

Human evidence for BPC-157 in orthopaedic and regenerative medicine: a systematic review of efficacy and safety

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ABSTRACT

Body Protective Compound-157 (BPC-157) is a synthetic pentadecapeptide popular among athletic populations for musculoskeletal injury recovery, despite lacking regulatory approval for human use and evidence being largely limited to animal models. This PRISMA-compliant systematic review, prospectively registered with PROSPERO (CRD420261406325), aimed to evaluate the efficacy and safety of BPC-157 for orthopaedic and regenerative purposes in humans. Electronic databases (Embase, PubMed, Cochrane Library and ClinicalTrials.gov) were searched up to 1 June 2026. Eligibility included quantitative and qualitative studies investigating BPC-157 for any indication in human participants. Methodological quality and certainty of evidence was assessed using the National Institutes of Health Quality Assessment Tool for Before–After Studies With No Control Group and GRADE framework respectively. Findings were narratively synthesised in accordance with SWiM guidance. Three studies (n=30) met the inclusion criteria, consisting of a retrospective study of intra-articular BPC-157 injections for knee pain (n=16), a retrospective pilot study of intravesical BPC-157 for interstitial cystitis (n=12), and a prospective pilot study evaluating intravenous BPC-157 safety (n=2). All studies reported symptom improvement in most participants without treatment-related adverse events, but were judged to be of poor methodological quality. Overall certainty of evidence was rated very low due to serious risk of bias, indirectness and imprecision. Accordingly, BPC-157 should not be used clinically in humans outside ethically approved, regulated, high-quality clinical trials.

Keywords: BPC-157, Injury, Systematic review, Peptide, Sport, Athletes.

BACKGROUND

Musculoskeletal disorders represent a substantial global health burden and are a leading cause of pain, disability, reduced quality of life and healthcare utilisation globally, with an estimated economic cost of \$2.1 trillion in 2021 alone¹. Consequently, optimising recovery from musculoskeletal injury remains fundamental to orthopaedic practice, with growing interest in emerging adjunctive therapies aimed at enhancing patient outcomes alongside established surgical, pharmacological and rehabilitation approaches². Within this evolving field, diverse regenerative approaches, including biologics, cell-based therapies, tissue engineering, and bioactive molecules, are under active investigation²⁻⁶. Against this backdrop, peptide therapies have recently attracted increasing scientific and commercial interest within orthopaedics due to their purported reparative and regenerative properties².

Within the human body, endogenous peptides act as precise messengers across physiological systems to modulate molecular pathways, including metabolism, immune response, and tissue regeneration⁷. Thus, since German chemist Emil Fischer created the first synthetic peptide, glycylglycine, in 1901, medical research has long explored the utility of exogenous peptides for therapeutic purposes in humans⁸. Notably, in 1922, insulin became the first peptide used to successfully manage type 1 diabetes mellitus, revolutionising diabetes care and establishing peptide-based therapies in medicine⁹. Since then, new peptide-based therapies have continued to enter clinical use and cement their role as core components of modern medical management across a range of conditions, including the glucagon-like peptide-1 (GLP-1) receptor agonist semaglutide for obesity and metabolic disease, oxytocin for induction of labour and control of postpartum haemorrhage, leuprolide for

prostate cancer, and enfuvirtide as part of combination antiretroviral therapy for human immunodeficiency virus infection¹⁰⁻¹³.

Nonetheless, to maintain patient safety, all novel peptide-based therapies must first undergo rigorous translational evaluation and safety testing prior to clinical implementation¹⁴⁻¹⁵. One such novel peptide within the broader pipeline of investigational agents under preclinical and early clinical evaluation is Body Protective Compound-157 (BPC-157), a synthetic pentadecapeptide with the amino acid sequence GEPPPGKPADDAGLV and a molecular mass of approximately 1419 Daltons¹⁶. Originally, BPC-157 was first isolated from human gastric juice in 1991 by a Croatian research group led by Dr. Predrag Sikirić and has subsequently been reported to exhibit regenerative and reparative properties across tissue types and organs, including tendon, skeletal muscle, ligament, bone, teeth, peripheral nerve, brain, cornea, liver and vascular endothelium, within animal models¹⁷⁻³⁶. Yet, at the time of writing (regulatory status verified on 3 June 2026), BPC-157 is unapproved for human use by major medicines regulators across the globe, including the United States Food and Drug Administration (FDA), the European Medicines Agency (EMA), and the Medicines and Healthcare products Regulatory Agency (MHRA), and is additionally prohibited for use in sport by the World Anti-Doping Agency (WADA), owing to a lack of robust human efficacy and safety data³⁷⁻⁴⁰.

Despite this, BPC-157 has gained prominence in anecdotal reports and non-clinical discourse, particularly among athletic populations and online wellness communities, where it is promoted for musculoskeletal injury repair and exercise recovery, often being colloquially referred to as the “Wolverine peptide” in reference to the fictional superhero’s regenerative abilities⁴¹⁻⁴³. Further evidencing the growing public interest in BPC-157, Google Trends data indicated peak global search interest for “BPC-157” in April 2026, coinciding with >50 million views of related content on both YouTube and TikTok, and over 100,000 members across peptide-focused Reddit communities^{44,45}. Concerningly, this rising interest has purportedly been accompanied by increased availability through unregulated online direct-to-consumer sales and private clinics, raising significant concerns about BPC-157’s effects in humans, as well as the authenticity, purity, dosage accuracy and potential contamination of products marketed as containing BPC-157^{43,46,47}. Concurrently, escalating patient interest has required orthopaedic surgeons to increasingly consult patients

on the efficacy and safety of peptide-based therapies for musculoskeletal injury repair and exercise recovery⁷.

Consequently, the apparent disconnect between preclinical research findings in animal models and increasing unregulated personal use in humans defines the central issue discussed by the present review. While prior reviews have sought to synthesise preclinical evidence on the efficacy and safety profile of BPC-157, a systematic review evaluating evidence exclusively from human studies has yet to be published^{41,42,45}. Additionally, where prior reviews have attempted to incorporate brief discussion of limited human evidence within broader syntheses of preclinical evidence, none appear to have applied standardised frameworks for evaluating methodological quality or assessing the certainty of the available evidence^{41,42,45}. This represents a key methodological limitation, as the absence of standardised assessment tools reduces transparency, makes it difficult to compare findings across studies, and limits the ability to evaluate the reliability and clinical relevance of reported effects⁴⁸⁻⁵⁰. Moreover, without applying a formal framework for rating evidence certainty, conclusions may overestimate the certainty of findings, particularly in limited evidence bases dominated by small, uncontrolled, and non-randomised studies, such as in the case of literature surrounding the use of BPC-157 in humans⁴⁸⁻⁵⁰. Accordingly, this review aims to address this gap by providing the first systematic evaluation of the efficacy and safety of BPC-157 for orthopaedic and regenerative applications based exclusively on human evidence. Also, in contrast to previous broad preclinical syntheses, this review will conduct standardised methodological quality assessment using relevant National Institutes of Health (NIH) tools⁵¹ and evaluate certainty of evidence using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework,⁵² thereby improving the rigour, reproducibility, and interpretability of the evidence synthesis. In doing so, it is hoped the findings of this review will inform orthopaedic and regenerative medicine practices, support evidence-based patient consultation, and identify priorities for future research.

METHODS

This systematic review was conducted and reported in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines⁵³. Additionally, to aid quality assurance, the protocol for this review was registered in the International Prospective Register

of Systematic Reviews (PROSPERO) under the ID CRD420261406325.

Types of Studies

Quantitative and qualitative studies were searched for including, but not limited to, randomised controlled trials, clinical trials, cohort, case-control, cross-sectional, case series, before-after and quasi-experimental. Only human studies were eligible for inclusion. Primary studies in any language and published up to 1 June 2026 were considered. Studies that were duplicates of previously included studies or utilised the same data set as a previously included study were excluded.

Participants

Studies were included if they involved adult human participants (aged ≥ 18 years). No restrictions were placed on sex, ethnicity, or clinical diagnosis in order to maximise generalisability and capture the breadth of available evidence. Conversely, animal and in vitro studies were excluded.

Exposure

The exposure of interest was administration of BPC-157, or one of its synonyms, for any orthopaedic indication irrespective of formulation, dosage, route of administration, or treatment duration. Study exposure was broadly defined in said manner to capture a breadth of medical interventions, utilities and safety profiles. Nonetheless, due to the anticipated limited quantity of studies investigating BPC-157 for orthopaedic indications, studies from other clinical contexts were considered solely to provide information on general human exposure and safety, not orthopaedic efficacy.

Additionally, to enhance interpretability and explore potential sources of heterogeneity, data were extracted on variables that may have influenced treatment effects, such as participant occupation and activity level, attributed aetiology and mechanism of injury/diagnosis, duration of symptoms, prior treatment, concomitant medical pathologies, and co-interventions or adjunctive therapies.

Comparators

Studies with and without a comparator were included. Uncontrolled before-after studies were included due to the anticipated limited availability of controlled clinical evidence.

Primary outcomes

Primary outcomes included validated and reliable quantitative measures of symptom severity, quality of

life, and functional status, such as the Visual Analogue Scale (VAS), Short Form Health Survey (SF-36), Global Response Assessment (GRA), and EuroQol 5-Dimension questionnaire (EQ-5D). In addition, non-validated patient-reported outcomes were included due to the anticipated scarcity of objective data. Nonetheless, these measures were considered to be at higher risk of measurement bias and were interpreted with particular caution during synthesis.

Secondary outcomes included adverse events, complications, and safety-related findings associated with BPC-157 administration.

Search strategy

Two independent reviewers (J.T.P and J.M) systematically searched for published, unpublished and grey literature on the electronic databases Embase, PubMed, Cochrane Library and ClinicalTrials.gov up to 1 June 2026. The search strategy incorporated the following terms (Body Protection Compound 157 OR Gastric pentadecapeptide OR GEPPPGKPADDAGLV OR BPC-157 OR BPC-15 OR Bepecin OR PL-14736 OR PLD-116 OR PL-10 OR PCO-02).

Furthermore, in order to identify grey literature and minimise publication bias, no restrictions were applied to publication status. Additionally, the reference lists of all included publications were also screened for potentially eligible literature.

Data selection and extraction

Two reviewers (J.T.P and J.M) independently evaluated the titles and abstracts of the identified publications before applying the eligibility criteria to the full text reports. Any disagreements between the independent reviewers were settled by the third co-author (A.K). Data on study design, duration, exposures, participant characteristics, outcome measures, results and complications was extracted using a standardised extraction form adapted from the Cochrane Collaboration to reduce information bias⁵⁴.

Quality assessment and Risk of Bias

All included studies were assessed for quality by two independent reviewers (J.T.P and J.M) using the National Institutes of Health (NIH) Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group⁵¹. The NIH Before-After tool was selected as the included studies primarily involved uncontrolled within-subject outcome assessment. This tool evaluates internal validity across multiple domains, including study population, intervention clarity, outcome measurement, and statistical

analysis⁵¹. In accordance with the checklist's guidance document, and to succinctly summarise findings for the reader, all studies were awarded overall quality ratings as follows:

Good – The study likely has a low risk of bias, most key criteria have been met, any flaws are minor and unlikely to affect the results and the findings are therefore considered valid and reliable.

Fair – The study likely has some risk of bias, not all criteria have been met, there may be methodological limitations, but no critical flaws, meaning the results should be interpreted with caution.

Poor – The study likely has a high risk of bias, there appear to be major methodological problems present and key criteria has not been met (e.g., unclear intervention, invalid outcomes, high attrition) meaning the results are considered unreliable.

Any disagreements were resolved through consensus discussion, with arbitration by a third reviewer (A.K) where necessary.

Data Synthesis

Although considered, methodological heterogeneity and the absence of a comparator group in the included studies rendered a meta-analysis inappropriate. Subsequently, data was instead narratively synthesised in accordance with the Synthesis Without Meta-analysis (SWiM) reporting framework⁵⁵. Additionally, the GRADE framework was followed to determine the overall strength of the body of evidence⁵². The GRADE approach was selected due to the tool's inclusion of explicit marking criteria for non-randomised evidence and its specific purpose of determining the overall quality and strength of recommendations in healthcare, based on the below criteria.

Overall GRADE quality ranking:

- High (Very confident that the body of evidence's effect represents the actual effect)
- Moderate (Quite confident that the body of evidence's effect is close to the actual effect, although it is also conceivable that it is significantly different)
- Low (The body of evidence's true effect may significantly differ from the actual effect)
- Very low (The body of evidence's true effect likely substantially differs from the actual effect)

Overall GRADE strength of recommendation ranking, considering factors such as balance between undesirable and desirable effects, patient preference and cost-effectiveness:

- Strong for using
- Weak for using
- Strong against using
- Weak against using

As a consequence of all included studies methodologies being uncontrolled and non-randomised, the certainty of evidence was initially rated as low and further downgraded based on risks of bias, imprecision and indirectness.

RESULTS

Study Selection

The overall search yielded 864 records with 3 meeting the inclusion criteria^{43,46,47}. These comprised of one retrospective study investigating intra-articular BPC-157 injections for knee pain,⁴⁶ one retrospective pilot study evaluating intravesical BPC-157 injections for interstitial cystitis,⁴⁷ and one pilot study assessing the safety of intravenous (IV) BPC-157 infusion⁴³. During the search, an additional 3 studies appeared to meet the inclusion criteria but were later excluded⁵⁶⁻⁵⁸. Reasons for exclusion of these full-text reports are provided in Supplementary Table I. The PRISMA flow diagram used for study identification is represented in Figure 1.

Study Methodological Characteristics and Risk of Bias

All 3 studies were conducted in single private clinical settings in Orlando, Florida, USA, share the same lead author, utilised uncontrolled observational designs, and did not declare any conflicts of interest^{43,46,47}.

The 2 symptomatic intervention studies employed retrospective chart review methodologies over defined periods of 2019–2020 and January 2023–June 2024,⁴⁶⁻⁴⁷ while the IV infusion safety study implemented a prospective pilot design over a 3-day intervention period⁴³. Small convenience sample sizes were recruited in all 3 studies, ranging from a total of 2 participants in the IV infusion safety study,⁴³ 12 participants in the interstitial cystitis study,⁴⁷ and 16 participants in the knee pain study (n=17 recruited, n=16 analysed)⁴⁶. Two studies utilised BPC-157 sourced from unnamed compounding pharmacies,^{43,47} while a third study stated the BPC-157 had been compounded by Tailor Made Compounding in Nicholasville, Kentucky, USA⁴⁶.

Outcome assessment methods varied across all 3 studies. One study relied entirely on subjective pre and post intervention patient-reported knee pain scores (rated on a scale of 0–10, with 10 being the

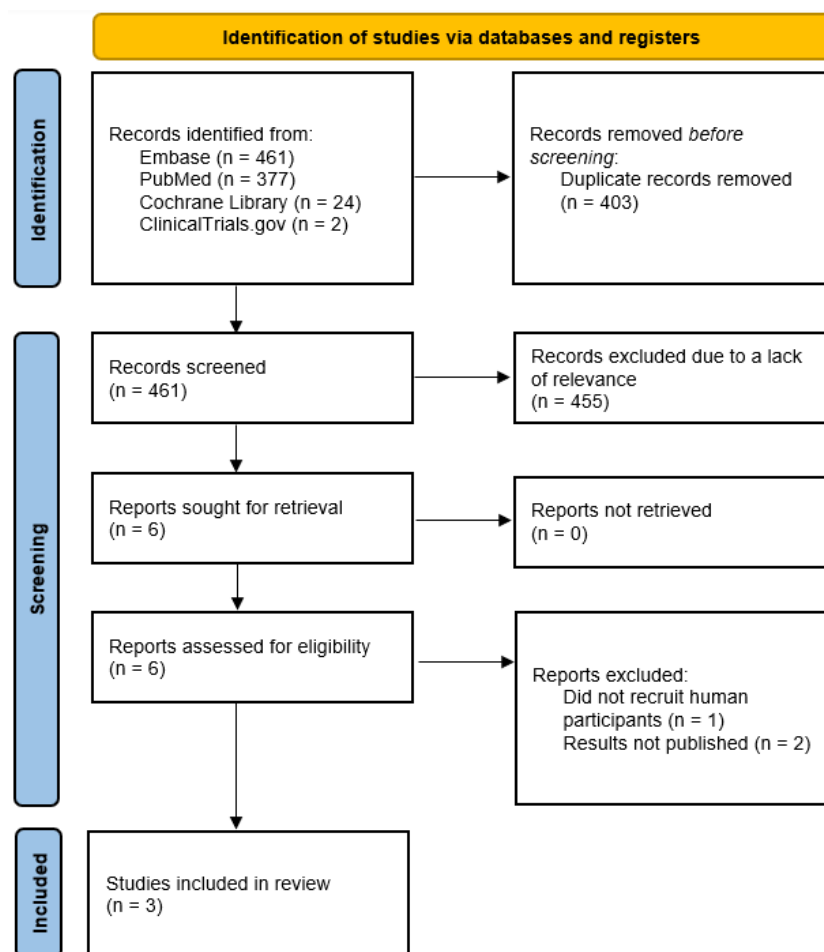


Fig. 1 — Flow diagram of the screening and selection of studies in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) methodology. Source: Elaborated by the authors (2026).

most painful) and survey questions inquiring about participants' mobility, exercise tolerance, ability use stairs, sleep quality, adverse events, and duration of knee pain improvement after the intervention⁴⁷. Another utilised the GRA questionnaire with categorical scoring from 1-5 to assess intervention response among participants with interstitial cystitis⁴⁷. The third study analysed fasting blood samples, blood pressure, heart rate, and patients' subjective reports of adverse events at baseline and over the course of IV infusion with BPC-157⁴³.

Using the NIH Quality Assessment Tool for Before–After (Pre–Post) Studies With No Control Group, all studies were judged to be of poor quality. The studies commonly failed to satisfy criteria relating to adequate sample size, outcome assessor blinding, use of valid and reliable outcome measures, and implementation of formal statistical tests to assess significance, indicative of substantial susceptibility to selection bias, reporting bias, performance bias, and confounding. These factors raised substantial doubt

about the ability of the 3 studies to accurately assess an association between the intervention/exposure and the measured outcomes. The methodological characteristics and quality of all included studies is represented in Table I. Domain-level assessments for all included studies, using the NIH Quality Assessment Tool for Before–After (Pre–Post) Studies With No Control Group, are provided in Supplementary Table II.

Participant Characteristics of Studies

The total number of participants when study data was combined was 30 (22 female and 8 male) with a mean age of 59.5 years (range: 19–77 years)^{43,46,47}. The knee pain study analysed 16 participants (after exclusion of 1 lost to follow-up), consisting of 9 females (56%) and 7 males (44%) with a mean age of 60 years (range 19–77 years)⁴⁶. The reported ethnicities of the participants included White (n=15), Hispanic (n=1), and Korean (n=1)⁴⁶. The interstitial cystitis study included 12 female participants with

Table I. — Methodological characteristics of included studies.

Authors	Aim	Design	Duration	Quality
Lee and Padgett	Efficacy for knee pain	Retrospective chart review	1 Year	Poor
Lee, Walker and Ayadi	Efficacy for interstitial cystitis	Retrospective chart review	1 Year and 5 months	Poor
Lee and Burgess	Intravenous safety	Safety profile	3 days	Poor
Source: Elaborated by the authors (2026).				

a mean age of 58.3 years (range 39–76 years) and a reported ethnicity distribution of White (n=10), Asian (n=1), and Latina (n=1)⁴⁷. The intravenous safety study included 2 participants, namely a 68-year-old Caucasian female and a 58-year-old Asian male⁴³.

Medical diagnoses varied across studies^{43,46,47}. In the knee pain study, 5 participants had a prior diagnosis of osteoarthritis, and 4 possessed MRI-confirmed pathologies including meniscal tear with medial collateral ligament sprain (n=1), isolated meniscal tear (n=1), anterior cruciate ligament tear (n=1), and popliteal bursitis (n=1)⁴⁶. Reporting of prior exposures exclusively included 1 account of the participant with a meniscal tear and concomitant medial collateral ligament sprain undergoing meniscus surgery, without subsequent relief of knee pain, 6 months prior to injection with BPC-157⁴⁶. All 12 participants in the interstitial cystitis study possessed a diagnosis of moderate to severe interstitial cystitis with hypervascularity and hyperemia seen on cystoscopy, with ulcers also observed on cystoscopy in an unspecified number of participants⁴⁷. All 12 participants had reportedly failed to adequately respond to prior management with pentosan polysulfate and had not been treated with pentosan polysulfate, any other oral medications, or intravesical instillations 6 months prior to the study intervention⁴⁷. In the intravenous infusion safety study, the female participant had a medical history of thalassemia and a medication history of oral progesterone (200 mg) and transdermal estradiol (50 mcg), in addition to taking magnesium, fish oil, nitric oxide, resveratrol, and vitamin D supplements⁴³. No medical or medication history was reported for the male participant, who reportedly took vitamin D and B-complex supplements only⁴³.

All 3 of the included studies implemented different interventions/exposures.^{43,46,47}. In the knee pain study, injections were performed without ultrasound guidance using a 25-gauge 1.5-inch needle inserted via the medial tibial plateau⁴⁶. Twelve participants received 2cc intra-articular BPC-157 alone, whereas four participants received combined BPC-157 and Thymosin beta-4 (TB4) injections ranging from

1–2cc of each peptide administered separately into the joint⁴⁶. The BPC-157 and TB4 were compounded at a concentration of 2000mcg/mL and 3000mcg/mL respectively, and both preparations were buffered with sodium phosphate and benzyl alcohol⁴⁶. In the interstitial cystitis study, 1mg of BPC-157 was injected in 10 equally distributed areas of the uroepithelium of the dome and trigone of the bladder wall (total of 10mg) at a depth of 3mm via a 17–24F catheter 30° cystoscope with an injeTAK 70cm needle⁴⁷. In the safety study, IV doses of 10mg on day 1 and 20mg on day 2 were administered in 250cc of saline over 1 hour⁴³. Table II represents the participant characteristics of the included studies.

Results of Studies

Symptom improvement in most participants was reported in both efficacy studies^{46,47}. In the knee pain study, 11/12 participants (91.6%) receiving BPC-157 monotherapy purportedly showed overall improvement, while 1/12 (8.3%) demonstrated no overall improvement⁴⁶. Among the participants receiving BPC-157 and TB4 combination therapy, 3/4 participants (75%) showed improvement and 1/4 (25%) demonstrated no improvement⁴⁶. All 4 patients with MRI-confirmed pathology were also separately reported to have experienced improvement following the intervention⁴⁶. No indication of what constituted an overall improvement was provided by the authors⁴⁶. Pain, mobility and sleep were also separately reported to have improved (14/16 [87.5%], 12/16 [75%] and 10/16 [62.5%] respectively)⁴⁶. No results for changes to exercise tolerance or ability use stairs were reported despite being named outcome domains in the study's methodology⁴⁶. In the interstitial cystitis study, all 12 participants (100%) scored 5/5 on the GRA scale, denoting a “Successful therapy” outcome⁴⁷. Additionally, 10/12 participants (83.3%) reported complete resolution of symptoms, while 2/12 (16.7%) reported an 80% improvement⁴⁷. The authors stated there was no relationship between the age or ethnicity of the participants who rated their improvement of symptoms at 80%, although how this conclusion was reached was not declared⁴⁷. Cystoscopic pre and post

Table II. — Participant characteristics of included studies.

Authors	N (Male: Female)	Age (years)	Ethnicity	Medical Diagnoses	Intervention
Lee and Padgett	16 (7:9)	60 (range, 19–77)	Hispanic (n=1), Korean (n=1) and Caucasian (n=14)	Knee pain; osteoarthritis (n=5); MRI-confirmed pathology (n=4: meniscal tear ± MCL sprain, ACL tear, popliteal bursitis)	Intra-articular BPC-157 monotherapy (n=12; 2cc) or BPC-157 & TB4 combination therapy (n=4; 1–2cc of each peptide)
Lee, Walker and Ayadi	12 (0:12)	58.3 (range, 39–76)	Latina (n=1), Asian (n=1) and Caucasian (n=10)	Moderate-to-severe interstitial cystitis with cystoscopic hypervascularity and hyperemia; all refractory to prior pentosan polysulfate therapy	Intravesical BPC-157 injection (10mg total; 1mg injected into each of 10 bladder-wall sites)
Lee and Burgess	2 (1:1)	63 (range, 58–68)	Caucasian (n=1) and Asian (n=1)	Healthy volunteers with reported medical histories	Intravenous BPC-157: 10mg (day 1) and 20mg (day 2) infused over 1 hour
Number of patients (N), Body Protection Compound-157 (BPC-157), magnetic resonance imaging (MRI), medial collateral ligament (MCL), thymosin beta-4 (TB4), milligrams (mg), cubic centimetres (cc). Source: Elaborated by the authors (2026).					

images were provided for only 1 participant and were suggested to demonstrate reduced hypervascularity, hyperemia, and detrusor hypertrophy⁴⁷.

Symptom improvement was reported to occur as early as 2 weeks post-treatment in the interstitial cystitis study, although supporting data was not provided⁴⁷. In the knee pain study, duration of reported symptom improvement with BPC-157 monotherapy was reported as follows: 1/12 participants (8.3%) experienced relief for 24 hours, 2/12 (16.7%) for up to 3 months, 2/12 (16.7%) for 3–6 months, and 7/12 (58.3%) for 6 months to 1 year⁴⁶. In the BPC-157 and TB4 combination group, duration of improvement endured up to 3 months in 1/4 participants (25%), 3–6 months in 1/4 (25%), and 6 months to 1 year in 2/4 (50%)⁴⁶.

Across both efficacy studies and the IV safety study, no drug related adverse events or subjective side effects were reported (0/30 participants)^{43,46,47}. In the intravenous safety study, the maximum pre- to post-infusion fluctuation in systolic and diastolic blood pressure was 3mmHg and 2mmHg respectively, while heart rate varied by a maximum of 2bpm⁴³. Additionally, no fluctuations in biomarkers of the heart, liver, kidneys, thyroid, or blood glucose levels were deemed clinically significant by the authors⁴³. For example, Creatine kinase (CK) increased within normal limits (Participant 1: 50–72U/L; Participant 2: 152–169U/L; reference range 40–331U/L), while B-type natriuretic peptide (BNP) decreased within normal limits (Participant 1: 31–18pg/mL; Participant 2: 14–10pg/mL; reference range <100pg/mL)⁴³. The outcomes of all included studies are represented in Table III.

Certainty of evidence

Adhering to GRADE guidance,⁵² BPC-157 should not be used clinically in humans outside ethically approved, regulated, high-quality clinical trials owing to the small evidence base (n=3 studies), poor quality and very low certainty of evidence (Table IV).

DISCUSSION

This review is the first, to the authors' knowledge, that has systematically evaluated the efficacy and safety of BPC-157 for orthopaedic and regenerative applications based exclusively on human evidence, with methodological quality and certainty of evidence assessed using the NIH Quality Assessment Tool for Before–After (Pre–Post) Studies With No Control Group and the GRADE framework respectively^{51,52}. Although all 3 included studies (total of 30 participants) reported favourable outcomes, namely symptom improvement in most participants' knee pain and interstitial cystitis symptoms, as well as an absence of reported adverse events, quality was rated as poor and the overall certainty of evidence was judged to be very low^{43,46,47}. The inclusion of non-orthopaedic human studies, including interstitial cystitis and intravenous safety evaluations, reflects the limited clinical evidence available in orthopaedic populations, serving only to inform general understanding of human exposure and safety, not orthopaedic efficacy. Consequently, the present review's findings suggest the current evidence base is insufficient for establishing the efficacy and safety of BPC-157 in humans for orthopaedic and regenerative

Table III. — Outcomes of included studies utilising a retrospective chart review study design.

Authors	Purpose	Outcome Measure(s)	Key Findings	Complications
Lee and Padgett	Efficacy for knee pain	Overall symptom improvement	BPC-157 monotherapy: Improved in 11/12 participants (91.7%) BPC-157 & TB4 therapy: Improved in 3/4 participants (75%)	No adverse events reported
		Self-reported pain	Improved in 14/16 participants (87.5%)	
		Self-reported mobility	Improved in 12/16 participants (75%)	
		Self-reported sleep	Improved in 10/16 participants (62.5%)	
Lee, Walker and Ayadi	Efficacy for interstitial cystitis	GRA	All participants (12/12; 100%) achieved a GRA score of 5/5	No adverse events reported
		Cystoscopic imaging	Pre & post-intervention images from 1 participant suggested reduced hypervascularity, hyperemia, and detrusor hypertrophy	
Lee and Burgess	Intravenous safety	Vital signs	Maximum pre- to post-infusion fluctuation in systolic and diastolic blood pressure was 3mmHg and 2mmHg respectively, while heart rate varied by a maximum of 2bpm.	No adverse events reported
		Laboratory biomarkers	No clinically significant changes in cardiac, hepatic, renal, thyroid, or glucose biomarkers. CK increased within reference range, while BNP decreased within reference range.	
Global Response Assessment (GRA), B-type natriuretic peptide (BNP), Body Protection Compound-157 (BPC-157), blood pressure (BP), beats per minute (bpm), creatine kinase (CK), millimetres of mercury (mmHg), thymosin beta-4 (TB4). Source: Elaborated by the authors (2026).				

Table IV. — GRADE assessment of certainty of evidence.

Domain	Assessment	Justification
Risk of bias	Very serious (−2)	All studies had significant methodological limitations relating to recruitment, randomisation, allocation concealment, blinding, missing data, outcome measurement, selective reporting, and potential confounding.
Inconsistency	Not serious (0)	The included studies consistently reported favourable outcomes, with no contradictory findings identified. Differences in clinical indications and outcome measures were considered under indirectness rather than inconsistency.
Indirectness	Very serious (−2)	The included studies evaluated different clinical indications, enrolled heterogeneous patient populations, and used different, predominantly subjective outcome measures, limiting the direct applicability and comparability of the evidence.
Imprecision	Very serious (−2)	Small sample sizes, no reported power calculations and incomplete reporting of statistical uncertainty (absence of p-values/confidence intervals)
Publication bias	Very strongly suspected (−2)	The small number of available studies and the consistent reporting of favourable outcomes without adverse events raise concerns regarding selective publication and incomplete reporting of negative findings. Additionally, the lead author of all studies is the founder of an advocacy organisation opposing regulatory restrictions on peptides.
Overall certainty	⊕ ○ ○ ○ Very low	Evidence was downgraded across multiple domains.
Source: Elaborated by the authors (2026).		

applications. Said findings are broadly consistent with prior systematic reviews, which similarly concluded the evidence for BPC-157 in humans remains extremely limited and further research is required before definitive conclusions can be drawn^{41,42}.

Yet, prior reviews have devoted substantial attention to preclinical and animal research, and subsequently

emphasised the therapeutic potential of BPC-157 in humans^{41,42}. In contrast, the present review focused exclusively on human evidence and, via adherence to the GRADE framework, recommendations were based on the quality, consistency, directness, and precision of human evidence rather than mechanistic plausibility or preclinical efficacy⁵⁵. Consequently,

despite the positive findings reported in the included studies, serious concerns regarding risk of bias, indirectness, and imprecision resulted in a very low certainty rating, indicating that the true effects of BPC-157 could be substantially different from those observed and, therefore, not supportive of claims bolstering the therapeutic potential or safety of BPC-157 in humans.

Furthermore, through assessing all included studies for quality using the NIH Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group,⁵¹ fundamental methodological limitations were identified in the included studies which may have been overlooked by prior reviewers when seeking to draw conclusions from the available evidence. For example, all included studies employed uncontrolled observational designs and lacked randomisation, blinding, and comparator groups^{43,46,47}. Consequently, causal inferences cannot be made, as findings may reflect placebo effects, regression to the mean, natural disease fluctuation, or other uncontrolled factors rather than a true treatment effect⁵⁹. This limitation is particularly important given that the primary outcomes assessed in the efficacy studies were subjective symptom measures which are highly susceptible to expectation and reporting bias⁶⁰.

Moreover, further limiting confidence in the findings, the knee pain study relied on non-validated patient-reported outcomes and the authors did not define the criteria used to classify overall improvement⁴⁶. Additionally, the interstitial cystitis study assessed treatment response using the GRA, a subjective outcome measure in which the highest response category encompasses a broad range of improvement (76–100%)⁴⁷. Consequently, participants reporting 80% improvement and complete symptom resolution were classified identically, limiting discrimination between degrees of treatment response^{47,61}. Saliently, baseline symptom severity was also not quantified in either efficacy study, undermining efforts to determine the magnitude or clinical significance of reported improvements^{46,47}.

Additionally, all 3 studies were conducted in private clinical settings in the same geographic region and shared the same lead author, raising concerns regarding author allegiance, publication bias, and repeatability^{43,46,47,62}. Moreover, despite no conflicts of interest being declared, the lead author of all 3 studies is the founder of SavePeptides.org, an advocacy organisation opposing regulatory restrictions on peptides, further highlighting the potential for author allegiance bias^{43,46,47,62}. Correspondingly, two

studies utilised BPC-157 sourced from unnamed compounding pharmacies without independent verification of product composition, introducing uncertainty regarding intervention standardisation and reproducibility^{43,47}. Also, in the IV safety study, both participants had reportedly received prior exposure to BPC-157, potentially introducing expectation bias and limiting assessment of treatment-naïve safety outcomes^{43,62}.

Nonetheless, discrepancies between statements reported in prior reviews and the findings of the primary literature have also been identified during the process of the present review. Specifically, prior reviews have described pharmacokinetic findings indicating that plasma BPC-157 concentrations return to baseline within 24 hours after IV administration in humans^{41,42}. However, the primary IV safety study referenced to support such claims did not measure or report on plasma BPC-157 concentrations⁴³. This observation highlights the importance of rigorous data extraction and verification procedures during evidence synthesis and demonstrates how unsupported interpretations may propagate through subsequent reviews when primary studies are not carefully examined. Accordingly, the implementation of a standardised extraction form adapted from the Cochrane Collaboration demonstrates a key strength of the present review's attempts to reduce information bias^{54,62}.

Given the substantial methodological limitations and paucity of human data identified in the current evidence base,^{43,46,47} future research would benefit from adequately powered, randomised, placebo-controlled methodologies which utilise standardised BPC-157 formulations, validated outcome measures, and longer-term follow-up⁶³. Robust safety assessment will also require systematic adverse event monitoring and standardised reporting practices, including frameworks aligned with ICH-GCP and CONSORT Harms recommendations,^{64,65} to improve the detection and reporting of uncommon, delayed, and cumulative adverse effects across diverse human populations⁶³. Additionally, independent replication of such findings may further strengthen the reliability of the evidence base⁶⁶.

Notably, progress in this field has been hindered by the absence of published results from a Phase I, randomised, placebo-controlled trial (NCT02637284) of 42 participants, which was terminated for unknown reasons before reporting pharmacokinetic and safety outcomes⁵⁶. However, a Phase II randomised, double-blind, placebo-controlled trial (n=120)

evaluating the efficacy of subcutaneous BPC-157 for MRI-confirmed acute grade II hamstring strain (NCT07437547) is scheduled for completion in 2028⁵⁷. If completed and reported in full, this trial could provide higher-quality evidence regarding the efficacy and safety of BPC-157 in humans. Although, given that >90% of investigational drugs fail during clinical development, largely due to poor translation of preclinical pharmacokinetic, efficacy, and toxicity findings to humans, a single study, regardless of design, would be insufficient to establish reliable evidence of efficacy or safety, and any results should therefore be interpreted with caution⁶⁷.

Accordingly, in clinical practice, orthopaedic surgeons should inform patients that no robust evidence demonstrating the efficacy and safety of BPC-157 in humans presently exists and BPC-157 remains unapproved for human use by major medicines regulators across the globe³⁷⁻³⁹. Clinicians should also inform patients that BPC-157 is prohibited by WADA under the S0 Non-Approved Substances category,⁴⁰ a consideration of particular importance for athletes subject to anti-doping regulations. Furthermore, patients should be counselled on the risks associated with the unregulated nature of online direct-to-consumer sales of products marketed as containing BPC-157, in which the authenticity, purity, dosage accuracy and absence of contamination cannot be assured^{43,46,47}. Cumulatively, patient-centred shared decision-making should continue to be guided by established evidence-based orthopaedic therapies, with BPC-157 use being avoided unless future high-quality randomised controlled trials consistently demonstrate a favourable benefit–risk profile.

CONCLUSION

The current literature on BPC-157 in humans is sparse (n=3), of poor quality, and of very low certainty overall. Premature adoption of this compound outside of controlled research environments risks exposing patients to unknown harms without proven benefit. A cautious, evidence-based approach is therefore essential to minimise potential public harm and ensure that clinical practice remains guided by robust and reliable data. Accordingly, BPC-157 should not be used clinically in humans outside ethically approved, regulated, high-quality clinical trials.

Ethics approval and consent to participate: This is a systematic review of published studies meaning ethical approval and informed consent to participate is not applicable.

Abbreviations: GLP-1: Glucagon-Like Peptide-1, BPC-157: Body Protective Compound-157, FDA: Food and Drug Administration, EMA: European Medicines Agency, MHRA: Medicines and Healthcare products Regulatory Agency, WADA: World Anti-Doping Agency, PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses, PROSPERO: International Prospective Register of Systematic Reviews, VAS: Visual Analogue Scale, SF-36: Short Form Health Survey-36, GRA: Global Response Assessment, EQ-5D: EuroQol 5-Dimension Questionnaire, NIH: National Institutes of Health, SWiM: Synthesis Without Meta-analysis, GRADE: Grading of Recommendations, Assessment, Development, and Evaluation, IV: Intravenous, TB4: Thymosin Beta-4, MRI: Magnetic Resonance Imaging, CK: Creatine Kinase, BNP: B-Type Natriuretic Peptide, ICH-GCP: International Council for Harmonisation Good Clinical Practice, CONSORT: Consolidated Standards of Reporting Trials.

Availability of data and materials: All of the data which supports the findings of this systematic review is contained within the manuscript.

Competing interests: No competing interests are declared by the authors.

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SUPPLEMENTARY MATERIALS**Supplementary table I.** — Full-text reports excluded after eligibility assessment.

Study Reference	Reason for exclusion
Yildirim AK, Dastan AO, Demeli Ertus M, Ensarioglu M, Karabacak K, Pehlivanoglu B. Endothelium-dependent nitric oxide-mediated vasorelaxant effects of BPC 157 in human internal mammary artery. <i>Journal of Clinical Medicine</i> . 2026 May 2;15(9):3488.	Ex vivo study using isolated human internal mammary artery segments obtained during elective coronary artery bypass graft surgery. No human participants received BPC-157 or were enrolled in the study.
ClinicalTrials. NCT02637284 PCO-02—Safety and Pharmacokinetics Trial. ClinicalTrials.Gov 2026 [cited 2026, June 3] Available from: https://clinicaltrials.gov/study/NCT02637284	Phase I clinical trial investigating the safety and pharmacokinetics of BPC-157 in human participants. The study results were unavailable because the sponsor or investigator cancelled the results submission before completion of the quality control review.
ClinicalTrials. NCT07437547 BPC 157 for Acute Hamstring Muscle Strain Repair (BPC-HAMSTR). ClinicalTrials. GOV 2026 [cited 2026, June 3] Available from: https://clinicaltrials.gov/study/NCT07437547?intr=BPC-157&viewType=Card&rank=2&tab=results	Phase 2 randomised, double-blind, placebo-controlled study investigating the effects of BPC-157 on structural healing and functional recovery after acute grade II hamstring muscle strain in humans. The study results were unavailable because they have not been submitted.

Supplementary table II. — Domain-level assessment of included studies using the NIH Quality Assessment Tool for Before–After (Pre–Post) Studies With No Control Group.

Criteria	Lee and Padgett			Lee, Walker and Ayadi			Lee and Burgess		
	Yes	No	Other (CD, NR, NA)*	Yes	No	Other (CD, NR, NA)*	Yes	No	Other (CD, NR, NA)*
1. Was the study question or objective clearly stated?		No		Yes			Yes		
2. Were eligibility/selection criteria for the study population prespecified and clearly described?		No		Yes			Yes		
3. Were the participants in the study representative of those who would be eligible for the test/service/intervention in the general or clinical population of interest?	Yes			Yes				No	
4. Were all eligible participants that met the prespecified entry criteria enrolled?			CD			CD			CD
5. Was the sample size sufficiently large to provide confidence in the findings?		No			No			No	
6. Was the test/service/intervention clearly described and delivered consistently across the study population?		No		Yes			Yes		
7. Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants?		No				CD	Yes		
8. Were the people assessing the outcomes blinded to the participants' exposures/interventions?		No			No			No	
9. Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis?			CD	Yes					NA
10. Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided p values for the pre-to-post changes?		No			No			No	
11. Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention (i.e., did they use an interrupted time-series design)?		No			No		Yes		
12. If the intervention was conducted at a group level (e.g., a whole hospital, a community, etc.) did the statistical analysis take into account the use of individual-level data to determine effects at the group level?			NA			NA			NA

*CD, cannot determine; NA, not applicable; NR, not reported.