the intended pyroglutamate-containing peptide from sequence variants and incomplete synthesis products. A blood-metabolism study does not authenticate a supplied vial or establish that a similar mass spectrum identifies every structural feature (PMID 28941172).

Sterility, endotoxin burden, residual solvents, counterions, water content, and container compatibility require appropriate separate assessments. Even authentic analytical documents apply to the tested sample and lot, not automatically to every item carrying the same label. A matching lot number is necessary for traceability but does not itself prove independent testing.

The clinical evidence cannot establish the quality of material obtained outside the trials. It also cannot supply a validated storage period, preparation method, or clinical use simply because a named compound has published references. The meaningful comparison is between documented preparations and their testing, rather than between package sizes or claimed purity percentages.

COMMON MISTAKES

- Calling cibinetide a straightforward EPO fragment. It was designed from features of EPO's three-dimensional helix B surface. Its nonerythropoietic design does not establish cardiovascular safety or an endurance benefit (PMID 25728128).

- Treating a statistically significant placebo comparison in one dose group as proof that it outperformed another active group. The phase 2b results do not establish an optimal dose or a confirmed bell-shaped response (PMID 28475703).
- Using the approximately two-minute plasma estimate to invent a redosing interval or workout schedule. Clinical schedules varied, and pharmacokinetic exposure does not independently establish clinical duration of action (PMID 25728128, PMID 23168581, PMID 26431906).
- Equating corneal nerve morphology with proven pain relief, permanent nerve repair, or athletic recovery. These are different outcomes. The largest trial's highlighted pain comparison did not reach statistical significance (PMID 28475703).
- Assuming that absence of erythropoiesis means the compound is permitted in sport. The current WADA framework prohibits innate repair receptor agonists at all times. Detection research is consistent with that prohibition (PMID 28941172).
- Converting animal doses to human doses by multiplying by body weight. The wound and transplantation studies used different species, routes, schedules, and disease models. Their exposure-response relationships do not establish human dosing (PMID 29223734, PMID 26683514).
- Reading no identified treatment-related safety issue as no adverse events. Both the clinical literature and the phase 2b registry contain adverse-event reporting, including serious events requiring careful interpretation rather than automatic attribution.
- Treating a certificate of analysis, a clear solution, or correct concentration arithmetic as proof of injectable quality. Identity, content, impurities, sterility, endotoxin burden, and stability require distinct evidence.
- Assuming that different mechanisms establish synergy or that apparently opposite mechanisms establish cancellation. No identified studies validate the catalog peptide combinations described here.
- Treating experiments on human cells transplanted into mice as human clinical trials. Human islet studies remain preclinical when treatment outcomes are measured in culture or animal recipients (PMID 34498509).

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and 49 controls, immune-marker analyses, and inconsistent retrospective versus random-allocation terminology.)

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impact. Supports lesion, apoptosis, and microglial morphology findings while documenting unchanged measured cytokine expression and total Iba-1-positive cell numbers.)

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130. Staresinic M et al. Gastric pentadecapeptide BPC 157 accelerates healing of transected rat Achilles tendon and in vitro stimulates tendocytes growth.. *Journal of orthopaedic research : official publication of the Orthopaedic Research Society*, 2003. PMID 14554208 DOI 10.1016/S0736-0266(03)00110-4 (Rat Achilles transection outcomes, experimental intraperitoneal dose provenance, timing, peptide sequence, and approximate molecular weight. Does not prove a flat human dose-response curve.)

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