HSS Journal®: The Musculoskeletal Journal of Hospital for Special Surgery
1–11

DOI: 10.1177/15563316251355551
journals.sagepub.com/home/hss
Sage

Emerging Use of BPC-157 in Orthopaedic Sports Medicine: A Systematic Review

Nikhil Vasireddi, MHA[1], Henrik Hahamyan, BS[2], Michael J. Salata, MD[1,3], Michael Karns, MD[1,3], Jacob G. Calcei, MD[1,3], James E. Voos, MD[1,3], and John M. Apostolakos, MD[1,3]

Abstract

Background: Body protection compound-157 (BPC-157) is a naturally occurring gastric peptide that promotes mucosal integrity and homeostasis. Preclinical studies show its potential for promoting healing in musculoskeletal injuries such as fractures, tendon ruptures, ligament tears, and muscle injuries. Despite lacking US Food and Drug Administration approval and its use being banned in professional sports, it is increasingly used by clinicians and athletes. *Purpose:* We sought to (1) provide a comprehensive synthesis of the BPC-157 literature from an orthopedic sports medicine perspective and (2) elucidate the mechanism of action, musculoskeletal effects, metabolism, and safety profile. *Methods.* We conducted a systematic review of English-language literature, published from database inception to June 3, 2024, from PubMed, Cochrane, and Embase. We searched PROSPERO to identify any current or unpublished reviews. Studies reporting BPC-157's mechanism, musculoskeletal outcomes, metabolism, and safety were included. Articles were screened in 3 phases by 2 reviewers. In cases of a disagreement between the 2 reviewers, blinding was removed, and eligibility was determined by group consensus, with a third author making the final decision. *Results.* A total of 544 articles from 1993 to 2024 were identified. After duplicates were removed, 36 studies were included (35 preclinical studies, 1 clinical study). The studies suggest that BPC-157 enhances growth hormone receptor expression and several pathways involved in cell growth and angiogenesis, while reducing inflammatory cytokines. In preclinical models, BPC-157 improved functional, structural, and biomechanical outcomes in muscle, tendon, ligament, and bony injuries. In a retrospective study of musculoskeletal pain following intraarticular injection of BPC-157 for unspecified chronic knee pain, 7 of 12 patients reported relief for >6 months. BPC-157 is metabolized in the liver, with a half-life of less than 30 minutes, and is cleared by the kidneys. Preclinical safety studies showed no adverse effects across several organ systems. No clinical safety data were found. *Conclusion:* This systematic review of level IV and level V studies suggests that BPC-157 shows promise for promoting recovery from musculoskeletal injuries. Adverse effects are possible due to unregulated manufacturing, contamination, or unknown clinical safety. We recommend that clinicians counsel athletes to understand their organizations' rules to remain compliant with medication/supplement safety and testing standards.

Plain Language Summary

Review of the Musculoskeletal Literature Surrounding a Relatively Novel Peptide, Body Protection Compound-157

Body protection compound-157 (BPC-157) is a naturally occurring substance in the body that helps maintain healthy tissues and organs. Even though it is not approved by the US Food and Drug Administration and is banned in some sports, BPC-157 is still being used. This study aimed to review all the research on BPC-157 to understand how it works, its effects on muscles and joints, how the body processes it, and whether it is safe. The review looked at 36 studies published from 1993 to 2024. The findings showed that BPC-157 helps promote healing by boosting growth factors and reducing inflammation. It has improved outcomes in muscle, tendon, ligament, and bone injury models in animals. In one human study, 7 out of 12 people with chronic knee pain felt relief for over six months after receiving one BPC-157 knee injection. Animal studies showed no harmful effects, but there is no clinical safety data in humans. Overall, BPC-157 could help heal musculoskeletal injuries, but there are potential risks due to unregulated production and lack of clinical safety data.

Keywords

body protection compound-157, BPC-157, gastric pentadecapeptide, orthobiologics, peptide, sports, athlete

Received March 25, 2025. Accepted April 29, 2025.

Table 1. Stances of regulatory agencies and top professional sports organizations on BPC-157.

Organization	Stance on BPC-157	Year established
FDA [56]	Category 2: Bulk drug substance that raises significant safety concerns	2023
WADA [64]	Specific ban on BPC-157	2022
UFC [55]	Specific ban on BPC-157	2022
NFL [32]	Specific ban on BPC-157	2022
NBA	Non-specific ban on PEDs	NA
NHL	Non-specific ban on PEDs	2013
MLB [26]	Non-specific ban on types of peptide hormones	2019
NAIA [30]	Non-specific ban on peptide hormones	2017
PGA [37]	Non-specific ban on peptide hormones	2015
NCAA [31]	Non-specific ban on peptide hormones	1999

FDA U.S. Food and Drug Administration; *MLB* Major League Baseball; *NAIA* National Association of Intercollegiate Athletics; *NCAA* National Collegiate Athletics Association; *NBA* National Basketball Association; *NFL* National Football League; *NHL* National Hockey League; *PEDs* performance enhancing drugs; *PGA* Professional Golfers Association; *UFC* Ultimate Fighting Championship; *WADA* World Anti-Doping Agency.

Introduction

First described in 1992, body protective compound-157 (BPC-157) is a naturally occurring peptide in gastric juices that endogenously functions to promote gastric mucosal integrity and homeostasis [2,46,47]. Increasingly, BPC-157 is being studied in a variety of disease states due to its proposed angiogenic, anti-inflammatory, and wound healing properties [2,46,47]. In preclinical models, BPC-157 demonstrates significant cytoprotective effects in a range of organs and tissues, including the alimentary canal, liver, pancreas, heart, and nerves [8–10,21,23,24,34,36,44,46,65]. The compound also shows promise in rapid healing of muscles, bones, and joints, which highlights its potential application in orthopedic sports medicine [6,19,22,23,39,49]. There seem to be little to no adverse effects reported in the preclinical literature [11].

Although there is little clinical evidence, select cash practices offer BPC-157 intraarticular injections and oral formulations for knee pain and arthritis [25], and athletes are increasingly using BPC-157 for general musculoskeletal recovery and injury, including muscular strains and tendon injuries [54,64]. Recently, many leading regulatory agencies and professional and collegiate sports leagues in the United States have banned its use either by name or by association as a peptide hormone (Table 1).

At this time, there is no U.S. Food and Drug Administration (FDA) approved indication for BPC-157. In 2023, the FDA named BPC-157 a Category 2 bulk drug substance, meaning it cannot be compounded by commercial pharmaceutical companies and that there is insufficient evidence on whether it would cause harm to humans [56,57]. Nonetheless, many BPC-157 products are legally sold as "dietary supplements" or "research chemicals," classifications that are not subject to FDA regulations. In addition, because BPC-157, along with many peptide hormones, are not Drug Enforcement Agency (DEA) scheduled substances, possession is not illegal (unlike substances such as anabolic steroids). Thus, any products marketed as BPC-157 are unregulated for quality and safety [7,51]. In the wake of this gray-area legal status, numerous medical clinics with licensed physicians across the United States offer treatment with this peptide, and it remains readily accessible for purchase online, with interest on the rise [7,25].

In June 2024, the "BPC-157" Google search volume index, which measures the popularity of a search query, was at an all-time high. Concurrently, there are over 50 million "BPC-157" tagged video views on both YouTube and TikTok, with over 100,000 members in peptide-related Reddit communities. These trends with BPC-157 resemble another gray market class of drugs, selective androgen receptor modulators, which also have minimal clinical safety data, similar widespread use, and recent regulatory

[1]Case Western Reserve University School of Medicine, Cleveland, OH, USA
[2]East Tennessee State University, Quillen College of Medicine, Johnson City, TN, USA
[3]University Hospitals Cleveland Medical Center, Cleveland, OH, USA

Corresponding Author:
Nikhil Vasireddi, MHA, Case Western Reserve University School of Medicine, MHA, 9501 Euclid Avenue, Cleveland, OH 44106, USA.
Email: nikv98@gmail.com

bans, yet are available in cash clinics and online [12,13,58,59]. Despite increasing athlete and musculoskeletal clinical use, there is no peer-reviewed literature on BPC-157 specifically geared toward sports medicine clinicians and athletes.

We are not aware of any prior systematic reviews pertaining to BPC-157 use in orthopedic sports medicine and athletes. Therefore, we sought to provide sports medicine clinicians and athletes with a comprehensive synthesis of the BPC-157 literature to understand the mechanism of action, musculoskeletal effects, metabolism, and safety profile, and to guide whether and how physicians should recommend this substance to their patients.

Methods

We searched PROSPERO to identify any current or unpublished reviews on this topic. This systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The search terms were "Body Protective Compound-157" and "BPC-157" in combination with all known alternative names (gastric pentadecapeptide, BPC-15, PL-14736, bepecin, PLD-116, PCO-02) and variants of dash/space locations with the Boolean operator "OR."

The search was conducted in PubMed, Embase, and the Cochrane Library from inception to June 3, 2024, with no limit on publication year. Non-English studies were excluded from the search, and duplicates were removed using Covidence (Veritas Health Innovation).

Articles were assessed for study eligibility by 2 reviewers, each without knowledge of the other's inclusion/exclusion decisions. They reviewed included articles in 3 phases. After removing duplicates, articles were screened by title and abstract. After agreement, the review was repeated to screen by full-text articles, then agreement was assessed again prior to extraction. In cases of a disagreement between the 2 reviewers, anonymity was removed, and eligibility was determined by group consensus, with a third author making the final decision. All abstracts and full-text articles were stored in Covidence, which allowed anonymizing of each independent reviewer to the inclusion/exclusion decisions made by the other reviewers throughout the assessment process.

Articles relevant to the BPC-157 mechanism of action related to the musculoskeletal system, overall musculoskeletal effects, safety profile, and metabolism were included. Preclinical and clinical studies were included. Reviews, meta-analyses, editorials, and conference abstracts were excluded.

Articles that met eligibility criteria underwent data extraction, including model demographics, sample size, treatment groups, side effects, and primary and secondary outcomes. The 2 reviewing authors categorized each article into non-mutually exclusive sections by article topic or type: mechanism of action, musculoskeletal outcomes, metabolic profile, and safety profile. Further subsections were included when necessary.

Results

A total of 544 articles were initially identified. After removing duplicates and completing the screening processes, we included 36 articles in this systematic review [1,2,4–7,15–20,22,23,25,33,35,36,39,40,41,44–53,60–62,66,67], with 21 reporting on the mechanism of action [1,2,5,6,16–20,23,35,40,41,47,50,52,53,60–62,66], 15 reporting musculoskeletal outcomes [2,4–6,19,22,22,25,33,36,39,46,48,49], 3 analyzing metabolism [7,15,51], and 4 assessing safety profile and adverse effects associated with BPC-157 [15,45,45,67] (Fig. 1).

Mechanism of action

Of the 36 included articles, 21 reported on the mechanism of action of BPC-157 (Fig. 2) [1,2,5,6,16–20,23,35,40,41,47,50,52,53,60–62,66].

Several preclinical animal models identified that BPC-157 stimulates vascular endothelial growth factor (VEGF) protein and gene expression, a pathway commonly implicated in angiogenesis [2,16–18,60,61,66]. Other studies suggested that BPC-157 upregulates the phosphorylation level of extracellular signal-regulated kinases (ERK) 1 and 2 as well as their downstream targets, including c-Fos [18], c-Jun [18], and Egr-1 [18,60,61], which are key molecules involved in cell growth, migration, and angiogenesis. Other pro-survival and pro-proliferation pathways include increased AKT phosphorylation [61,66] and increased Kirsten rat sarcoma viral oncogene homolog (KRAS) gene expression [60,61]. BPC-157 was associated with increased FAK and paxillin gene expression in an *in vitro* cultured tendon fibroblast model, suggesting direct or indirect activation of the focal adhesion kinase (FAK)-paxillin pathway, important in cellular adhesion, migration, proliferation, and survival [6]. In cultured tendon fibroblasts isolated from rats, BPC-157 was associated with increased growth hormone receptor gene and protein expression, identifying modulation of another proliferation-promoting pathway [5].

In addition to growth-related pathways, BPC-157 upregulates vasodilatory nitric oxide pathways, including the upregulation of nitric oxide synthase (NOS) gene and protein expression and increased nitric oxide production [1,16,35,40,47,50,60–62,66]. BPC-157 also counteracts proinflammatory pathways and cytokines as it has been observed to decrease cyclooxygenase-2 (COX-2) gene expression [19,62], decrease myeloperoxidase activity [23], and decrease levels of interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) [40].

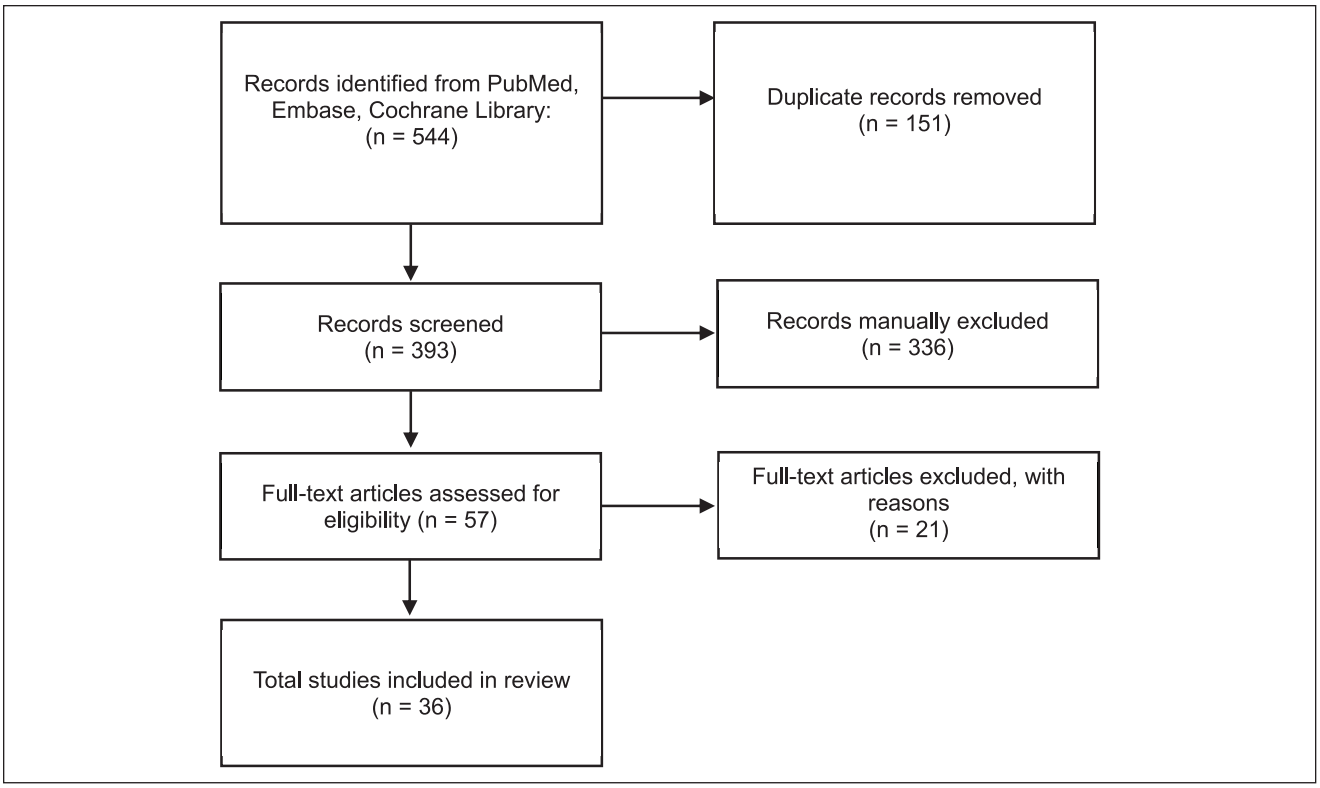

Fig. 1. PRISMA diagram.

BPC-157 also modulates dopamine and serotonin pathways [20,53]. Following intraperitoneal administration in rat models, BPC-157 increased serotonin synthesis in the substantia nigra reticulate and medial anterior olfactory nucleus [54]; decreased serotonin synthesis in the dorsal thalamus, hippocampus, lateral geniculate body and hypothalamus [53]; and blocked amphetamine-induced heightened startle response and stereotypy [20,41].

Musculoskeletal outcomes

Fourteen studies measured musculoskeletal outcomes associated with BPC-157 [2,4–6,19,22,25,33,36,39,46,48,49] (Table 2).

BPC-157 body protection compound-157; MCL, medial collateral ligament; *VEGF* vascular endothelial growth factor

In 3 rat muscle transection and crush models, BPC-157 treatment improved muscle structure, function, and biomechanics [33,36,48]. Outcomes included improved load to failure, motor function indices, muscle myofibril and macroscopic diameters, and reduced atrophy and subcutaneous gapping [33,36,48]. Similarly, BPC-157 treatment improved tendon structure, limb alignment, biomechanics, and motor function indices following transection of rat Achilles and quadriceps tendons [19,22,23,49]. *In vitro*, BPC-157 improved tendon fibroblast survival under stress, cell migration indices, cell proliferation, and growth hormone receptor expression [5,6,49].

One study found that BPC-157 promotes fracture healing [39]. In rabbit nonunion models, intramuscular administration of BPC-157 performed similarly to percutaneous injection of autologous bone marrow or autologous bone grafting in improving callous mineralization and resolution of the bone defect with predominantly lamellar bone formation versus fibrous scar tissue [39].

BPC-157 also demonstrated anti-inflammatory effects in musculoskeletal injury models [19,23,46,49]. In Freund's adjuvant–induced polyarthritis rat models, BPC-157 reduced paw inflammation, nodule formation, and stiffness [46]. Histologic analysis of transected rat muscle and tendon models demonstrated decreased inflammatory infiltrates following BPC-157 treatment [19,23,49]. In addition, on histology, BPC-157 increased local vascularity and VEGF expression in muscle, tendon, and ligament injury models [2,4,22].

In 1 rat medial collateral ligament (MCL) transection model, BPC-157 treatment reduced postinjury valgus instability and contracture, and restored biomechanics (MCL load to failure, stiffness, breaking force, and absorbed energy indices), motor function indices, and macroscopic and microscopic structure [4].

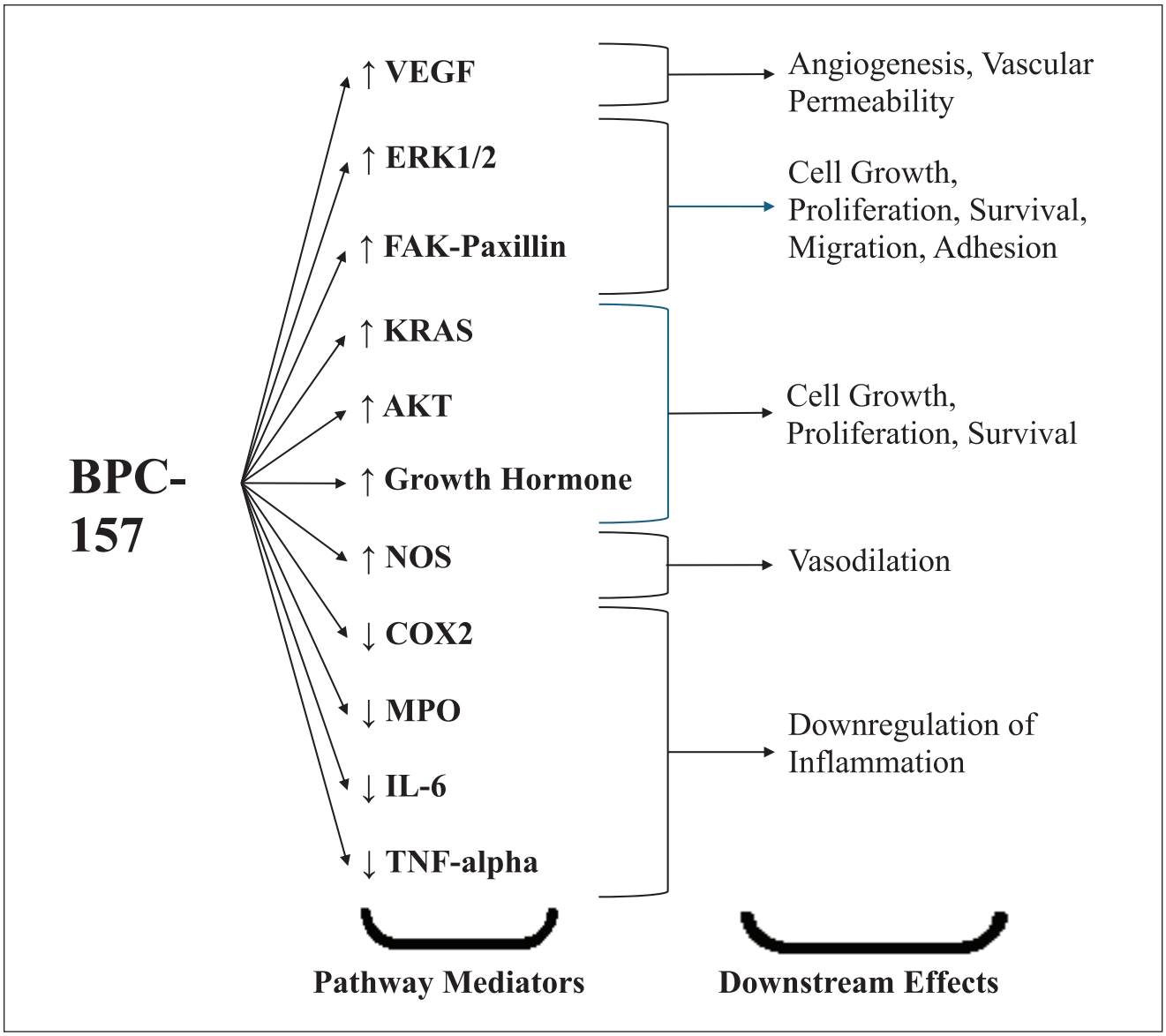

Fig. 2. High-level overview of pathways modulated by BPC-157. It is important to note that these pathways are nonlinear and often interconnected.
VEGF vascular endothelial growth factor; *ERK1/2* extracellular signal-regulated kinase 1/2; *FAK* focal adhesion kinase; *KRAS* Kirsten rat sarcoma virus; *AKT* alpha serine/threonine-protein kinase; *NOS* nitric oxide synthase; *COX2* cyclooxygenase-2; *MPO* myeloperoxidase; *IL-6* interleukin-6; *TNF-α* tumor necrosis factor-alpha.

Only 1 clinical study could be identified that retrospectively assessed musculoskeletal pain following intraarticular injection of BPC-157 for unspecified chronic knee pain. Out of 12 patients, 7 reported subjective improvement in symptoms for more than 6 months following intraarticular injection of BPC-157 alone (2 cc of 2000 mcg/mL solution) [25].

Metabolism and Excretion

Three studies assessed the metabolic and elimination profiles of BPC-157 [7,15,51]. In animal models, BPC-157 tissue concentration was reportedly highest in the kidneys, then the liver, with high concentrations found in bile, and extensive metabolism was also observed in *in vitro* human liver microsome models [15]. Thus, BPC-157 is likely metabolized in the liver by cytochrome P450 enzymatic pathways and excreted in the urine, but further renal metabolism cannot be ruled out. The half-life of BPC-157 was reported to be less than 30 minutes, following linear pharmacokinetics, after single and repeat intramuscular and intravenous dose administration. One study reported that BPC-157 metabolites were stable and detectable in urine

Table 2. Studies reporting musculoskeletal outcomes associated with BPC-157.

Author	Models	Primary investigations	Associated Outcomes Reported
Sikiric et al (1997) [46]	Male Wistar rats	Effect of BPC-157 on induced inflammatory arthritis	Reduced paw inflammation, nodule formation, stiffness
Sebecić et al (1999) [39]	Rabbits	Effect of BPC-157 on a rabbit nonunion model	Local BPC-157 performed similarly to percutaneous injection of autologous bone marrow or autologous bone grafting in resolving nonunion defect
Staresinic et al (2003) [49]	Male Wistar rats	Effect of BPC-157 on Achilles tendon healing post-transection	Improved Achilles tendon structural, functional, and biomechanical indices; reduced inflammatory infiltrates
Krivic et al (2006) [22]	Male Wistar rats	Effect of BPC-157 on Achilles tendon healing post-transection	Improved functional and biomechanical indices, macroscopic and microscopic structures; resolved tendon-bone defect
Staresinic et al (2006) [48]	Male Wistar rats	Effect of BPC-157 on quadriceps muscle healing post-transection	Improved quadriceps muscle macroscopic and microscopic structural, functional, and biomechanical indices
Krivic et al (2008) [23]	Male Wistar rats	Effect of BPC-157 on Achilles tendon healing post-transection	Decreased inflammatory infiltrates, increased vascular indices, and increased functional indices (BPC-157 with methylprednisolone)
Novinscak et al (2008) [33]	Male Wistar rats	Effect of BPC-157 on muscle crush injury	Improved macroscopic and microscopic muscle structures and restored functional indices
Brcic et al (2009) [2]	Male Wistar rats	Angiogenic effect of BPC-157 in muscle and tendon transection	Increases local vascularity and VEGF expression in muscle and tendon transection models
Pevec et al (2010) [36]	Male Wistar rats	Effect of BPC-157 on a corticosteroid-impaired muscle healing model	Improved structural and functional muscle healing despite concurrent corticosteroid treatment
Cerovecki et al (2010) [4]	Male Wistar rats	Effect of BPC-157 on MCL healing at 90 days post-transection	Reduced postinjury valgus instability and contracture, restored motor function indices, MCL biomechanical indices, macroscopic and microscopic structures
Chang et al (2011) [6]	Cultured tendon explants and fibroblasts from Sprague-Dawley rats	Effect of BPC-157 on cultured Achilles tendon	Increased ex vivo outgrowth of tendon explants, migration of tendon fibroblasts, and cell survival under stress
Chang et al (2014) [5]	Cultured Sprague-Dawley rat tendon fibroblast	Effect of BPC-157 on tendon fibroblasts	Increased growth hormone receptor expression and activity in cultured tendon fibroblasts
Japjec et al (2021) [19]	Male Wistar rats	Effect of BPC-157 on quadriceps tendon healing post-transection	Improved tendon macroscopic and microscopic structures, reduced inflammatory infiltrates, and resolved myotendinous defect
Lee et al (2021) [25]	Human knees (retrospective)	Effect of BPC-157 on chronic knee pain	7 of 12 patients reported subjective improvement in symptoms for more than 6 months (intraarticular BPC-157 injection)

for 4 days, with a limit of detection of 0.1 ng/mL using high-resolution liquid chromatography mass spectrometry [7]. Another study reported limits of detection for several BPC-157 metabolites ranging from 0.03 to 0.11 ng/mL, all stable and detectable in urine for 5 days using ultra-high-performance liquid chromatography mass spectrometry [51]. These limits of detection are below the minimum required levels (2 ng/mL) for peptide compounds set by the World Anti-Doping Agency (WADA), providing analytical parameters suitable for use in athlete drug testing [63].

Safety Profile

Three studies assessed the safety profile and adverse effects of BPC-157 [15,45,67]. Notably, all 3 studies assessed several organ-specific outcome measures in animal and *in vitro* models and reported no acute toxicity across several organ systems. Following single and repeat intramuscular and intravenous doses of BPC-157, ranging from 6 µg/kg to 20 mg/kg over 6 weeks, gross necropsy analysis revealed no adverse changes in the liver, spleen, thymus, and gastric

wall of both rat and dog models [15,45,67]. No microscopic histopathologic changes were noted in the liver, spleen, lung, kidney, brain, thymus, prostate, and ovaries across similar dosing and frequency through 6 weeks in both rat and dog models [67]. In addition, BPC-157 did not cause acute local irritation at injection sites. In a local tolerance study that assessed gross necropsy, antigen excitation assays, and anaphylaxis assays, a single injection of BPC-157 (100 μg/mL) into the quadriceps femoris of rabbits did not induce local irritation, erythema, edema, hyperemia, necrosis, or ulceration, over a 48-hour period [67].

Although renally and hepatically cleared, BPC-157 was not found to be acutely hepatotoxic or nephrotoxic and demonstrated protective effects [15,45,67]. Sikiric et al [44] reported that following induced hepatic injury (hepatic artery ligation, bile duct ligation, or carbon tetrachloride administration), all BPC-157 pretreated rat groups (regardless of dose and timepoint) had a similar reduction of alanine transaminase (AST), bilirubin, and AST-to-aspartate transaminase (ALT) ratio and less histologic evidence of liver necrosis compared to saline pretreated controls.

One study assessed the *in vitro* mutagenicity and genotoxicity, and preclinical teratogenicity associated with BPC-157 [67]. BPC-157 was associated with no change in the number of revertant bacterial colonies in the Ames test, no chromosomal aberration or damage in cultured mice bone marrow cells, and negative micronucleus assays; these results suggest that BPC-157 has no *in vitro* mutagenic or genotoxic effects. Regarding teratogenicity, 3 intramuscular injections of BPC-157 (0.2–4 mg/kg) were administered between the 6th and 15th days of rat pregnancy. After sacrifice on day 20, maternal-fetal assessment revealed no differences in the number of alive, dead, or aborted fetuses, and no changes in mass, size, and morphology of reproductive organs and fetal tissues. Thus, BPC-157 did not demonstrate *in vivo* teratogenicity at the studied doses/frequencies.

Despite a wide range of doses (6 μg/kg to 20 mg/kg), routes of administration (intramuscular, intraperitoneal, intravenous, oral), and frequency assessed in several animal models, no acute lethal or toxic dose was reported [15,67]. No study assessed adverse events beyond 6 weeks following single or repeat administration of BPC-157 in animal models. No study assessed the safety or adverse events of BPC-157 in humans.

Discussion

This systematic review suggests that BPC-157 has the potential to reduce inflammation, promote vascularity, and augment structural, biomechanical, and functional recovery in fracture, muscle, tendon, and ligamentous injury models. The mechanism of action is multifactorial, directly or indirectly upregulating cell growth, proliferation, survival, angiogenesis, and anti-inflammation pathways. BPC-157 is metabolized in the liver with a half-life of less than 30 min, excreted in the urine, and detectable in the urine for up to 4 days by mass spectrometry methods. In preclinical animal models, BPC-157 was not associated with acute (<6 weeks) gross or histologic toxicity across several organs, including the liver, spleen, lung, kidney, brain, thymus, prostate, and ovaries. No toxic or lethal dose was achieved over a wide range of doses (6 μg/kg to 20 mg/kg). The in-human safety of BPC-157 was not assessed in the included studies and thus remains unknown. We recommend that clinicians and athletes exercise caution when considering the use of BPC-157 due to the lack of high-quality clinical data. To promote athlete safety and compliance, we recommend that clinicians take thorough histories of dietary and sports supplements and counsel athletes to understand their organization's medication and supplement policies.

This systematic review had several limitations. The heterogeneity in study design, objectives, and outcome measures restricted our ability to conduct a quantitative meta-analysis. In addition, the lack of clinical outcome and safety data prevents us from proposing evidence-based practice use guidelines, and we therefore recommend caution regarding clinical use. More important, this highlights an important gap in the BPC-157 musculoskeletal literature for future multidisciplinary clinical investigations. It is unlikely that we missed any relevant studies, especially clinical studies, due to our thorough search strategy, which included an extensive list of known alternative names for BPC-157 and related terms. Lastly, the field of BPC-157 research in orthopedics and sports medicine is rapidly evolving, as indicated by the findings of this review. Our study should be interpreted as a global snapshot of the expanding literature relevant to orthopedic sports medicine clinicians, and our conclusions are not meant to replace individual outcomes or interpretations of specific studies on BPC-157.

In preclinical models, BPC-157 has been found to reduce inflammation and augment structural, biomechanical, and functional recovery in fracture, muscle, tendon, and ligamentous injury models. Athletes' use of BPC-157 is growing [64], presumably in pursuit of these regenerative effects, and many top professional and collegiate sports leagues have banned its use in recent years. These outcome measures have not been clinically studied in humans, yet a Google search reveals that licensed medical practitioners, including orthopedic and sports medicine specialists, are offering BPC-157 treatment for musculoskeletal injuries [25]. In fact, there was only 1 registered clinical trial (phase I) with an unknown status since 2016 [28]. This highlights an important gap in the BPC-157 musculoskeletal literature for future multidisciplinary clinical investigation.

Hepatic metabolism, relatively short (<30 min) half-life, urinary excretion, and window of detection up to 4 days is consistent with other commonly abused peptide

hormones, such as human growth hormone (HGH) and erythropoietin (EPO) [3,7,29,38]. Furthermore, since BPC-157 is shown to accelerate recovery in many preclinical musculoskeletal injury models, it is likely used far out of competition, as opposed to EPO and HGH. The relatively short window of detection of peptide hormones in urine poses unsolved challenges for both in-competition and out-of-competition doping control in collegiate and professional sports leagues [14].

Preclinical models did not reveal any adverse effects or toxicities associated with BPC-157, but clinical data were limited, and in-human safety remains unknown. Side effects of other frequently used peptide hormones by athletes, such as HGH and EPO, are reportedly rare, but case reports include acromegaly, anaphylaxis, flu-like symptoms, mood dysregulation, and thrombosis [12,41]. Without an FDA-approved indication, BPC-157 remains an unregulated supplement, and anywhere between 12% and 58% of ergo-nutritional supplements are contaminated with other, oftentimes unsafe, substances [27]. It is important to acknowledge that many anonymous online users of BPC-157 report adverse effects, including injection site pain and swelling, joint pain, anxiety, panic attacks, heart palpitations, insomnia, drowsiness, weakness, fatigue, loss of appetite, depression, and anhedonia. These side effects could be possible in the setting of unregulated production, contamination, and/or the ability of BPC-157 to modulate inflammatory, dopamine, and serotonin pathways [8–10,21,23,24,34,36,44,46,65]. To improve outcome reporting and athlete safety, we recommend that during history-taking, clinicians explicitly inquire about "dietary or sports supplements" and provide counseling and heightened suspicion regarding potential contaminants.

In conclusion, early preclinical evidence suggests that BPC-157 promotes structural, biomechanical, and functional recovery in tendon rupture, ligament tear, muscle tear, and fracture models. Like other peptide hormones, BPC-157 is metabolized in the liver, excreted in the urine, and detectable for up to 4 days by mass spectrometry methods. BPC-157 modulates cell growth, proliferation, survival, anti-inflammatory, and angiogenesis pathways. While no acute adverse events (<6 weeks) were reported in preclinical animal models, clinical safety in humans remains unknown. Due to limited high-quality clinical evidence, clinicians and athletes should exercise caution when considering the use of BPC-157. To promote outcome reporting and athlete safety, we recommend that during history-taking, clinicians specifically inquire about dietary or sports supplements and provide counsel about the risks associated with unregulated manufacturing, contamination, and poor clinical safety data. Clinicians should urge athletes to understand their organizations' rules and be cautious of the medication or supplements they take to remain compliant with safety and testing standards. Further basic science and clinical studies are needed to validate these preliminary findings pertaining to BPC-157.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Michael J. Salata, MD, declares a relationship with Stryker. Michael Karns, MD, declares relationships with Smith & Nephew and Arthrex. Jacob G. Calcei, MD, declares a relationship with Smith & Nephew. James E. Voos, MD, declares relationships with Arthrex and Mitek. The other authors declare no potential conflicts of interest.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Human/Animal Rights

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration.

Informed Consent

Informed consent was not required for this systematic review.

Required Author Forms

Disclosure forms provided by the authors are available with the online version of this article as supplemental material.

ORCID iD

Nikhil Vasireddi https://orcid.org/0000-0002-8316-9586

References

1. Barisic I, Balenovic D, Udovicic M, et al. Stable gastric pentadecapeptide BPC 157 may counteract myocardial infarction induced by isoprenaline in rats. *Biomedicines*. 2022;10(2):265.
2. Brcic L, Brcic I, Staresinic M, Novinscak T, Sikiric P, Seiwerth S. Modulatory effect of gastric pentadecapeptide BPC 157 on angiogenesis in muscle and tendon healing. *J Physiol Pharmacol Off J Pol Physiol Soc*. 2009;60(Suppl 7):191–196.
3. Cameron D, Burger H, Catt C, Gordon E, Watts J. Metabolic clearance of human growth hormone in patients with hepatic and renal failure, and in the isolated perfused pig liver. *Metabolism*. 1972;21(10):895–904.
4. Cerovecki T, Bojanic I, Brcic L, et al. Pentadecapeptide BPC 157 (PL 14736) improves ligament healing in the rat. *J Orthop Res*. 2010;28:1155–1161.
5. Chang CH, Tsai WC, Hsu YH, Pang JH. Pentadecapeptide BPC 157 enhances the growth hormone receptor expression in tendon fibroblasts. *Molecules*. 2014;19:19066–19077.

6. Chang C-H, Tsai W-C, Lin M-S, Hsu Y-H, Pang J-HS. The promoting effect of pentadecapeptide BPC 157 on tendon healing involves tendon outgrowth, cell survival, and cell migration. *J Appl Physiol*. 2011;110:774–780.
7. Cox HD, Miller GD, Eichner D. Detection and in vitro metabolism of the confiscated peptides BPC 157 and MGF R23H. *Drug Test Anal*. 2017;9:1490–1498.
8. Drmic D, Kolenc D, Ilic S, et al. Celecoxib-induced gastrointestinal, liver and brain lesions in rats, counteraction by BPC 157 or L-arginine, aggravation by L-NAME. *World J Gastroenterol*. 2017;23:5304.
9. Duzel A, Vlainic J, Antunovic M, et al. Stable gastric pentadecapeptide BPC 157 in the treatment of colitis and ischemia and reperfusion in rats: New insights. *World J Gastroenterol*. 2017;23:8465–8488.
10. Grabarevic Z, Tisljar M, Artukovic B, et al. The influence of BPC 157 on nitric oxide agonist and antagonist induced lesions in broiler chicks. *J Physiol-Paris*. 1997;91:139–149.
11. Gwyer D, Wragg NM, Wilson SL. Gastric pentadecapeptide body protection compound BPC 157 and its role in accelerating musculoskeletal soft tissue healing. *Cell Tissue Res*. 2019;377:153–159.
12. Hahamyan HA, Basaria S. Selective androgen receptor modulators—transformative drugs or heralds of the next drug epidemic? *JAMA*. 2024;331:1359–1360.
13. Hahamyan HA, Vasireddi N, Voos JE, Calcei JG. Social media's impact on widespread SARMs abuse. *Phys Sportsmed*. 2023;51(4):291–293. doi: https://10.1080/00913847.2022.2078679.
14. Handelsman DJ. Performance Enhancing Hormone Doping in Sport. 2020. In: Feingold KR, Ahmed SF, Anawalt B, et al, editors. *Endotext* [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000–. PMID: 26247087.
15. He L, Feng D, Guo H, et al. Pharmacokinetics, distribution, metabolism, and excretion of body-protective compound 157, a potential drug for treating various wounds, in rats and dogs. *Front Pharmacol*. 2022;13:1026182. doi: https://10.3389/fphar.2022.1026182.
16. Hsieh MJ, Lee CH, Chueh HY, et al. Modulatory effects of BPC 157 on vasomotor tone and the activation of Src-Caveolin-1-endothelial nitric oxide synthase pathway. *Sci Rep*. 2020;10:17078.
17. Hsieh MJ, Liu HT, Wang CN, et al. Therapeutic potential of pro-angiogenic BPC157 is associated with VEGFR2 activation and up-regulation. *J Mol Med Berl*. 2017;95:323–333.
18. Huang T, Zhang K, Sun L, et al. Body protective compound-157 enhances alkali-burn wound healing in vivo and promotes proliferation, migration, and angiogenesis in vitro. *Drug Des Devel Ther*. 2015;9:2485–2499.
19. Japjec M, Horvat Pavlov K, Petrovic A, et al. Stable Gastric Pentadecapeptide BPC 157 as a Therapy for the Disable Myotendinous Junctions in Rats. *Biomedicines*. 2021;9:1547.
20. Jelovac N, Sikirić P, Ručman R, et al. A novel pentadecapeptide, BPC 157, blocks the stereotypy produced acutely by amphetamine and the development of haloperidol-induced supersensitivity to amphetamine. *Biol Psychiatry*. 1998;43:511–519.
21. Klicek R, Kolenc D, Suran J, et al. Stable gastric pentadecapeptide BPC 157 heals cysteamine-colitis and colon-colon-anastomosis and counteracts cuprizone brain injuries and motor disability. *J Physiol Pharmacol Off J Pol Physiol Soc*. 2013;64:597–612.
22. Krivic A, Anic T, Seiwerth S, Huljev D, Sikiric P. Achilles Detachment in Rat and Stable Gastric Pentadecapeptide BPC 157: Promoted Tendon-to-Bone Healing and Opposed Corticosteroid Aggravation. *J Orthop Res*. 2006;24:982–989.
23. Krivic A, Majerovic M, Jelic I, Seiwerth S, Sikiric P. Modulation of early functional recovery of Achilles tendon to bone unit after transection by BPC 157 and methylprednisolone. *Inflamm Res*. 2008;57:205–210.
24. Lazić R, Gabrić N, Dekaris I, Bosnar D, Boban-Blagaić A, Sikirić P. Gastric pentadecapeptide BPC 157 promotes corneal epithelial defects healing in rats. *Coll Antropol*. 2005;29:321–325.
25. Lee E, Padgett B. Intra-Articular Injection of BPC 157 for Multiple Types of Knee Pain. *Altern Ther Health Med*. 2021;27:8–13.
26. Major League Baseball. *Major League Baseball's Minor League Drug Prevention And Treatment Program*.; 2019. Available at: https://content.mlb.com/documents/2/5/6/296983256/2019_Minor_League_Program.pdf. Accessed June 5, 2024.
27. Martínez-Sanz JM, Sospedra I, Ortiz CM, Baladía E, Gil-Izquierdo A, Ortiz-Moncada R. Intended or unintended doping? A review of the presence of doping substances in dietary supplements used in sports. *Nutrients*. 2017;9:1093.
28. Menchaca R. *Phase I, Pilot Study in Healthy Volunteers to Assess the Safety and Pharmacokinetics of PCO-02, Which Active Ingredient Is BPC-157, a Penta-Deca-Peptide From Gastric Source*. clinicaltrials.gov; 2015. Available at: https://clinicaltrials.gov/study/NCT02637284. Accessed December 31, 2023.
29. Mullis PE, Pal BR, Matthews DR, Hindmarsh PC, Phillips PE, Dunger DB. Half-life of exogenous growth hormone following suppression of endogenous growth hormone secretion with somatostatin in type I (insulin-dependent) diabetes mellitus. *Clin Endocrinol*. 1992;36(3):255–263. doi: https://10.1111/j.1365-2265.1992.tb01441.x.
30. National Association of Intercollegiate Athletics. *NAIA Banned Drugs*. National Association of Intercollegiate Athletics; 2019. Available at: https://www.naia.org/student-athlete-wellness-center/2019-20/files/NAIA_Banned_Substances_List.pdf. Accessed June 5, 2024.
31. National Collegiate Athletic Association. *NCAA Banned Substances*. National Collegiate Athletic Association; 2023. Available at: https://www.ncaa.org/sports/2015/6/10/ncaa-banned-substances.aspx. Accessed June 5, 2024.
32. National Football League Player's Association. *List of Prohibited Substances*. National Football League Player's Association; 2022. Available at: https://nflpaweb.blob.core.windows.net/website/PDFs/List-of-Prohibited-Substances_PES_2022.pdf. Accessed June 5, 2024.
33. Novinscak T, Brcic L, Staresinic M, et al. Gastric pentadecapeptide BPC 157 as an effective therapy for muscle crush injury in the rat. *Surg Today*. 2008;38:716–725.
34. Perovic D, Kolenc D, Bilic V, et al. Stable gastric pentadecapeptide BPC 157 can improve the healing course of spinal cord injury and lead to functional recovery in rats. *J Orthop Surg*. 2019;14:199.
35. Perovic D, Milavic M, Dokuzovic S, et al. Novel therapeutic effects in rat spinal cord injuries: recovery of the definitive and

early spinal cord injury by the administration of pentadecapeptide BPC 157 therapy. *Curr Issues Mol Biol*. 2022;44:1901–1927.
36. Pevec D, Novinscak T, Brcic L, et al. Impact of pentadecapeptide BPC 157 on muscle healing impaired by systemic corticosteroid application. *Med Sci Monit Int Med J Exp Clin Res*. 2010;16:BR81–BR88.
37. Professional Golfers Association. *PGA TOUR Anti-Doping Program Manual*. Professional Golfers Association; 2015. Available at: https://www.usga.org/content/dam/usga/pdf/Championship%20Resources/2015-2016%20PGATOURAntiDopingProgram.pdf. Accessed June 5, 2024.
38. Saugy M, Robinson N, Saudan C, Baume N, Avois L, Mangin P. Human growth hormone doping in sport. *Br J Sports Med*. 2006;40:i35–i39.
39. Sebecić B, Nikolić V, Sikirić P, et al. Osteogenic effect of a gastric pentadecapeptide, BPC-157, on the healing of segmental bone defect in rabbits: a comparison with bone marrow and autologous cortical bone implantation. *Bone*. 1999;24:195–202.
40. Sever AZ, Sever M, Drmic D, Poljak L, Seiwerth S, Sikiric P. Pentadecapeptide BPC 157 therapy in bile duct ligated (BDL) rats: in the liver tissue, BPC 157 counteracts the increased NOS3 expression, IL-6, TNF-α, IL-1β levels, and Ki-67 presentation. *Gastroenterology*. 2019;156:S–113.
41. Sikirić P, Jelovac N, Jelovac-Gjeldum A, et al. Pentadecapeptide BPC 157 attenuates chronic amphetamine-induced behavior disturbances. *Acta Pharmacol Sin*. 2002;23:412–422.
42. Sikirić P, Petek M, Rotkvić I, et al. Antiulcerogenic and anti-inflammatory effect of a new gastric juice peptide-body protection compound. *Exp Clin Gastroenterol*. 1991b;1:179–181.
43. Sikirić P, Petek M, Rucman R, et al. A new gastric juice peptide, BPC. An overview of the stomach-stress-organoprotection hypothesis and beneficial effects of BPC. *J Physiol Paris*. 1993;87:313–327.
44. Sikirić P, Seiwerth S, Grabarevic Z, et al. Hepatoprotective effect of BPC 157, A 15-aminoacid peptide, on liver lesions induced by either restraint stress or bile duct and hepatic artery ligation or CCl4 administration. A comparative study with dopamine agonists and somatostatin. *Life Sci*. 1993;53:PL291–PL296.
45. Sikirić P, Seiwerth S, Grabarević Ž, et al. The influence of a novel pentadecapeptide, BPC 157, on N(G)-nitro-L-arginine methylester and L-arginine effects on stomach mucosa integrity and blood pressure. *Eur J Pharmacol*. 1997;332:23–33.
46. Sikirić P, Seiwerth S, Grabarevic Z, et al. Pentadecapeptide BPC 157 positively affects both non-steroidal anti-inflammatory agent-induced gastrointestinal lesions and adjuvant arthritis in rats. *J Physiol-Paris*. 1997;91:113–122.
47. Skorjanec S, Kokot A, Drmic D, et al. Duodenocutaneous fistula in rats as a model for "wound healing-therapy" in ulcer healing: the effect of pentadecapeptide BPC 157, L-nitro-arginine methyl ester and L-arginine. *J Physiol Pharmacol*. 2015;66:581–590.
48. Staresinic M, Petrovic I, Novinscak T, et al. Effective therapy of transected quadriceps muscle in rat: Gastric pentadecapeptide BPC 157. *J Orthop Res*. 2006;24:1109–1117.
49. Staresinic M, Sebecic B, Patrlj L, et al. Gastric pentadecapeptide BPC 157 accelerates healing of transected rat Achilles tendon and in vitro stimulates tendocytes growth. *J Orthop Res*. 2003;21:976–983.
50. Stupnisek M, Kokot A, Drmic D, et al. Pentadecapeptide BPC 157 reduces bleeding and thrombocytopenia after amputation in rats treated with Heparin, Warfarin, L-NAME and L-Arginine. *PLoS One*. 2015;10(4):e0123454.
51. Tian T, Jing J, Li Y, Wang Y, Deng X, Shan Y. Stable isotope labeling-based nontargeted strategy for characterization of the in vitro metabolic profile of a novel doping BPC-157 in doping control by UHPLC-HRMS. *Molecules*. 2023;28:7345.
52. Tkalcević VI, Cuzić S, Brajsa K, et al. Enhancement by PL 14736 of granulation and collagen organization in healing wounds and the potential role of egr-1 expression. *Eur J Pharmacol*. 2007;570:212–221.
53. Tohyama Y, Sikirić P, Diksic M. Effects of pentadecapeptide BPC157 on regional serotonin synthesis in the rat brain: alpha-methyl-L-tryptophan autoradiographic measurements. *Life Sci*. 2004;76:345–357.
54. Ultimate Fighting Championship. *Anti-Doping Statement on Courtney Casey*. Ultimate Fighting Championship; 2023. Available at: https://www.ufc.com/news/statement-cortney-casey?language_content_entity=en
55. Ultimate Fighting Championship. *UFC Anti-Doping Policy*. Ultimate Fighting Championship; 2024. Available at: https://ufcantidoping.com
56. US Food and Drug Administration. *Safety Risks Associated with Certain Bulk Drug Substances Nominated for Use in Compounding*.; 2023. Available at: https://www.fda.gov/drugs/human-drug-compounding/safety-risks-associated-certain-bulk-drug-substances-nominated-use-compounding
57. US Food and Drug Administration. *Bulk Drug Substances Used in Compounding Under Section 503B of the FD&C Act*. U.S. Food and Drug Administration; 2024. Available at: https://www.fda.gov/drugs/human-drug-compounding/bulk-drug-substances-used-compounding-under-section-503b-fdc-act#:~:text=Category%202%20–%20These%20are%20bulk,in%20compounding%20pending%20further%20evaluation. Accessed June 5, 2024.
58. Vasireddi N, Hahamyan H, Gould H, et al. Athlete selective androgen receptor modulators abuse: a systematic review. *Am J Sports Med*. 2025;53:999–1009.
59. Vasireddi N, Hahamyan HA, Kumar Y, Ng MK, Voos JE, Calcei JG. Social media may cause emergent SARMs abuse by athletes: a content quality analysis of the most popular YouTube videos. *Phys Sportsmed*. 2023;51(2):175–182. doi: https://10.1080/00913847.2022.2108352.
60. Vukojević J, Siroglavić M, Kašnik K, et al. Rat inferior caval vein (ICV) ligature and particular new insights with the stable gastric pentadecapeptide BPC 157. *Vascul Pharmacol*. 2018;106:54–66.
61. Vukojević J, Vrdoljak B, Malekinušić D, et al. The effect of pentadecapeptide BPC 157 on hippocampal ischemia/reperfusion injuries in rats. *Brain Behav*. 2020;10(8):e01726. doi: https://10.1002/brb3.1726.

62. Vukusic D, Sever AZ, Sever M, et al. Duodenocolic fistula healing by pentadecapeptide bpc 157 in rats. A cytoprotection viewpoint. *J Physiol Pharmacol*. 2024;75:89–104.
63. WADA Science / MRPL Working Group. *Technical Document TD2022MRPLf65*; 2022. World Anti-Doping Agency (WADA).
64. WADA's 2022 Prohibited List Now in Force. World Anti-Doping Agency; 2022. Available at: https://www.wada-ama.org/en/news/wadas-2022-prohibited-list-now-force#:~:text=For%20the%20first%20time%2C%20a,re%2Devaluation%20of%20its%20status. Accessed June 5, 2024.
65. Wang X-Y, Qu M, Duan R, et al. Cytoprotective Mechanism of the Novel Gastric Peptide BPC157 in Gastrointestinal Tract and Cultured Enteric Neurons and Glial Cells. *Neurosci Bull*. 2019;35:167–170.
66. Wu H, Wei M, Li N, et al. Clopidogrel-Induced Gastric Injury in Rats is Attenuated by Stable Gastric Pentadecapeptide BPC 157. *Drug Devel Ther*. 2020;14:5599–5610.
67. Xu C, Sun L, Ren F, et al. Preclinical safety evaluation of body protective compound-157, a potential drug for treating various wounds. *Regul Toxicol Pharmacol*. 2020;114:104665.