

RESEARCH MONOGRAPH . COMPOUND PROFILE

Pentadeca Arginate

An arginine-salt formulation of the gastric pentadecapeptide BPC-157 (Body Protection Compound-157) developed to improve oral bioavailability and acid stability, retaining the parent peptide's pleiotropic cytoprotective, angiogenic, and tissue-regenerative pharmacology across gastrointestinal, musculoskeletal, and central nervous system research models.

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ABSTRACT

Pentadeca Arginate (PDA) is the arginate salt form of the stable gastric pentadecapeptide BPC-157 (Body Protection Compound-157, bepecin, PL 14736), a synthetic 15-amino-acid oligopeptide with the sequence Gly-Glu-Pro-Pro-Pro-Gly-Lys-Pro-Ala-Asp-Asp-Ala-Gly-Leu-Val and a molecular weight of 1419.55 daltons (free base). The parent peptide was first characterized by Sikiric and colleagues at the University of Zagreb in 1993 as a partial sequence of a protein isolated from human gastric juice, and it has since accumulated a preclinical literature of more than 100 peer-reviewed publications demonstrating cytoprotective, pro-angiogenic, anti-inflammatory, and tissue-regenerative activity across gastrointestinal, musculoskeletal, hepatic, cardiovascular, and central nervous system injury models. The arginate salt formulation replaces the conventional acetate counterion with L-arginine, producing two pharmacologically consequential changes: first, a marked improvement in structural stability under simulated gastric acid conditions (greater than 95 percent structural integrity after five hours of gastric acid exposure, compared to less than 2 percent for the acetate form); and second, a reported increase in oral bioavailability of approximately 7-fold relative to the acetate salt, attributed to the arginine shielding of the peptide backbone from enzymatic degradation and the concurrent delivery of L-arginine as a nitric oxide synthase substrate that complements the parent peptide's established nitric oxide system modulation. The pharmacology of Pentadeca Arginate is that of BPC-157, a pleiotropic cytoprotective agent whose principal characterized mechanisms include bidirectional modulation of nitric oxide production through the Akt-eNOS

signaling axis; upregulation of vascular endothelial growth factor receptor 2 (VEGFR2), epidermal growth factor receptor (EGFR), and growth hormone receptor expression; activation of extracellular signal-regulated kinase (ERK1/2) pathways driving fibroblast proliferation and collagen deposition; modulation of dopaminergic, serotonergic, and GABAergic neurotransmitter systems; and activation of early response gene cascades (Egr1, Akt1, Src, Nos3) within minutes of tissue injury. Preclinical pharmacokinetic characterization in rats and beagle dogs (Xu et al. 2022) demonstrated rapid absorption after intramuscular administration (Tmax approximately 3 minutes in rats, 6 to 9 minutes in dogs), a short plasma elimination half-life (approximately 15 minutes in rats, approximately 5 minutes in dogs), linear pharmacokinetics across studied dose ranges, and rapid metabolism to constituent amino acids through normal peptide degradation pathways. Human pharmacokinetic data remain extremely limited. Clinical evidence for BPC-157 in humans is confined to three pilot studies encompassing fewer than 30 total participants: a Phase I safety study in healthy volunteers (Veljaca et al. 2003), a Phase II enema study in ulcerative colitis (Ruenzi et al., unpublished full data), and recent intravenous safety studies (Lee and Burgess 2024, Lee et al. 2025) that reported no adverse events or clinically meaningful changes in cardiac, hepatic, renal, thyroid, or metabolic biomarkers at doses up to 20 mg. BPC-157 is not approved by any drug regulatory agency for human use. In September 2023, the United States Food and Drug Administration classified BPC-157 as a Category 2 bulk drug substance, prohibiting its use in compounding by 503A and 503B pharmacies. The World Anti-Doping Agency banned BPC-157 in 2022 under the S0 category of non-exempt substances. Pentadeca Arginate emerged in the

clinical and compounding pharmacy market as an alternative formulation following the FDA Category 2 classification, leveraging the arginate salt distinction. This monograph reviews the chemistry, synthesis, and salt-form pharmacology of Pentadeca Arginate; the comprehensive preclinical pharmacology of the parent BPC-157 peptide across gastrointestinal, musculoskeletal, vascular, and central nervous system models; the limited human clinical evidence; sourcing and quality considerations; reconstitution and handling; stack-interaction implications; the adverse-event and safety profile; and a comparative assessment of five tissue-regenerative peptide candidates against Pentadeca Arginate on five competency standards.

1. Compound Identification

1.1 Names, synonyms, and registry identifiers

Common name: Pentadeca Arginate (PDA).

Parent compound name: BPC-157 (Body Protection Compound-157); also designated bepecin, gastric pentadecapeptide BPC 157, and stable gastric pentadecapeptide BPC 157.

Development codes: PL 14736, PL-10, PLD-116 (Pliva, Croatia). The development codes are the identifiers under which BPC-157 entered clinical trials for inflammatory bowel disease conducted by Pliva (later acquired by Barr Pharmaceuticals and subsequently Teva Pharmaceutical Industries) [1].

Chemical Abstracts Service registry number: 137525-51-0 (BPC-157 free base). The arginate salt does not carry a separate CAS registry number in the public domain as of the monograph date.

PubChem compound identifier: 9941957.

DrugBank identifier: DB11882.

Amino acid sequence: Gly-Glu-Pro-Pro-Pro-Gly-Lys-Pro-Ala-Asp-Asp-Ala-Gly-Leu-Val (single-letter code: GEPPPGKPADDAGLV). The peptide is a 15-residue oligopeptide (pentadecapeptide) derived from a partial sequence of a protein identified in human gastric juice [2].

1.2 Structural class and chemistry

Pentadeca Arginate is a salt-form variant of BPC-157, a linear, non-glycosylated pentadecapeptide belonging to the class of gastric cytoprotective peptides. The parent peptide is structurally characterized by a triple-proline motif (Pro-Pro-Pro) at positions 3 through 5, which confers conformational rigidity to the peptide backbone and contributes to the unusual resistance of BPC-157 to enzymatic degradation in gastric juice [3].

Molecular formula (free base): C₆₂H₉₈N₁₆O₂₂.

Molecular weight (free base): 1419.55 g/mol (monoisotopic).

Salt form: The arginate salt pairs the BPC-157 peptide with L-arginine (C₆H₁₄N₄O₂, molecular weight 174.20 g/mol) as the counterion, replacing the acetate counterion (C₂H₄O₂, molecular weight 60.05 g/mol) used in the conventional BPC-157 acetate preparation. The stoichiometry of the salt pairing has not been fully characterized in the public literature; commercial preparations are typically described as a 1:1 molar complex.

Physical properties: White to off-white lyophilized powder. Freely soluble in water and aqueous buffers. The peptide demonstrates unusual stability in human gastric juice, remaining structurally intact for greater than 24 hours in the free base and acetate forms [3]. The arginate form maintains greater than 95 percent structural integrity after five hours of exposure to simulated gastric fluid (pH 1.2, 37 degrees Celsius), compared to less than 2 percent retention for the acetate form under identical conditions [4].

Stereochemistry: All amino acid residues are in the L-configuration. The peptide contains no disulfide bonds, no post-translational modifications, and no non-standard amino acids.

1.3 Synthesis

BPC-157 is produced by solid-phase peptide synthesis using standard Fmoc (9-fluorenylmethoxycarbonyl) chemistry on a resin support [5]. The synthesis proceeds by sequential coupling of protected amino acids in the C-to-N direction (Val-Leu-Gly-Ala-Asp-Asp-Ala-Pro-Lys-Gly-Pro-Pro-Pro-Glu-Gly), with side-chain protecting groups removed during the final cleavage step using trifluoroacetic acid. The crude peptide is purified by reverse-phase high-performance liquid chromatography (RP-HPLC) and lyophilized. The arginate salt is prepared by dissolving the purified free-base peptide and equimolar L-arginine in aqueous solution, followed by lyophilization of the resulting salt complex. The acetate-to-arginate salt conversion can also be accomplished by ion-exchange chromatography or dialysis followed by co-lyophilization with L-arginine. Commercial preparations are supplied at greater than 98 percent purity by HPLC, with identity confirmed by mass spectrometry (expected [M+H]⁺ of 1420.56 for the protonated free base).

2. Abstract

Pentadeca Arginate (PDA) is the arginate salt of BPC-157 (Body Protection Compound-157, bepecin, PL 14736), a synthetic pentadecapeptide derived from a protein fraction of human gastric juice. The parent compound was first described by Sikiric et al. in 1993 at the University of Zagreb and has been the subject of more than 100 preclinical publications demonstrating cytoprotective, pro-angiogenic, anti-inflammatory, and tissue-regenerative effects in models spanning the gastrointestinal tract, musculoskeletal system, vascular system, liver, kidney, and central nervous system [2, 6].

The principal pharmacological distinction of the arginate salt form is improved oral bioavailability and gastric acid stability relative to the conventional acetate salt [4]. The L-arginine counterion is reported to shield the peptide backbone from proteolytic degradation in the stomach and to deliver supplementary substrate for nitric oxide synthase, complementing the parent peptide's established bidirectional modulation of the nitric oxide system [7, 8].

BPC-157 operates through multiple overlapping mechanisms. The most extensively characterized is the modulation of the nitric oxide system through the Akt-eNOS signaling axis, producing context-dependent effects: in conditions of nitric oxide deficiency (ischemia, NOS blockade), BPC-157 increases nitric oxide bioavailability and restores tissue perfusion; in conditions of pathological nitric oxide excess (endotoxemia, L-arginine overdose), BPC-157 reduces overproduction [7, 8]. The peptide upregulates VEGFR2 expression in vascular endothelial cells, promoting angiogenesis independently of VEGF-A ligand concentration [9]. Additional characterized mechanisms include upregulation of growth hormone receptor expression in tendon fibroblasts [10], activation of ERK1/2 signaling driving fibroblast proliferation and collagen deposition [11], early response gene activation (Egr1, Akt1, Src, Nos3) within minutes of tissue injury [12], and modulation of dopaminergic, serotonergic, and GABAergic neurotransmitter systems in the central nervous system [13].

Preclinical pharmacokinetics in rats and beagle dogs demonstrate rapid absorption (Tmax approximately 3 minutes intramuscularly in rats), short elimination half-life (approximately 15 minutes in rats, approximately 5 minutes in dogs), lin-

ear dose-proportional pharmacokinetics, absolute intramuscular bioavailability of approximately 15 to 19 percent in rats and 45 to 51 percent in dogs, and rapid metabolism to constituent amino acids [14]. Oral bioavailability of the acetate form is reported as very low (less than 3 percent); the arginate form is reported to achieve substantially higher oral bioavailability, though these claims are based on formulation comparisons rather than published peer-reviewed pharmacokinetic studies [4].

Human clinical data are extremely limited. Across all published human studies (fewer than 30 total participants), no adverse events have been reported [15, 16, 17]. BPC-157 is not approved by any drug regulatory agency for human use. The FDA classified BPC-157 as a Category 2 bulk drug substance in September 2023, and the World Anti-Doping Agency banned the compound in 2022 [18, 19]. The vast majority of the BPC-157 literature originates from a single research group at the University of Zagreb, and independent replication of key findings remains limited [20].

This monograph reviews the chemistry and salt-form properties of Pentadeca Arginate; the comprehensive preclinical pharmacology of BPC-157; the limited clinical evidence; pharmacokinetics; reconstitution and sourcing considerations; stack interactions; the safety profile; and a structured comparative assessment of five tissue-regenerative peptide candidates against Pentadeca Arginate.

3. Discovery and Development History

3.1 Origin

BPC-157 was first identified and characterized by Professor Predrag Sikiric and his research group at the Department of Pharmacology, University of Zagreb School of Medicine, Croatia, in the early 1990s [2]. The discovery originated from research into the protective proteins naturally present in human gastric juice, which maintain mucosal integrity against endogenous acid, pepsin, and exogenous noxious agents. The researchers isolated a specific 15-amino-acid sequence from the larger Body Protection Compound protein and determined that this fragment retained potent cytoprotective activity in gastric ulcer models when administered systemically or locally at doses in the microgram-per-kilogram and nanogram-per-kilogram ranges.

3.2 Early preclinical development

The initial publications from the Sikiric laboratory focused on gastric cytoprotection: BPC-157 protected against ethanol-induced, NSAID-induced, and stress-induced gastric mucosal lesions in rat models at intraperitoneal doses of 10 micrograms per kilogram, 10 nanograms per kilogram, and 10 picograms per kilogram, with efficacy across several orders of magnitude of dose [6, 21]. The compound was positioned within the Robert cytoprotection paradigm (the concept that prostaglandin-independent mechanisms can protect gastric mucosa against diverse noxious stimuli) and was characterized as extending this paradigm to organoprotection: protection of tissues beyond the stomach, including liver, pancreas, heart, and vascular endothelium [22].

3.3 Clinical development under Pliva

Pliva, a Croatian pharmaceutical company, licensed BPC-157 for clinical development under the designations PL-10, PLD-116, and PL 14736. Pliva conducted a Phase I safety study in healthy volunteers, presented by Veljaca et al. (2003) at Digestive Disease Week and published as a conference abstract in *Gut*, which demonstrated safety and tolerability [15]. A subsequent Phase II multicenter, randomized, double-

blind, placebo-controlled study of PL 14736 administered as an enema in mild-to-moderate ulcerative colitis was conducted by Ruenzi et al. [23]. The full results of this Phase II trial have not been published in a standalone peer-reviewed paper, and independent evaluation of the efficacy and safety data remains limited. Pliva was acquired by Barr Pharmaceuticals in 2006 and subsequently by Teva Pharmaceutical Industries in 2008; the BPC-157 clinical development program did not advance beyond Phase II under subsequent ownership.

3.4 Expansion of the preclinical literature

From the mid-1990s through the present, the Sikiric laboratory and collaborators expanded the preclinical characterization of BPC-157 to encompass tendon healing (Chang et al. 2010, Staresinic et al. 2003), ligament repair, muscle regeneration, bone healing, liver protection against hepatotoxins, pancreatic injury, vascular occlusion and ischemia-reperfusion injury, traumatic brain injury, spinal cord compression, dopaminergic and serotonergic neurotransmitter modulation, and alcohol and drug withdrawal models [6, 13, 24, 25]. The compound has been studied in over 100 peer-reviewed publications, the overwhelming majority originating from the University of Zagreb group.

3.5 Emergence of the arginate salt form

The arginate salt formulation of BPC-157 (Pentadeca Arginate) emerged in the compounding pharmacy and clinical wellness market following the FDA's September 2023 classification of BPC-157 as a Category 2 bulk drug substance, which prohibited compounding pharmacies from preparing BPC-157 for patient use [18]. The arginate salt was positioned as a distinct formulation with improved oral bioavailability and stability, leveraging the salt-form distinction from the acetate preparation that was the subject of the FDA classification. The regulatory status of Pentadeca Arginate remains uncertain; the FDA has not issued a separate classification for the arginate salt form, and the compound remains unapproved for human use by any drug regulatory agency.

3.6 WADA prohibition

The World Anti-Doping Agency added BPC-157 to the Prohibited List in January 2022 under the S0 category (non-approved substances), citing the absence of regulatory approval for human use and the potential for performance-enhancing effects

through tissue repair mechanisms [19]. The prohibition applies to all salt forms of BPC-157, including the arginate variant.

4. Mechanism of Action

Pentadeca Arginate is a multi-mechanism cytoprotective and tissue-regenerative agent. The pharmacological activity is that of the parent peptide BPC-157, with the additional contribution of L-arginine as a nitric oxide synthase substrate delivered by the arginate counterion. The principal characterized mechanisms are summarized below.

4.1 Nitric oxide system modulation

The nitric oxide (NO) system interaction is the most extensively characterized mechanism of BPC-157 and the mechanistic axis most directly complemented by the arginate salt formulation. BPC-157 demonstrates bidirectional modulation of NO production: in states of NO deficiency (ischemia, L-NAME-induced NOS blockade), BPC-157 increases NO bioavailability by activating the Akt-endothelial nitric oxide synthase (eNOS) pathway, restoring blood flow and protecting against ischemic tissue damage [7, 8]. In states of pathological NO excess (L-arginine overdose, endotoxemia-driven iNOS overexpression), BPC-157 reduces NO overproduction and prevents the resulting hypotension and cytotoxicity [7].

The bidirectional modulation operates through the Src kinase-caveolin-1 signaling axis, which regulates eNOS localization and activity in vascular endothelium. BPC-157 enhances eNOS activity through this pathway while simultaneously upregulating heme oxygenase-1 (HO-1), reducing oxidative stress and preventing mitochondrial dysfunction [8]. The L-arginine delivered by the arginate counterion provides additional substrate for NOS, potentially amplifying the eNOS-dependent component of the mechanism under conditions where arginine availability is rate-limiting.

4.2 Angiogenesis and growth factor receptor modulation

BPC-157 is a potent pro-angiogenic agent in preclinical models. The principal angiogenic mechanism is upregulation of VEGFR2 (vascular endothelial growth factor receptor 2) expression at both mRNA and protein levels in vascular endothelial cells

[9]. This upregulation occurs independently of changes in VEGF-A ligand concentration, distinguishing BPC-157 from exogenous VEGF administration and suggesting a receptor-sensitization mechanism rather than a ligand-delivery mechanism.

Additional growth factor receptor modulation includes upregulation of epidermal growth factor receptor (EGFR) in intestinal epithelium [26], upregulation of growth hormone receptor expression in tendon fibroblasts with concurrent enhancement of JAK2 phosphorylation (beginning at 100 nanomolar concentration) [10], and modulation of fibroblast growth factor (FGF) and hepatocyte growth factor (HGF) signaling in wound healing models [9].

4.3 ERK1/2 signaling and collagen metabolism

In fibroblast and wound healing models, BPC-157 activates the extracellular signal-regulated kinase (ERK1/2) pathway, driving fibroblast proliferation, migration, and collagen deposition [11]. Huang et al. (2015) demonstrated that BPC-157 promoted faster granulation tissue formation, re-epithelialization, dermal remodeling, and collagen deposition through ERK1/2 signaling in a rat skin wound model. The compound also increased human umbilical vein endothelial cell (HUVEC) proliferation and migration and upregulated VEGF-a expression in these cells [11].

4.4 Early response gene activation

Gene expression studies following tissue injury demonstrate that BPC-157 activates cascades of early response genes within minutes of administration. Vukojevic et al. (2018) identified the following sequential gene activation pattern in wound models: at 2 minutes, upregulation of Akt1, Grb2, Nos3, Pik3cd, Prkcg, Ptk2, and Src; at 5 minutes, upregulation of Braf, Egfr, Egr1, Hdac7, Mapk1, Mapk3, Mapk14, Plcg1, Srf, and Vegfa; and at 10 minutes, upregulation of Kras [12]. Following hippocampal ischemia-reperfusion injury, BPC-157 treatment upregulated Egr1, Akt1, Kras, Src, Foxo, Srf, Vegfr2, Nos3, and Nos1 while suppressing pro-inflammatory genes [27].

4.5 Neurotransmitter system modulation

BPC-157 interacts with multiple central neurotransmitter systems, as characterized in the comprehensive review by Sikiric et al. (2021) [13].

In the dopaminergic system, BPC-157 counteracts the consequences of nigrostriatal neuronal damage, dopamine vesicle depletion (reserpine model), and dopamine receptor blockade (haloperidol model). The compound demonstrates beneficial effects even after complete dopamine blockade produced by combined reserpine and haloperidol treatment [13].

In the serotonergic system, BPC-157 induces the release of serotonin in specific brain nigrostriatal regions and produces antidepressant effects in the Porsolt forced swim test and in chronic unpredictable stress depression models. The compound also counteracts serotonin syndrome symptoms [13].

In the GABAergic system, BPC-157 counteracts diazepam-induced tolerance and withdrawal and accelerates the return to homeostasis after perturbation of GABA-mediated inhibitory tone [13].

4.6 Cytoprotection and organoprotection

The foundational mechanism of BPC-157 is gastric cytoprotection: the maintenance of gastric mucosal integrity against diverse noxious agents including ethanol, NSAIDs, and stress [22]. The compound fully counteracts NSAID-induced gastric and intestinal lesions in rodent models, consistent with the prostaglandin-independent cytoprotection paradigm originally described by Robert [22]. This cytoprotective activity extends to organoprotection in liver (hepatotoxin models), pancreas (cerulein pancreatitis), heart (doxorubicin cardiotoxicity), and kidney (nephrotoxin models), suggesting a generalizable tissue-protective mechanism that is not organ-specific [6, 22].

5. Pharmacokinetics and Routes of Administration

5.1 Absorption

Pharmacokinetic characterization of BPC-157 has been conducted in rats and beagle dogs by Xu et al. (2022) [14]. After intramuscular administration in rats at doses of 20, 100, and 500 micrograms per kilogram, plasma BPC-157 reached peak concentrations rapidly: T_{max} was approximately 3 minutes at all three doses. Peak concentrations (C_{max}) were 12.3 nanograms per milliliter at 20 micrograms per kilogram, 48.9 nanograms per milliliter at 100 micrograms per kilogram, and 141 nanograms per milliliter at 500 micrograms per kilogram, demonstrating dose-proportional exposure.

In beagle dogs, after intramuscular administration at 6, 30, and 150 micrograms per kilogram, T_{max} was 6.3, 8.7, and 8.2 minutes respectively, with C_{max} values of 1.05, 3.30, and 26.1 nanograms per milliliter [14].

Oral bioavailability of BPC-157 in the acetate salt form is reported as very low (less than 3 percent), reflecting extensive first-pass degradation by gastric and intestinal peptidases. The arginate salt form is reported to achieve substantially higher oral bioavailability (estimated at approximately 7-fold greater than acetate), attributed to the arginine shielding of the peptide backbone from enzymatic degradation in the gastric environment [4]. These bioavailability claims for the arginate form are based on formulation comparisons and commercial data rather than published peer-reviewed pharmacokinetic studies; investigators should treat the reported improvement as preliminary.

5.2 Distribution

Volume of distribution after intravenous administration in rats was 36.4 milliliters per kilogram, indicating predominantly vascular and extracellular distribution with limited tissue partitioning [14]. This is consistent with the hydrophilic character of the peptide. Distribution studies using tritium-labeled [3H]BPC-157 demonstrated uptake in gastrointestinal tissues, liver, and kidney, with lower concentra-

tions in brain tissue [14]. Central nervous system effects observed in behavioral models therefore likely reflect either direct CNS penetration at functionally relevant concentrations or peripheral-to-central signaling through the vagal nerve and the brain-gut axis.

5.3 Metabolism

BPC-157 is rapidly metabolized through normal peptide degradation pathways. Tritium-labeled [3H]BPC-157 was converted to small peptide fragments and ultimately to single amino acids that entered normal amino acid metabolism. The primary radiolabeled metabolite in plasma was [3H]proline, representing 86.65 percent of plasma radioactivity at one hour post-dose [14]. This rapid and complete degradation to endogenous amino acids is pharmacologically favorable from a toxicological perspective, as no novel or persistent metabolites are generated.

5.4 Elimination

After intravenous administration in rats, the plasma elimination half-life was approximately 15.2 minutes. In beagle dogs, the intravenous half-life was approximately 5.3 minutes [14]. These values are consistent with the characteristics of general peptide drugs. Clearance in rats was 50.1 milliliters per minute per kilogram.

Excretion over 72 hours after radiolabeled administration in rats was predominantly renal: approximately 15.9 percent of the administered dose was recovered in urine and approximately 2.3 percent in feces [14]. Biliary excretion accounted for approximately 9.1 percent. The remainder was presumed to enter the endogenous amino acid pool through complete peptide degradation.

Repeated intramuscular dosing at 100 micrograms per kilogram daily for 7 days in rats produced similar pharmacokinetic profiles to single-dose administration, with slight increases in C_{max} and AUC, indicating minimal accumulation [14].

5.5 Routes of administration

Subcutaneous injection: The most common research and clinical-practice route for BPC-157 and Pentadeca Arginate. Typical investigational doses in human practice range from 200 to 500 micrograms per injection, administered once or twice daily.

Subcutaneous pharmacokinetics have not been formally characterized in published studies but are expected to approximate the intramuscular profile with slightly delayed Tmax.

Intramuscular injection: Formally characterized in rats and dogs [14]. Produces rapid absorption with Tmax of 3 to 9 minutes.

Oral administration: The arginate salt form is specifically designed for oral delivery, with capsule formulations typically containing 500 micrograms. The improved acid stability (greater than 95 percent retention at 5 hours in simulated gastric fluid) supports oral bioavailability superior to the acetate form [4].

Intravenous administration: Used in the Lee and Burgess (2024) and Lee et al. (2025) pilot safety studies at doses up to 20 milligrams, with no adverse events reported [16, 17].

Topical application: BPC-157 has been applied topically as a cream (1 microgram per gram) in preclinical burn and wound models with demonstrated efficacy [28].

5.6 Special populations

No human pharmacokinetic data in special populations (renal impairment, hepatic impairment, pediatric, geriatric) are available. The rapid metabolism to endogenous amino acids suggests that accumulation in renal or hepatic impairment is unlikely, but this has not been confirmed experimentally.

6. Preclinical Pharmacology

6.1 Gastrointestinal cytoprotection

Gastrointestinal protection is the foundational and most extensively documented preclinical application of BPC-157. The compound has demonstrated consistent efficacy across all studied models of acute and chronic gastrointestinal injury [6, 22].

In the ethanol-induced gastric ulcer model, BPC-157 at intraperitoneal doses of 10 micrograms per kilogram, 10 nanograms per kilogram, and 10 picograms per kilogram produced significant protection against mucosal lesions, with efficacy preserved across several orders of magnitude of dose [21]. In the NSAID-induced gastric and intestinal lesion model, BPC-157 fully counteracted indomethacin-induced damage, stabilized intestinal permeability, and enhanced cytoprotection [29]. In chronic alcohol administration models, BPC-157 prevented, attenuated, and reversed gastric lesion appearance, with efficacy comparable to ranitidine and propranolol [30].

The fistula healing literature provides additional evidence of gastrointestinal regenerative capacity: BPC-157 successfully healed colocutaneous fistulas (Klicek et al. 2008), gastrocutaneous fistulas (Skorjanec et al. 2009), esophagocutaneous fistulas (Cesarec et al. 2013), duodenocutaneous fistulas (Skorjanec et al. 2015), and rectovaginal fistulas (Baric et al. 2016) in rat models, with the NO system implicated in the healing mechanism across all fistula types [12].

6.2 Musculoskeletal healing

BPC-157 accelerates healing of tendons, ligaments, muscles, and bone in preclinical models. Chang et al. (2010) demonstrated that BPC-157 promoted tendon outgrowth, cell survival, and cell migration in a rat Achilles tendon injury model, with the effect involving enhanced tendon explant outgrowth and increased cell survival in culture [24]. Staresinic et al. (2003) reported acceleration of Achilles tendon healing in rats with BPC-157 treatment. The peptide upregulates growth hormone receptor expression in tendon fibroblasts with concurrent activation of JAK2 phosphorylation, suggesting that BPC-157 sensitizes tendon tissue to circulating growth hormone [10].

In ligament injury models, BPC-157 promoted superior healing of damaged medial collateral ligaments in rat knee joints, with improved collagen organization and mechanical strength [25]. Bone healing studies demonstrated acceleration of fracture repair in rabbit radial osteotomy models.

6.3 Vascular and ischemia-reperfusion protection

BPC-157 demonstrates protective effects in models of major vessel occlusion, ischemia-reperfusion injury, and thrombotic vascular events. Vukojevic et al. (2018) showed that following inferior caval vein ligation in rats, BPC-157 rapidly recruited collateral vascular pathways (left ovarian vein as a major bypass), redistributed trapped blood volume, and maintained continuous therapeutic effect [12]. The compound has also been studied in Pringle maneuver ischemia-reperfusion models and Budd-Chiari syndrome models with positive outcomes [31].

6.4 Neuroprotection and brain injury

Tudor et al. (2010) demonstrated that BPC-157 markedly attenuated brain damage induced by traumatic brain injury in mice, with improved early outcome and minimal postponed mortality throughout the 24-hour post-injury period [32]. In rat spinal cord compression models, a single intraperitoneal injection of BPC-157 administered 10 minutes post-injury counteracted tail paralysis, axonal and neuronal necrosis, demyelination, and cyst formation, with functional recovery persisting in both short-term and long-term assessments (Perovic et al. 2019) [33].

In hippocampal ischemia-reperfusion injury models, BPC-157 treatment led to upregulation of neuroprotective genes (Egr1, Akt1, Kras, Src, Foxo, Srf, Vegfr2, Nos3, Nos1) and suppression of pro-inflammatory gene expression [27].

6.5 Hepatoprotection

BPC-157 has demonstrated protective effects against multiple hepatotoxins in rat models, including protection against carbon tetrachloride-induced liver damage, paracetamol overdose, and alcohol-induced hepatotoxicity. The hepatoprotective mechanism involves maintenance of hepatocyte membrane integrity, reduction of oxidative stress through HO-1 upregulation, and support of hepatic vascular perfusion through the NO system [6].

6.6 Hemostasis modulation

Stupnisek et al. (2012, 2015) demonstrated that BPC-157 influences all four major events in hemostasis: vessel constriction, primary platelet plug formation, secondary fibrin plug formation, and clot resolution [34]. The compound accomplished this modulation without affecting standard clotting parameters (prothrombin time, activated partial thromboplastin time), suggesting a vascular-endothelial rather than coagulation-cascade mechanism.

7. Clinical Evidence Base

7.1 Phase I healthy volunteer study

Veljaca et al. (2003) conducted a Phase I safety study of BPC-157 (designated PL 14736) in healthy volunteers under the sponsorship of Pliva [15]. The study was presented at Digestive Disease Week and published as a conference abstract in Gut. The compound was reported as safe and well tolerated. Full data from this study have not been published in a standalone peer-reviewed paper.

7.2 Phase II ulcerative colitis study

Ruenzi et al. conducted a multicenter, randomized, double-blind, placebo-controlled Phase II study of PL 14736 administered as an enema in mild-to-moderate ulcerative colitis [23]. The study reportedly demonstrated efficacy with no toxicity; however, the full results have not been published in a standalone clinical paper, and independent evaluation of the data is not possible from the available literature. Multiple subsequent publications from the Sikiric group reference this trial as evidence supporting clinical translation, but the absence of complete published data is a significant limitation [20].

7.3 Intra-articular injection pilot study

Lee and Padgett (2021) conducted a pilot study of intra-articular BPC-157 injection for knee pain, representing one of the few published direct human applications of the compound [35]. The study was small and exploratory in design.

7.4 Intravenous safety studies

Lee and Burgess (2024) conducted a pilot study involving two healthy adults who received intravenous BPC-157 infusions at doses up to 20 milligrams [16]. The treatment was well tolerated with no adverse events or clinically meaningful changes observed in vital signs, electrocardiograms, or laboratory biomarkers assessing cardiac, hepatic, renal, thyroid, or metabolic function.

A subsequent intravenous safety study (Lee et al. 2025) confirmed the absence of measurable effects on tested biomarkers of heart, liver, kidney, thyroid, or blood glucose function, with the BPC-157 peptide infusion tolerated with no side effects reported [17].

7.5 Limitations of the clinical evidence

The clinical evidence base for BPC-157 and Pentadeca Arginate is severely limited. Across all published human studies, fewer than 30 total participants have been studied [20]. No Phase III registration trial has been completed for any indication. The overwhelming concentration of the preclinical literature within a single research group (the Sikiric laboratory at the University of Zagreb) is both a strength (deep institutional expertise and consistent methodology) and a significant limitation (minimal independent replication) [20]. Pharmaceutical regulatory agencies and the broader scientific community place substantial weight on independent verification of preclinical findings, which has been minimal for BPC-157.

8. Sourcing and Quality Verification

Pentadeca Arginate is not available as a pharmaceutical-grade registered medicine in any jurisdiction. The compound is supplied by compounding pharmacies, peptide research suppliers, and direct-to-consumer peptide vendors.

Compounding pharmacy sources: Following the FDA Category 2 classification of BPC-157 in September 2023, some compounding pharmacies have offered Pentadeca Arginate (the arginate salt) as a distinct preparation. The regulatory basis for this distinction has not been formally adjudicated by the FDA, and investigators should be aware that the regulatory status may change [18].

Research-grade suppliers: Multiple peptide synthesis companies (GenScript, CPC Scientific, American Peptide, GL Biochem, and others) supply BPC-157 free base and acetate salt at greater than 98 percent purity. Arginate salt preparations are available from selected suppliers. Pricing is moderate for research quantities (milligram to gram scale).

Quality verification: Investigators should confirm compound identity and purity on every lot through:

- Reverse-phase HPLC purity analysis (target greater than 98 percent)
- Mass spectrometry confirmation of molecular weight (expected $[M+H]^+$ of 1420.56 for the protonated free base)
- Amino acid analysis to confirm the 15-residue sequence
- Endotoxin testing (limulus amebocyte lysate assay) for parenteral preparations
- Residual solvent analysis by gas chromatography
- Counterion confirmation (arginine content by ion chromatography or amino acid analysis) for the arginate salt form

Third-party analytical testing is strongly recommended for peptide preparations obtained from direct-to-consumer vendors, where quality control standards may be variable. Peptide purity, sequence fidelity, and counterion identity are the critical

quality attributes. The research-grade peptide market for BPC-157 is well established, but the arginate salt is less widely available than the acetate form, and on-receipt verification is particularly important for this preparation.

9. Reconstitution and Handling

Pentadeca Arginate is typically supplied as a sterile lyophilized powder in single-use vials. The lyophilized material is white to off-white in appearance.

Reconstitution for injection: Reconstitute with bacteriostatic water for injection (0.9 percent benzyl alcohol preserved) or sterile water for injection. Typical reconstitution volumes are 2 to 3 milliliters per vial for subcutaneous injection preparations, or up to 7.5 milliliters for larger vial presentations. Direct the diluent stream against the glass wall of the vial rather than directly onto the lyophilized pellet. Swirl gently; do not shake vigorously, as peptide solutions may foam and adsorb to the air-liquid interface.

Storage of reconstituted solution: Refrigerate at 2 to 8 degrees Celsius. Solutions reconstituted with bacteriostatic water may be stored for up to 28 days at refrigerated conditions. Solutions reconstituted with sterile water (preservative-free) should be used within 24 hours. Protect from light as a reasonable precaution, although BPC-157 is not characterized as highly photosensitive.

Storage of lyophilized material: Store at 2 to 8 degrees Celsius for long-term stability. The lyophilized peptide is stable at room temperature for limited periods (days to weeks) but refrigerated storage is recommended. Freezer storage (minus 20 degrees Celsius) is appropriate for long-term archival of stock material.

Oral capsule preparations: Pentadeca Arginate oral capsules (typically 500 micrograms per capsule) are stored at room temperature in a cool, dry location. The improved gastric acid stability of the arginate form supports oral delivery without enteric coating.

Compatibility: Aqueous BPC-157 solutions are compatible with standard laboratory plasticware (polypropylene, polystyrene) and with glass. Peptide adsorption to container surfaces is modest at the concentrations used in research preparations (micrograms per milliliter range) but may be relevant at very low concentrations; siliconized or low-binding containers are appropriate for dilute solutions.

Aliquoting: Single-use aliquoting of reconstituted stock solution is recommended to minimize freeze-thaw cycling and potential microbial contamination from repeated vial access. The peptide tolerates at least 5 freeze-thaw cycles without measurable potency loss.

10. Stack Interactions and Combinations

Pentadeca Arginate is frequently used in combination with other peptide and non-peptide agents in investigational and clinical-practice contexts. The following interaction considerations are relevant.

Thymosin Beta-4 (TB-500): The combination of BPC-157 and TB-500 is the most commonly reported peptide combination in tissue-regenerative applications. The two peptides operate through complementary mechanisms: BPC-157 promotes angiogenesis through VEGFR2 upregulation and NO system modulation, while TB-500 promotes cell migration through actin polymerization modulation [36]. The combination is reported to produce synergistic tissue repair outcomes in anecdotal clinical practice, though no controlled preclinical or clinical study has formally characterized the combination pharmacology.

GHK-Cu (Copper tripeptide): GHK-Cu promotes collagen synthesis and extracellular matrix remodeling through copper-dependent activation of fibroblast transcriptional programs [37]. Combination with Pentadeca Arginate is reported in dermatological and wound-healing applications. No pharmacokinetic interaction is expected, as GHK-Cu operates through metal-ion-dependent mechanisms distinct from the BPC-157 pathways.

KPV (Lysine-Proline-Valine tripeptide): KPV is an anti-inflammatory tripeptide derived from alpha-melanocyte-stimulating hormone. Combination with Pentadeca Arginate targets both regenerative (BPC-157) and anti-inflammatory (KPV) axes of tissue repair. No formal interaction data are available.

L-Arginine supplementation: The arginate counterion delivers L-arginine alongside the peptide, and concurrent oral L-arginine supplementation is pharmacologically redundant for the NOS substrate effect. High-dose L-arginine (greater than 10 grams per day) may shift the NO system balance toward overproduction, which could theoretically attenuate the bidirectional NO modulation that characterizes BPC-157 pharmacology [7].

NSAIDs: BPC-157 counteracts NSAID-induced gastrointestinal damage in preclinical models [29]. Concurrent use in clinical practice is common and is mechanistically coherent (BPC-157 protecting the gastric mucosa against NSAID toxicity). No adverse pharmacokinetic interaction is expected.

Growth hormone and growth hormone secretagogues: BPC-157 upregulates growth hormone receptor expression in tendon fibroblasts [10]. Concurrent growth hormone or growth hormone releasing peptide administration (CJC-1295, ipamorelin, tesamorelin) may produce additive or synergistic effects on musculoskeletal tissue repair through receptor sensitization. This combination has not been formally studied.

Proton pump inhibitors: BPC-157's gastric cytoprotective mechanism operates independently of gastric acid suppression. Concurrent proton pump inhibitor use is not expected to interfere with peptide activity and may improve oral bioavailability by reducing acid-mediated degradation (though the arginate form already provides substantial acid protection).

11. Adverse Events and Safety

11.1 Preclinical safety

The preclinical safety profile of BPC-157 is notable for the absence of reported toxicity across a broad dose range. In the comprehensive preclinical pharmacokinetic and safety evaluation by Xu et al. (2022), BPC-157 demonstrated no toxicity at doses tested in rats and dogs [14]. The compound has been administered at doses spanning several orders of magnitude (10 picograms per kilogram to 500 micrograms per kilogram) in hundreds of preclinical studies without reported organ toxicity, mutagenicity, or teratogenicity [6].

The LD50 (lethal dose in 50 percent of subjects) has not been determined, as lethal doses have not been reached in toxicology studies. The compound is described as having "no lethal dose" in the BPC-157 literature, though this characterization is limited by the dose ranges actually tested [6].

11.2 Human safety data

Across all published human studies (fewer than 30 total participants), no adverse events have been reported [15, 16, 17, 35]. The Lee and Burgess (2024) intravenous safety study at doses up to 20 milligrams (a dose approximately 40-fold higher than typical subcutaneous investigational doses) reported no clinically meaningful changes in vital signs, electrocardiograms, or laboratory biomarkers of cardiac, hepatic, renal, thyroid, or metabolic function [16].

11.3 Theoretical safety considerations

The FDA's September 2023 Category 2 classification cited three principal safety concerns: potential immunogenicity (the risk that a synthetic peptide may provoke immune responses with repeated administration), manufacturing impurities (the characterization challenges inherent in peptide synthesis), and the absence of adequate human safety data [18].

Immunogenicity: BPC-157 is a 15-amino-acid peptide with a molecular weight of 1419 daltons, below the conventional threshold for immunogenic proteins (typically greater than 5000 daltons). The risk of anti-drug antibody formation is theoretically low but has not been formally assessed in chronic-exposure human studies.

Peptide impurities: Solid-phase peptide synthesis can produce deletion sequences, truncation products, and racemized residues that co-purify with the target peptide. These impurities may have unpredictable biological activity. The quality verification protocols described in Section 8 are designed to mitigate this risk.

Tumorigenic potential: BPC-157 promotes angiogenesis and cell proliferation through VEGFR2, EGFR, and ERK1/2 activation. The theoretical concern that pro-angiogenic and pro-proliferative agents may promote tumor growth or vascularization has not been formally addressed in long-term carcinogenicity studies. This concern is shared with other pro-angiogenic growth factors and peptides and is not specific to BPC-157.

11.4 Regulatory prohibitions

BPC-157 (all salt forms) is classified as a Category 2 bulk drug substance by the FDA, prohibited from compounding by 503A and 503B pharmacies [18]. The compound is banned by the World Anti-Doping Agency under the S0 category [19]. It is controlled as a prescription-only substance in Australia and New Zealand, though no legitimate prescription pathway exists in these jurisdictions [19]. Investigators and practitioners should consult current regulatory guidance in their jurisdiction before any research or clinical application.

12. Comparative Assessment

This section presents a structured comparative assessment of five tissue-regenerative peptide candidates against Pentadeca Arginate, evaluated on five competency standards: novelty, effect size, promising potential (current clinical trajectory), side-effect profile (clinical or preclinical), and overall validation. The five comparators were selected as the principal tissue-regenerative peptides with substantive preclinical or clinical pharmacology programs that overlap with the Pentadeca Arginate research-clinical positioning.

12.1 Thymosin Beta-4 (TB-500)

Mechanism: Thymosin beta-4 is a 43-amino-acid peptide that binds G-actin monomers and modulates actin polymerization, promoting cell migration, wound healing, and anti-inflammatory activity. The peptide is expressed endogenously in most cell types and is released at sites of tissue injury [36].

Development trajectory: Thymosin beta-4 (as the commercial preparation RGN-259 and Tβ4) has been studied in clinical trials for dry eye disease, neurotrophic keratopathy, cardiac repair following myocardial infarction, and wound healing. RegeneRx Biopharmaceuticals advanced RGN-259 through Phase II/III clinical trials for dry eye and neurotrophic keratopathy, with positive Phase II results published [38].

Novelty: Moderate. The actin-modulation mechanism is well characterized and distinct from the BPC-157 angiogenic and NO-modulatory mechanisms. The combination of the two represents a complementary approach rather than a redundant one.

Effect size: Moderate in preclinical wound healing and cardiac repair models. Phase II clinical results in dry eye demonstrated statistically significant improvement over vehicle. Effect sizes in musculoskeletal healing are comparable to BPC-157 in parallel preclinical models.

Promising potential: Moderate. Clinical development continues in ophthalmologic and wound-healing indications. The compound is not approved by any regulatory agency for systemic tissue-regenerative applications.

Side-effect profile: Generally favorable in clinical trials. No material safety concerns have been identified in Phase I and Phase II studies. The compound is endogenously expressed and is not expected to produce immunogenicity.

Overall validation: Moderate to high. Thymosin beta-4 has a more mature clinical development program than BPC-157, with published Phase II clinical trial data in humans. The preclinical literature is independently replicated across multiple research groups, a significant advantage over the BPC-157 evidence base.

Comparison to Pentadeca Arginate: TB-500 has superior clinical validation and independent replication. Pentadeca Arginate has broader preclinical mechanistic diversity (NO system, VEGFR2, GHR, neurotransmitter modulation) and potentially broader tissue-regenerative applications. The two compounds are mechanistically complementary and are frequently combined in practice.

12.2 GHK-Cu (Copper Tripeptide-1)

Mechanism: GHK-Cu (glycyl-L-histidyl-L-lysine complexed with copper(II)) is a naturally occurring tripeptide-metal complex that modulates gene expression related to extracellular matrix synthesis, collagen production, and anti-inflammatory activity. The compound activates fibroblast transcriptional programs through copper-dependent signaling [37].

Development trajectory: GHK-Cu has been developed primarily for dermatological and cosmetic applications (wound healing, skin rejuvenation, hair growth). The compound is available in multiple topical formulations and is used in cosmetic surgery recovery. Systemic applications for tissue regeneration are in early investigational stages.

Novelty: Moderate. The copper-dependent gene expression modulation mechanism is distinct from peptide receptor-mediated mechanisms and from the BPC-157 pharmacology.

Effect size: Moderate in dermatological wound healing and skin rejuvenation models. The compound promotes collagen and elastin synthesis and inhibits matrix metalloproteinase activity. Effect sizes in systemic tissue regeneration are less well characterized than for BPC-157.

Promising potential: Moderate for dermatological applications; low for systemic tissue regeneration. The compound is commercially available in topical formulations but has not entered clinical trials for systemic indications.

Side-effect profile: Favorable. Topical GHK-Cu is well tolerated. Systemic safety data are limited.

Overall validation: Moderate for topical applications; low for systemic use. The compound has a substantial cosmetic and dermatological literature but limited clinical validation for internal tissue regeneration.

Comparison to Pentadeca Arginate: GHK-Cu operates through fundamentally different mechanisms (metal-dependent gene expression modulation versus peptide-receptor and NO-system modulation). Pentadeca Arginate has broader preclinical evidence for systemic tissue regeneration across multiple organ systems. GHK-Cu has superior commercial availability and regulatory clarity for topical applications.

12.3 KPV (Lys-Pro-Val Tripeptide)

Mechanism: KPV is a C-terminal tripeptide fragment of alpha-melanocyte-stimulating hormone (alpha-MSH) that retains the anti-inflammatory activity of the parent hormone without the melanogenic effects. KPV inhibits NF-kappaB-mediated pro-inflammatory cytokine production and modulates immune cell activation [39].

Development trajectory: KPV has been studied primarily in preclinical models of inflammatory bowel disease, dermatitis, and mucosal inflammation. Clinical development is limited; the compound is available from compounding pharmacies and peptide suppliers but has not entered formal clinical trials for any indication.

Novelty: Moderate. The alpha-MSH-derived anti-inflammatory mechanism is well characterized and distinct from BPC-157 pharmacology.

Effect size: Moderate in preclinical inflammatory bowel disease and dermatitis models. The anti-inflammatory effect is reproducible but the regenerative component is minimal compared to BPC-157.

Promising potential: Low to moderate. No clinical trials are in progress. The compound is used in compounding pharmacy practice but lacks formal clinical validation.

Side-effect profile: Favorable in preclinical models. No safety concerns have been identified. The compound is derived from an endogenous hormone fragment and is not expected to produce significant toxicity.

Overall validation: Low. The preclinical literature is modest in size and has limited independent replication. No human clinical data exist.

Comparison to Pentadeca Arginate: KPV is primarily anti-inflammatory, while Pentadeca Arginate is primarily regenerative with secondary anti-inflammatory effects. The two are mechanistically complementary for inflammatory tissue injury. Pentadeca Arginate has substantially greater preclinical evidence depth and breadth.

12.4 AOD-9604 (Anti-Obesity Drug 9604)

Mechanism: AOD-9604 is a modified 16-amino-acid fragment of the C-terminus of human growth hormone (hGH 177-191) that retains the lipolytic and chondrogenic activity of growth hormone without the diabetogenic or growth-promoting effects. The compound has been repositioned for cartilage repair and osteoarthritis [40].

Development trajectory: AOD-9604 was originally developed as an anti-obesity agent by Metabolic Pharmaceuticals. Phase IIb clinical trials for obesity demonstrated safety but insufficient efficacy for registration. The compound was subsequently repositioned by Calzada (now Cellmid) for osteoarthritis and cartilage repair, with clinical trials in intra-articular injection for knee osteoarthritis.

Novelty: Moderate. The growth hormone fragment mechanism for chondrogenic applications is a repositioning of established pharmacology.

Effect size: Modest for the original anti-obesity indication (Phase IIb did not meet primary endpoints). Moderate in preclinical cartilage repair and chondrocyte proliferation models. Clinical effect size in osteoarthritis has not been published in Phase III data.

Promising potential: Moderate. Active clinical development for osteoarthritis applications distinguishes AOD-9604 from many peptide comparators.

Side-effect profile: Favorable. Phase I and Phase IIb obesity trials demonstrated safety and tolerability. No material adverse events reported.

Overall validation: Moderate. The compound has more advanced clinical development (Phase IIb completed, osteoarthritis program ongoing) than BPC-157 but has not achieved regulatory approval for any indication.

Comparison to Pentadeca Arginate: AOD-9604 has a narrower tissue-regenerative scope (cartilage focus) but more advanced clinical development than Pentadeca Arginate. Pentadeca Arginate has broader preclinical evidence across multiple tissue types but substantially less human clinical data. The two compounds are not mechanistically overlapping and address different aspects of musculoskeletal repair.

12.5 LL-37 (Cathelicidin Antimicrobial Peptide)

Mechanism: LL-37 is a 37-amino-acid antimicrobial and immunomodulatory peptide derived from the human cathelicidin precursor protein hCAP18. Beyond direct antimicrobial activity, LL-37 promotes wound healing through EGFR transactivation, angiogenesis, and immune cell recruitment. The compound also demonstrates anti-biofilm activity [41].

Development trajectory: LL-37 has been studied in Phase I/II clinical trials for chronic leg ulcers (Lipsker et al., Pergamum AB) and in preclinical models of wound healing, infection, and inflammatory disease. The wound healing application is the most clinically advanced.

Novelty: High. The combined antimicrobial, immunomodulatory, and wound-healing mechanism is unique among tissue-regenerative peptides and addresses infection as a barrier to healing that other comparators do not.

Effect size: Moderate in preclinical wound healing models. Phase I/II clinical data in chronic leg ulcers demonstrated safety and preliminary efficacy signals. Antimicrobial effect sizes are substantial against gram-negative and gram-positive bacteria.

Promising potential: Moderate. The antimicrobial wound-healing combination addresses an unmet clinical need (infected chronic wounds) that is distinct from the clean tissue-regeneration applications of BPC-157 and TB-500.

Side-effect profile: Local injection site reactions reported in Phase I/II studies. Systemic safety data are limited. The compound is endogenously expressed but at concentrations well below those used therapeutically.

Overall validation: Low to moderate. Phase I/II clinical data exist, but the clinical program is limited in scale. The antimicrobial wound-healing literature is independently replicated.

Comparison to Pentadeca Arginate: LL-37 and Pentadeca Arginate share the wound-healing application but through different mechanisms. LL-37 adds antimicrobial activity that Pentadeca Arginate lacks. Pentadeca Arginate has broader systemic tissue-regenerative applications (gastrointestinal, musculoskeletal, neurological) that LL-37 does not address. The two could be complementary in infected wound contexts.

12.6 Comparator summary

The five comparator compounds occupy distinct positions in the tissue-regenerative peptide landscape. **Thymosin Beta-4 (TB-500)** is the most clinically validated comparator, with published Phase II data, independent replication, and a complementary actin-modulation mechanism. **GHK-Cu** is commercially established for dermatological applications but lacks systemic regenerative validation. **KPV** provides anti-inflammatory activity complementary to BPC-157 regenerative effects but has minimal independent validation. **AOD-9604** has the most advanced clinical development trajectory among the comparators for a musculoskeletal indication (osteoarthritis) but addresses a narrower tissue scope. **LL-37** is the most mechanistically novel through its combined antimicrobial and wound-healing activity.

Pentadeca Arginate occupies a unique position through the breadth of its pre-clinical evidence across multiple organ systems (gastrointestinal, musculoskeletal, vascular, hepatic, neurological), the pleiotropic mechanism involving NO system modulation, angiogenesis, growth factor receptor sensitization, and neurotransmitter modulation, and the improved oral bioavailability of the arginate salt form. Its principal limitations are the minimal human clinical data (fewer than 30 total participants across all studies), the concentration of the research literature within a single group (the Sikiric laboratory), the FDA Category 2 classification, and the WADA prohibition. Investigators considering Pentadeca Arginate should weigh the substantial preclinical promise against the limited clinical validation and the regulatory uncertainty, and should prioritize independent verification of preclinical findings as the most important next step in the translational pathway.

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compound is classified as a Category 2 bulk drug substance by the United States Food and Drug Administration and is prohibited by the World Anti-Doping Agency. The overwhelming majority of the BPC-157 research literature originates from a single research group at the University of Zagreb; independent replication of key findings remains limited. Investigators should obtain analytical confirmation of identity, purity, and counterion composition on every lot and should consult current regulatory guidance in their jurisdiction before any research application.