

BPC-157

Repair-associated signalling with incomplete human translation

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Medical review

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ABSTRACT

Across several experimental systems the peptide changes vascular, nitric-oxide, inflammatory and repair-associated responses rather than acting through one proven universal receptor.

This monograph examines the exact 15-amino-acid peptide BPC-157. It separates cell and animal mechanisms, animal pharmacokinetics, limited human administration and the large gap between experimental tissue effects and controlled patient outcomes.

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
• Defined 15-amino-acid identity • Substantial preclinical programme • Human administration reported	• Human PK • Controlled efficacy • Repeated-use and rare-event safety

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	Across several experimental systems the peptide changes vascular, nitric-oxide, inflammatory and repair-associated responses rather than acting through one proven universal receptor.
02 Exposure and reachability	Rat and dog studies describe short plasma half-life and species-dependent bioavailability. Human pharmacokinetic characterisation remains insufficient.
03 Physiological direction is contextual	Repair is a coordinated tissue process involving perfusion, inflammatory timing, matrix deposition, remodelling, mechanical loading and resolution. A change in nitric-oxide or angiogenic signalling may be useful in one phase and maladaptive in another. Structure, pain and function must therefore be separated rather than compressed into a generic healing claim.
04 Individual adjudication boundary	A validated proximal molecular target and human dose-exposure-target-engagement chain. Breadth across animal injury models does not create a pan-tissue human repair claim or establish the direction of angiogenesis in every biological context.

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	BPC-157 · GEPPPGKPADDAGLV · FAK paxillin · nitric oxide · angiogenesis · tendon fibroblast · wound biology
EVIDENCE CUTOFF	23 August 2026
ENTITY EXCLUSION	BPC-157 is not gastric juice, a generic collagen peptide or a universal healing factor. Sequence, route, formulation and achievable tissue exposure must remain explicit.
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	Identity and biochemical frame · claim 1	BPC-157 is the synthetic pentadecapeptide Gly-Glu-Pro-Pro-Gly-Lys-Pro-Ala-Asp-Asp-Ala-Gly-Leu-Val. The sequence is the first scientific gate: a commercial label, vial mass or generic term such as repair peptide cannot establish that the administered entity is the peptide studied in the literature.	[2][4]
IMolecular identity	Identity and biochemical frame · claim 2	The frequently repeated description as a gastric-juice peptide should be interpreted carefully. The research entity is a synthetic 15-residue sequence derived from work on gastric protective compounds. Evidence for that synthetic sequence does not prove that an identical free peptide circulates physiologically at therapeutic exposure in humans.	[4][8]
IIICell or ex-vivo system	Cell migration, adhesion and tendon biology · claim 1	In tendon fibroblast and explant systems, BPC-157 increased cell survival, spreading and migration and increased phosphorylation of FAK and paxillin without changing total protein abundance. This is a coherent adhesion-and-migration mechanism relevant to repair biology, but it remains a cellular and ex-vivo finding.	[4]
IIICell or ex-vivo system	Cell migration, adhesion and tendon biology · claim 2	A separate tendon-fibroblast experiment reported increased growth-hormone-receptor expression and enhanced proliferative response when growth hormone was subsequently added. This suggests that BPC-157 can alter tissue responsiveness rather than act through one isolated pathway. It does not establish that systemic GH-axis manipulation improves a human tendon outcome.	[5]
IVIntegrated in-vivo model	Nitric-oxide, vascular and gastrointestinal mechanisms · claim 1	Animal studies repeatedly interact BPC-157 with nitric-oxide biology, using L-NAME and L-arginine to probe vascular, haemostatic and gastrointestinal effects. In clopidogrel-induced gastric injury, BPC-157 modified VEGF-A/VEGFR1, AKT and p38/MAPK-associated findings while reducing mucosal damage in rats.	[6]

LAYER	EXPERIMENTAL FRAME	FINDING AND BOUNDARY	SOURCES
VI Human exposure or signal	Nitric-oxide, vascular and gastrointestinal mechanisms · claim 2	The same literature contains effects on angiogenesis, bleeding, thrombosis and vascular adaptation that can appear directionally different across models. That breadth is not proof of a universal balancing function. It indicates a context-sensitive vascular programme whose target hierarchy and human dose-response remain unresolved.	[6][7][8]
IV Integrated in-vivo model	Animal pharmacokinetics · claim 1	Rat and beagle-dog studies found a prototype-peptide half-life below 30 minutes after intravenous or intramuscular administration. Intramuscular bioavailability was approximately 14%-19% in rats and 45%-51% in dogs, with urine and bile as major excretory routes.	[2]
IV Integrated in-vivo model	Animal pharmacokinetics · claim 2	These data are stronger than an assumption of prolonged systemic exposure, but they remain species- and formulation-specific. They do not establish human subcutaneous, oral or intravenous pharmacokinetics, nor do they show which metabolites retain biological activity.	[2]
VI Human exposure or signal	Human observations · claim 1	Published human evidence is sparse. A retrospective knee-pain series reported subjective improvement after intra-articular administration without randomisation, blinding, standardised functional testing or systematic imaging. It establishes reported administration and a signal, not a causal effect size.	[1]
VI Human exposure or signal	Human observations · claim 2	A 2025 intravenous pilot described two previously exposed adults and did not identify acute clinical or laboratory safety abnormalities. Two participants cannot estimate efficacy, common adverse events, repeated-use effects or rare risk. The evidentiary value is descriptive and should remain labelled as such.	[3]
VII Controlled human proposition	Counterevidence and translation boundaries · claim 1	The main counterweight is not a large negative trial; it is the absence of adequate controlled human translation despite a broad preclinical programme. Animal success across many injury models can reflect shared experimental conditions, publication concentration and endpoints that are not equivalent to human pain, function or structural recovery.	[1][2][3][4]
IV Integrated in-vivo model	Counterevidence and translation boundaries · claim 2	Angiogenesis and remodelling are not intrinsically favourable. Active bleeding, unexplained lesions, proliferative disease, infection and mechanically unstable injuries change the meaning of a repair signal. These contexts require explicit study rather than blanket reassurance or blanket prohibition.	[6][7]

SECTION 01

Molecular dossier: the entity before the outcome

ENTITY — Synthetic 15-residue peptide with a defined primary sequence

BIOCHEMICAL CLASS — Gastric-derived repair-associated research peptide

PRIMARY SYSTEM — NO signalling · endothelial response · cytoprotection · tissue remodelling

IDENTITY BOUNDARY — BPC-157 is not gastric juice, a generic collagen peptide or a universal healing factor. Sequence, route, formulation and achievable tissue exposure must remain explicit.

SECTION 02

Historical and international corpus

BPC-157 belongs to a Croatian gastric-cytoprotection research programme developed over several decades, not to a century of human therapeutic use. Its historical depth is predominantly experimental and concentrated within a recurring research network.

The breadth of models is real information. It must be discounted neither to zero nor converted into human efficacy without authenticated material, human PK and target engagement.

SECTION 03

1990s onward: Long experimental cytoprotection lineage

Early gastric-lesion work was followed by vascular, fistula, tendon and drug-injury models. Repetition over decades strengthens the existence of a context-sensitive biological programme, while concentration of authorship and models limits independent generalisation.[4][6][7][8]

SECTION 04

2021-2025: Sparse human observations do not represent the whole corpus

Recent human reports add administration and safety signals but remain too small or uncontrolled to calculate efficacy. They are one layer appended to a much larger preclinical history, not the sole definition of the molecule.[1][3]

SECTION 05

Mechanistic calculus — MEASURED: The exposure bridge is quantitatively weak

Prototype studies reported a parent-peptide half-life below 30 minutes and incomplete intramuscular bioavailability in rats and dogs. Fast disappearance does not prove inactivity, but it makes metabolites, local action and dosing interval decisive unknowns.[2]

SECTION 06

Mechanistic calculus — INFERRED: A distributed network replaces a single receptor model

NO signalling, endothelial migration, FAK-paxillin, GH-receptor expression and inflammatory responses form a convergent network. Without a validated proximal target, causal direction must be tested node by node.[4][5][7]

SECTION 07

Mechanistic calculus — UNRESOLVED: Pleiotropy has no automatically positive sign

Angiogenesis, haemostasis and remodelling can support repair or worsen a different tissue state. The same measured action cannot be assigned one universal clinical value.[6][7][8]

SECTION 08

Causal architecture: The mechanism is a network, not a slogan

Published experiments connect BPC-157 with nitric-oxide biology, endothelial behaviour, angiogenic signalling, cytoprotection and inflammatory modulation. These observations form a mechanistic network, but no single universally validated receptor currently explains every reported phenotype.[2][4]

SECTION 09

Causal architecture: Vascular response can be causal and conditional

Endothelial migration and collateralisation can plausibly support repair in an ischaemic or disrupted tissue. The same remodelling language cannot be assumed favourable in proliferative disease, abnormal vasculature or active bleeding; biological context determines direction.[2][4]

SECTION 10

Causal architecture: Animal repair models resolve tissue questions

Tendon, ligament, gastrointestinal and drug-injury models test different causal environments. Repetition across tissues supports pleiotropic biology, yet it does not erase differences in mechanical loading, route, local concentration or species metabolism.[2][4]

SECTION 11

Causal architecture: Human translation begins with exposure

Without adequate human PK and a validated target-engagement marker, a nominal dose cannot be connected rigorously to the preclinical concentration-response programme. A subjective clinical signal can generate a question, but it cannot close this biochemical gap.[1][3]

SECTION 12

Molecular identity and entity resolution

BPC-157 is a synthetic 15-amino-acid peptide derived from a sequence described in gastric-juice research. Identity, route and exposure must remain explicit.

SECTION 13

Biochemical mechanism and target architecture

Experimental literature reports gastrointestinal integrity, angiogenic signalling, nitric-oxide pathways and effects in tendon, ligament and drug-injury models. The breadth is hypothesis-rich but does not create a universal repair mechanism.

SECTION 14

In-vivo pharmacology and exposure

Rat and dog studies describe short plasma half-life and species-dependent bioavailability. Human pharmacokinetic characterisation remains insufficient.

SECTION 15

Integrated physiology and individual terrain

Repair is a coordinated tissue process involving perfusion, inflammatory timing, matrix deposition, remodelling, mechanical loading and resolution. A change in nitric-oxide or angiogenic signalling may be useful in one phase and maladaptive in another. Structure, pain and function must therefore be separated rather than compressed into a generic healing claim.

SECTION 16

Terminal human stress-test

A small retrospective knee-pain series reported subjective improvement without randomisation, blinding, standardised function or systematic imaging. A 2025 intravenous pilot in two previously exposed adults detected no clinical or laboratory safety signal; two participants cannot establish efficacy or safety. No adequate prospective controlled clinical trial has yet established BPC-157 efficacy for tendon, ligament, muscle, gastrointestinal injury or recovery outcomes.

SECTION 17

Counterevidence and causal boundaries

Human effect size, repeated-use tolerability and rare-event risk remain unresolved. Angiogenic and tissue-remodelling biology is not automatically favourable and requires context in proliferative disease, unexplained lesions and active bleeding.

SECTION 18

Scientific conclusion

BPC-157 has a substantive preclinical programme and a small human signal, but the identity-to-human-outcome chain is incomplete. The next meaningful evidence is prospective, route-specific, identity-verified and outcome-defined.

SECTION 19

Identity and biochemical frame

BPC-157 is the synthetic pentadecapeptide

Gly-Glu-Pro-Pro-Pro-Gly-Lys-Pro-Ala-Asp-Asp-Ala-Gly-Leu-Val. The sequence is the first scientific gate: a commercial label, vial mass or generic term such as repair peptide cannot establish that the administered entity is the peptide studied in the literature.[2][4]

The frequently repeated description as a gastric-juice peptide should be interpreted carefully. The research entity is a synthetic 15-residue sequence derived from work on gastric protective compounds. Evidence for that synthetic sequence does not prove that an identical free peptide circulates physiologically at therapeutic exposure in humans.[4][8]

SECTION 20

Cell migration, adhesion and tendon biology

In tendon fibroblast and explant systems, BPC-157 increased cell survival, spreading and migration and increased phosphorylation of FAK and paxillin without changing total protein abundance. This is a coherent adhesion-and-migration mechanism relevant to repair biology, but it remains a cellular and ex-vivo finding.[4]

A separate tendon-fibroblast experiment reported increased growth-hormone-receptor expression and enhanced proliferative response when growth hormone was subsequently added. This suggests that BPC-157 can alter tissue responsiveness rather than act through one isolated pathway. It does not establish that systemic GH-axis manipulation improves a human tendon outcome.[5]

SECTION 21

Nitric-oxide, vascular and gastrointestinal mechanisms

Animal studies repeatedly interact BPC-157 with nitric-oxide biology, using L-NAME and L-arginine to probe vascular, haemostatic and gastrointestinal effects. In clopidogrel-induced gastric injury, BPC-157 modified VEGF-A/VEGFR1, AKT and p38/MAPK-associated findings while reducing mucosal damage in rats.[6]

The same literature contains effects on angiogenesis, bleeding, thrombosis and vascular adaptation that can appear directionally different across models. That breadth is not proof of a universal balancing function. It indicates a context-sensitive vascular programme whose target hierarchy and human dose-response remain unresolved.[6][7][8]

SECTION 22

Animal pharmacokinetics

Rat and beagle-dog studies found a prototype-peptide half-life below 30 minutes after intravenous or intramuscular administration. Intramuscular bioavailability was approximately 14%-19% in rats and 45%-51% in dogs, with urine and bile as major excretory routes.[2]

These data are stronger than an assumption of prolonged systemic exposure, but they remain species- and formulation-specific. They do not establish human subcutaneous, oral or intravenous pharmacokinetics, nor do they show which metabolites retain biological activity.[2]

SECTION 23

Human observations

Published human evidence is sparse. A retrospective knee-pain series reported subjective improvement after intra-articular administration without randomisation, blinding, standardised functional testing or systematic imaging. It establishes reported administration and a signal, not a causal effect size.[1]

A 2025 intravenous pilot described two previously exposed adults and did not identify acute clinical or laboratory safety abnormalities. Two participants cannot estimate efficacy, common adverse events, repeated-use effects or rare risk. The evidentiary value is descriptive and should remain labelled as such.[3]

SECTION 24

Counterevidence and translation boundaries

The main counterweight is not a large negative trial; it is the absence of adequate controlled human translation despite a broad preclinical programme. Animal success across many injury models can reflect shared experimental conditions, publication concentration and endpoints that are not equivalent to human pain, function or structural recovery.[1][2][3][4]

Angiogenesis and remodelling are not intrinsically favourable. Active bleeding, unexplained lesions, proliferative disease, infection and mechanically unstable injuries change the meaning of a repair signal. These contexts require explicit study rather than blanket reassurance or blanket prohibition.[6][7]

SECTION 25

Falsification map

Failure to reproduce a proximal endothelial or NO-related effect with authenticated material would weaken the proposed network.

Human exposure below concentrations required for mechanistic activity would break the translation chain.

No improvement in prespecified structure or function despite target engagement would falsify efficacy for that tissue and route.

RESEARCH AGENDA

What would materially change the conclusion?

01 Human route-specific PK and metabolite mapping

02 Prospective controlled tendon or ligament trials

03 Imaging plus function plus pain as separate outcomes

04 Repeated-dose safety and immunogenicity

05 Mechanistic studies outside the dominant research groups

06 Context-specific angiogenesis and haemostasis studies

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.

Lee & Padgett. *Altern Ther Health Med*. 2021;27:8-13. · PMID 34324435

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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.