

TB-500 (Ac-LKKTETQ)

The N-acetylated thymosin- β 4 17-23 fragment

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Medical review

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ABSTRACT

The LKKTETQ motif belongs to the actin-related functional region of thymosin-β4 and retains selected activity in defined experimental systems.

This monograph uses TB-500 to denote the N-acetylated heptapeptide Ac-LKKTETQ. It distinguishes that commercial fragment from unacetylated LKKTETQ and from full-length 43-residue thymosin beta-4.

This monograph begins with the molecule and follows the causal chain through biochemistry, cellular mechanism, exposure and integrated physiology. Population studies enter only at the terminal stress-test: useful for the proposition actually tested, incapable of defining the molecule or replacing the causal model.

ESTABLISHED	UNRESOLVED
• Ac-LKKTETQ analytically identified • Distinct from 43-residue thymosin-β4 • Fragment metabolism studied preclinically	• Human PK • Direct controlled efficacy • Systemic safety profile

EVIDENCE HIERARCHY

Mechanistic evidence is not a lower-grade substitute for population medicine. Physical constraints, biochemical measurements, historical and non-English records, exposure studies and clinical outcomes answer different questions. Controlled clinical trials test the complete implemented proposition; they cannot manufacture a missing identity, mechanism or exposure bridge.

I	Molecular identity and chemistry
II	Biochemistry and target architecture
III	Cells and ex-vivo tissues
IV	Animal and in-vivo pharmacology
V	Integrated physiology and translation
VI	Human PK and observational signal
VII	Controlled clinical trials

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ACTION LEDGER

Describe the action before judging its value.

Benefit is a downstream clinical judgement. The scientific object is the action itself: what moves, under which exposure, in which biological state, and where the inference stops.

01 Attributed biochemical action	The LKKTETQ motif belongs to the actin-related functional region of thymosin- β 4 and retains selected activity in defined experimental systems.
02 Exposure and reachability	Fragment-specific metabolism has been characterised in vitro and in rats. This does not establish human systemic pharmacokinetics, dose-exposure relationships or clinical target engagement.
03 Physiological direction is contextual	Actin dynamics, cell migration, angiogenesis and matrix remodelling are necessary components of repair but are not synonymous with high-quality tissue restoration. Spatial organisation, tensile function, inflammatory state and proteolytic balance determine whether greater cellular movement produces useful repair, fibrosis or disordered remodelling.
04 Individual adjudication boundary	Whether the isolated acetylated fragment reaches and reproduces the parent peptide's spatially organised functions in humans. A full-length thymosin- β 4 wound study is not clinical evidence for systemic Ac-LKKTETQ.

METHODS AND COVERAGE

A reproducible boundary, not an implied exhaustive review.

This curated mechanistic monograph uses primary indexed records and reference-chaining. It does not claim systematic-review completeness. Absence of a retrieved result is not evidence that an effect is absent.

SEARCH SURFACE	PubMed/MEDLINE primary records, Russian-language indexed abstracts, and reference-chaining for entity-defining, historical and translational studies. Language, geography, regulatory status and journal fashion are not evidence grades.
QUERY FRAME	TB-500 · Ac-LKKTETQ · LKKTETQ · thymosin beta-4 · actin binding · angiogenesis · matrix remodelling
EVIDENCE CUTOFF	23 August 2026
ENTITY EXCLUSION	Ac-LKKTETQ, unacetylated LKKTETQ and full-length 43-residue thymosin-β4 are three distinct entities. Shared motif does not confer shared pharmacokinetics or an identical evidence base.
TRACEABILITY	12 extended claim units plus 2 historical records and 3 mechanistic-calculus records; 8 cited records in the complete corpus.
INTERPRETIVE RULE	Identity → physical constraint → measured reaction or binding → reachable exposure → system response → outcome. Statistical significance does not manufacture mechanism; mechanistic plausibility does not manufacture a patient outcome.

EVIDENCE ATLAS

Every claim keeps its experimental address.

12 claim units are mapped to evidentiary layer, experimental frame and source records. The layer describes the question answered; it is not a popularity score.

LAYER	EXPERIMENTAL FRAME	FINDING AND BOUNDARY	SOURCES
IMolecular identity	The identity problem · claim 1	Full-length thymosin beta-4 is a 43-amino-acid peptide. Its central actin-binding region contains residues 17-23, LKKTETQ. Commercial TB-500 is commonly associated with an N-acetylated version of this fragment. Full-length peptide, unacetylated heptapeptide and Ac-LKKTETQ are structurally distinct entities.	[1][3][4]
IMolecular identity	The identity problem · claim 2	Terminal acetylation can alter proteolysis, mass and molecular interaction. A study identifying or metabolising Ac-LKKTETQ cannot be silently relabelled as a study of full-length thymosin beta-4, and a full-length wound trial cannot establish systemic efficacy of the fragment.	[1][2]
II/VMechanism and physiological translation	Actin-binding biology · claim 1	Full-length thymosin beta-4 forms a 1:1 complex with monomeric actin and helps maintain a reservoir of unpolymerised G-actin. Structural work places contacts across both ends of actin. This is a developed biochemical mechanism for the parent peptide.	[3]
IIICell or ex-vivo system	Actin-binding biology · claim 2	The LKKTETQ motif is central to actin-related biology, but the fragment does not necessarily reproduce the conformational reach, intracellular localisation or regulatory functions of the 43-residue parent. A shared motif is evidence of relationship, not evidence of equivalence.	[3][4]
VIHuman exposure or signal	Angiogenesis and matrix remodelling · claim 1	In endothelial migration and vessel-sprouting assays, the seven-residue actin-binding motif displayed activity similar to full-length thymosin beta-4 at the tested concentrations. This local experimental result supports motif-level angiogenic activity but does not define systemic human exposure or clinical dose.	[4]
VIIControlled human proposition	Angiogenesis and matrix remodelling · claim 2	Full-length thymosin beta-4 and its central domain have also increased matrix-metalloproteinase expression in wound-related cells. Matrix remodelling requires both synthesis and controlled degradation; an increase in MMP expression is therefore a mechanistic event, not automatically an improvement in tissue strength.	[5]

LAYER	EXPERIMENTAL FRAME	FINDING AND BOUNDARY	SOURCES
IVIntegrated in-vivo model	Preclinical wound models · claim 1	In diabetic and aged mice, full-length thymosin beta-4 accelerated several wound-repair measures. The unacetylated LKKTETQ synthetic peptide produced repair activity in aged animals comparable to the parent in that model. This is important fragment-level evidence, but the studied entity and local model must remain explicit.	[6]
VIHuman exposure or signal	Preclinical wound models · claim 2	A dermal wound outcome in mice cannot establish recovery of a human tendon, muscle, cardiac lesion or neurological injury. Tissue, route, mechanical environment and endpoint all change the translation problem.	[5][6]
VIHuman exposure or signal	Pharmacology and human evidence · claim 1	Analytical studies have characterised Ac-LKKTETQ and fragment metabolism in vitro and in animals. Human systemic pharmacokinetics, bioavailability, target engagement and immunogenicity have not been adequately established for the commercial fragment.	[1][2]
VIHuman exposure or signal	Pharmacology and human evidence · claim 2	Human wound studies using defined full-length thymosin beta-4 preparations are evidence for those exact preparations and routes. They do not close the evidence chain for systemic Ac-LKKTETQ. At present, there is no adequate controlled human efficacy programme for the entity defined in this monograph.	[1][2]
VIHuman exposure or signal	Scientific conclusion and boundary · claim 1	The fragment has a biologically meaningful relationship to the parent peptide, supported by actin-binding, angiogenesis and wound-model experiments. The scientific error is not to study the fragment; it is to transfer the parent molecule's full evidence base without resolving sequence, terminal chemistry, route and exposure.	[3][4][5][6]
VIHuman exposure or signal	Scientific conclusion and boundary · claim 2	A credible human programme must begin with analytical identity and route-specific PK, then demonstrate target engagement before moving to outcome claims. Until that chain exists, efficacy statements for systemic TB-500 remain conditional rather than established.	[1][2]

SECTION 01

Molecular dossier: the entity before the outcome

ENTITY — N-acetylated heptapeptide Ac-LKKTETQ

BIOCHEMICAL CLASS — Thymosin-β4 17-23 fragment

PRIMARY SYSTEM — Actin-associated migration · angiogenesis · matrix remodelling

IDENTITY BOUNDARY — Ac-LKKTETQ, unacetylated LKKTETQ and full-length 43-residue thymosin- β 4 are three distinct entities. Shared motif does not confer shared pharmacokinetics or an identical evidence base.

SECTION 02

Historical and international corpus

Thymosin biology has been studied since the 1960s and full-length thymosin beta-4 was sequenced in 1981. The commercial Ac-LKKTETQ fragment is a later, distinct chemical entity and cannot inherit the entire historical corpus.

This is where historical depth most easily becomes category error: parent peptide, unacetylated motif and acetylated seven-residue product must remain separated.

SECTION 03

1960s-1980s: Deep thymosin lineage

Thymic fractions preceded isolation and sequencing of distinct alpha and beta thymosins. Full-length thymosin beta-4 was established as a 43-residue N-acetylated peptide, creating a substantial parent-molecule literature.[7]

SECTION 04

1990s-2000s: Actin structure and fragment activity become separable questions

Structural studies mapped extended full-length contacts across actin, while fragment experiments found activity of the LKKTETQ motif in defined endothelial assays. Those records prove relationship but also demonstrate why seven residues cannot reproduce every parent contact.[4][8]

SECTION 05

Mechanistic calculus — CONSTRAINED: Seven residues cannot preserve a 43-residue contact surface

Full-length thymosin beta-4 contacts actin across regions outside LKKTETQ. Removing 36 residues necessarily changes conformational reach even when the retained motif remains active.[7][8]

SECTION 06

Mechanistic calculus — MEASURED: Motif-level angiogenic activity exists

At the concentrations tested, LKKTETQ supported endothelial migration and sprouting similar to the parent peptide. This is direct fragment biology in an experimental system, not evidence of systemic human efficacy.[4]

SECTION 07

Mechanistic calculus — UNRESOLVED: Acetylation and systemic exposure remain unbridged

N-terminal acetylation can alter proteolysis and distribution. Without Ac-LKKTETQ-specific human PK, no dose can be mapped rigorously onto the in-vitro activity range.[1][2]

SECTION 08

Causal architecture: Sequence resolution precedes mechanism

Full-length thymosin- β 4 folds its 43 residues around actin, whereas TB-500 as defined here contains only the acetylated seven-residue central motif. Removing flanking residues and adding terminal acetylation changes mass, proteolysis and possible molecular contacts.[1][3]

SECTION 09

Causal architecture: A functional motif can retain partial activity

The LKKTETQ region has shown actin-related, endothelial-migration and wound-model activity in selected experiments. This supports biological continuity with the parent, but continuity is not equivalence: concentration, localisation and conformational reach differ.[4][6]

SECTION 10

Causal architecture: Matrix remodelling is bidirectional

Migration, angiogenesis and metalloproteinase regulation can participate in repair, fibrosis resolution or pathological remodelling. Faster closure or greater cellular movement does not by itself establish stronger or better organised tissue.[4][5]

SECTION 11

Causal architecture: Systemic translation remains open

Fragment metabolism has been approached analytically and preclinically, while adequate human systemic PK and target engagement remain absent. Clinical inference must therefore stop before human efficacy, even though motif-level biochemistry remains meaningful.[1][2]

SECTION 12

Molecular identity and entity resolution

In this monograph TB-500 denotes the N-terminally acetylated 17-23 fragment Ac-LKKTETQ. Full-length thymosin- β 4 is a separate 43-residue entity. The terminal acetyl group is part of identity; LKKTETQ alone is incomplete.

SECTION 13

Biochemical mechanism and target architecture

Full-length thymosin- β 4 regulates actin dynamics, migration, inflammatory signalling, angiogenesis and wound biology. Those mechanisms cannot automatically be assigned to Ac-LKKTETQ.

SECTION 14

In-vivo pharmacology and exposure

Fragment-specific metabolism has been characterised in vitro and in rats. This does not establish human systemic pharmacokinetics, dose-exposure relationships or clinical target engagement.

SECTION 15

Integrated physiology and individual terrain

Actin dynamics, cell migration, angiogenesis and matrix remodelling are necessary components of repair but are not synonymous with high-quality tissue restoration. Spatial organisation, tensile function, inflammatory state and proteolytic balance determine whether greater cellular movement produces useful repair, fibrosis or disordered remodelling.

SECTION 16

Terminal human stress-test

Controlled wound literature concerns defined full-length thymosin- β 4 preparations and specific routes. Adequate human evidence for systemic Ac-LKKTETQ administration has not been established.

SECTION 17

Counterevidence and causal boundaries

Evidence from full-length thymosin- β 4, a preconditioned-cell study or another route is not direct evidence for systemic Ac-LKKTETQ. Sequence and terminal chemistry change degradation and target interaction.

SECTION 18

Scientific conclusion

TB-500 requires strict entity resolution. Ac-LKKTETQ and full-length thymosin- β 4 cannot share a pharmacokinetic estimate or evidence base merely because commercial language groups them together.

SECTION 19

The identity problem

Full-length thymosin beta-4 is a 43-amino-acid peptide. Its central actin-binding region contains residues 17-23, LKKTETQ. Commercial TB-500 is commonly associated with an N-acetylated version of this fragment. Full-length peptide, unacetylated heptapeptide and Ac-LKKTETQ are structurally distinct entities.[1][3][4]

Terminal acetylation can alter proteolysis, mass and molecular interaction. A study identifying or metabolising Ac-LKKTETQ cannot be silently relabelled as a study of full-length thymosin beta-4, and a full-length wound trial cannot establish systemic efficacy of the fragment.[1][2]

SECTION 20

Actin-binding biology

Full-length thymosin beta-4 forms a 1:1 complex with monomeric actin and helps maintain a reservoir of unpolymerised G-actin. Structural work places contacts across both ends of actin. This is a developed biochemical mechanism for the parent peptide.[3]

The LKKTETQ motif is central to actin-related biology, but the fragment does not necessarily reproduce the conformational reach, intracellular localisation or regulatory functions of the 43-residue parent. A shared motif is evidence of relationship, not evidence of equivalence.[3][4]

SECTION 21

Angiogenesis and matrix remodelling

In endothelial migration and vessel-sprouting assays, the seven-residue actin-binding motif displayed activity similar to full-length thymosin beta-4 at the tested concentrations. This local experimental result supports motif-level angiogenic activity but does not define systemic human exposure or clinical dose.[4]

Full-length thymosin beta-4 and its central domain have also increased matrix-metalloproteinase expression in wound-related cells. Matrix remodelling requires both synthesis and controlled degradation; an increase in MMP expression is therefore a mechanistic event, not automatically an improvement in tissue strength.[5]

SECTION 22

Preclinical wound models

In diabetic and aged mice, full-length thymosin beta-4 accelerated several wound-repair measures. The unacetylated LKKTETQ synthetic peptide produced repair activity in aged animals comparable to the parent in that model. This is important fragment-level evidence, but the studied entity and local model must remain explicit.[6]

A dermal wound outcome in mice cannot establish recovery of a human tendon, muscle, cardiac lesion or neurological injury. Tissue, route, mechanical environment and endpoint all change the translation problem.[5][6]

SECTION 23

Pharmacology and human evidence

Analytical studies have characterised Ac-LKKTETQ and fragment metabolism in vitro and in animals. Human systemic pharmacokinetics, bioavailability, target engagement and immunogenicity have not been adequately established for the commercial fragment.[1][2]

Human wound studies using defined full-length thymosin beta-4 preparations are evidence for those exact preparations and routes. They do not close the evidence chain for systemic Ac-LKKTETQ. At present, there is no adequate controlled human efficacy programme for the entity defined in this monograph.[1][2]

SECTION 24

Scientific conclusion and boundary

The fragment has a biologically meaningful relationship to the parent peptide, supported by actin-binding, angiogenesis and wound-model experiments. The scientific error is not to study the fragment; it is to transfer the parent molecule's full evidence base without resolving sequence, terminal chemistry, route and exposure.[3][4][5][6]

A credible human programme must begin with analytical identity and route-specific PK, then demonstrate target engagement before moving to outcome claims. Until that chain exists, efficacy statements for systemic TB-500 remain conditional rather than established.[1][2]

SECTION 25

Falsification map

Analytical material inconsistent with Ac-LKKTETQ invalidates the entity attribution.

Lack of fragment-specific actin or migration effects would prevent inheritance from parent-peptide biology.

Human exposure insufficient for the active experimental range would break systemic translation.

RESEARCH AGENDA

What would materially change the conclusion?

- 01 Human PK of analytically confirmed Ac-LKKTETQ
- 02 Comparison of acetylated and unacetylated fragments
- 03 Direct fragment-versus-full-length target studies
- 04 Controlled route-specific human outcomes
- 05 Immunogenicity and repeated-dose safety
- 06 Matrix quality rather than wound-closure speed alone

CITED PRIMARY EVIDENCE CORPUS

8 source records

This corpus documents the claims made in this monograph; it is not presented as an exhaustive systematic-review search.

Esposito et al. Drug Test Anal. 2012;4:733-738. · PMID 22962027

Sanders et al. PNAS. 1992;89:4678-4682. · PMID 1584803

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Malinda et al. The actin-binding site on thymosin beta-4 promotes angiogenesis. J Biol Chem. 2003. · PMID 14500546

Philp et al. Thymosin beta-4 and LKKTETQ promote dermal repair in diabetic and aged mice. Wound Repair Regen. 2003. · PMID 12581423

Low et al. Complete amino acid sequence of bovine thymosin beta-4. Proc Natl Acad Sci USA. 1981;78:1162-1166. · PMID 6940133

Safer et al. Thymosin beta-4 binds actin in an extended conformation and contacts both ends. Biochemistry. 1997. · PMID 9153421

AUTHORSHIP AND ACCOUNTABILITY

Valentine Wibowo performed the conceptualisation, evidence synthesis, scientific interpretation and drafting. dr. I Wayan Cahyadi Surya Distira Putra, MPH completed medical review and approved the publication. Internal medical review is not represented as independent journal peer review.

No new patient data or human research were undertaken. The author and reviewer declare no personal financial competing interests. Clinic Terrain and Klinik Pratama Cepat Sehat provide clinical services; that institutional relationship is disclosed.