

RESEARCH MONOGRAPH · COMPOUND PROFILE

BPC-157

A 15-amino-acid sequence derived from a gastric protective protein, broadly studied in tendon, ligament, vascular, and gut repair models.

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ABSTRACT

BPC-157, formally pentadecapeptide BPC 157 (Body Protection Compound 157), is a 15-residue partial sequence isolated from a larger gastric protective protein found in human gastric juice. The sequence Gly-Glu-Pro-Pro-Pro-Gly-Lys-Pro-Ala-Asp-Asp-Ala-Gly-Leu-Val (CAS 137525-51-0; molecular formula C₆₂H₉₈N₁₆O₂₂; molecular weight 1419.55) was originally characterized in the 1990s by the Sikiric group at the University of Zagreb, who have authored the majority of the published preclinical record. Reported activities span tendon and ligament healing in transection models, vascular reorganization through nitric oxide synthase modulation and VEGF receptor 2 engagement, gastrointestinal mucosal protection, dopaminergic system modulation, and GH receptor crosstalk. Routes studied include intraperitoneal, intramuscular, subcutaneous, oral, and topical administration in rodent models; oral bioavailability is unusual for a peptide of this length and is attributed to the parent compound's evolutionary role in the gut. Human pharmacokinetic data are sparse; one published Phase 1 single-ascending-dose study has been reported. BPC-157 is not approved by any regulatory authority for human or veterinary use. The literature base is dominated by a single research group, which is the principal limitation on the strength of the evidence; independent replications of the most-cited findings are limited but growing. This monograph reviews the chemistry, mechanism, pharmacokinetics, dosing literature, sourcing risks, and reconstitution practice for in vitro and in vivo investigative work.

Compound identification

Nomenclature and synonyms

BPC-157 is the most common designation. Less common alternatives in the literature include PL 14736, PL-10, pentadecapeptide BPC 157, and BPC-15. The "BPC" stem refers to "Body Protection Compound," a name applied by the discovering group to the parent gastric protein from which the 15-residue active sequence was extracted. The PubChem CID is 9941957. The compound has no INN; it has not been advanced as a regulated drug substance in the United States, the European Union, or Japan.

A persistent point of confusion is the relationship between BPC-157 and "BPC-157 arginate" or "stable BPC-157" formulations marketed by some research-grade suppliers. The native peptide sequence is identical; the difference is in the salt form (acetate vs. arginate) and in formulation excipients claimed to extend solution stability. The free-base mass and the activity in published assays do not differ between salt forms.

Structural chemistry

The amino acid sequence is Gly-Glu-Pro-Pro-Pro-Gly-Lys-Pro-Ala-Asp-Asp-Ala-Gly-Leu-Val. The proline-rich segment at positions 3 through 5 contributes substantially to the peptide's resistance to gastric and serum proteases, an unusual property for a peptide of this length and the structural basis for its reported oral bioavailability. The molecular formula is C₆₂H₉₈N₁₆O₂₂; the average molecular weight is 1419.55 g/mol; the monoisotopic mass is 1418.72 daltons.

The peptide has no disulfide bridges and no post-translational modifications in its native form. There is one free carboxylate at the C-terminus and one free amine at the N-terminus; the side chains contribute additional ionizable groups (two glutamate carboxylates from Glu-2 and Asp-10/Asp-11, one lysine epsilon-amine at position 7). The isoelectric point is approximately 4.4. At physiological pH the peptide carries a net negative charge.

Physicochemical properties

BPC-157 is supplied as a white to off-white fluffy lyophilized powder. The lot received under the current Kodiak lot 20260211 conforms to this description. Solubility is high in water, in bacteriostatic water, and in 0.9 percent saline; concentrations up to 5 mg/mL are routinely prepared without precipitation. Solubility is also adequate in physiological buffers (PBS, HBSS, Krebs-Ringer). The peptide is not soluble in pure DMSO at concentrations above approximately 1 mg/mL; DMSO is not the appropriate vehicle for in vivo work.

The peptide is stable in the lyophilized state at minus 20 degrees Celsius for at least 24 months in the original sealed vial under standard light protection. Reconstituted solutions in bacteriostatic water are stable refrigerated for at least 30 days; published stability data extend to 60 days under refrigeration with no measurable degradation by HPLC. Freeze-thaw cycles should be avoided; aliquoting is the standard practice for working solutions.

Discovery and developmental history

Origin in the Sikiric laboratory

The pentadecapeptide BPC 157 was first characterized in the early 1990s by Predrag Sikiric and colleagues at the University of Zagreb School of Medicine in Croatia. The parent protein, "body protection compound," was isolated from human gastric juice and screened for cytoprotective activity in rodent gastric ulcer models. The 15-residue active fragment was identified by enzymatic digestion and bioassay-guided fractionation. The Sikiric group has subsequently authored more than 100 peer-reviewed publications characterizing the compound in tendon, ligament, vascular, gastrointestinal, neurological, and metabolic models.

The dominance of a single research group in the BPC-157 literature is the principal methodological concern that any rigorous review must acknowledge. The findings are extensive and the experimental methods are standard, but the absence of large-scale independent replication outside the Zagreb consortium has limited the compound's progression toward regulatory approval despite three decades of pre-clinical work.

Independent replication and clinical translation

A small but growing literature outside the Sikiric consortium has begun to address the replication concern. Notable independent contributions include work from the University of Lubeck on hepatoprotection in rodent models, from the University of Tehran on anxiolytic and neuroprotective endpoints, and from several Chinese institutions on tendon healing. A 2017 Phase 1 single-ascending-dose study in healthy human volunteers, conducted under Croatian regulatory authority, reported no serious adverse events at doses up to 1 mg administered intravenously and intramuscularly; the study was not powered for efficacy and has not been followed by a Phase 2.

There is no FDA-approved IND for BPC-157 in any indication as of this revision. The compound is not a generally recognized as safe (GRAS) substance and is not a regulated dietary supplement. Clinical use in humans, where it occurs, is off-label

and outside the scope of regulatory oversight; this monograph does not endorse such use.

Mechanism of action

VEGF receptor 2 engagement and angiogenesis

The most extensively documented mechanism involves modulation of vascular endothelial growth factor receptor 2 (VEGFR2). Published work demonstrates that BPC-157 administration accelerates angiogenesis in healing tissue and that pharmacologic VEGFR2 antagonism abolishes the healing effect in tendon and gut models. The peptide does not appear to act as a direct VEGFR2 ligand; rather, it appears to upregulate VEGFR2 expression and to potentiate downstream signaling through endothelial nitric oxide synthase (eNOS) and the PI3K/Akt pathway. The functional consequence is enhanced vascular reorganization at sites of tissue injury, supporting fibroblast migration and matrix deposition.

Nitric oxide synthase modulation

BPC-157 effects on the nitric oxide system are documented in cardiovascular, gastrointestinal, and neurological contexts. The peptide attenuates the consequences of NOS inhibition by L-NAME in models of stress-induced gastric injury, hypertension, and arrhythmia. Co-administration of L-arginine generally augments the BPC-157 effect, while NOS inhibition attenuates it. The most parsimonious interpretation is that the peptide either upregulates eNOS expression, stabilizes the eNOS dimer, or facilitates substrate availability through an upstream mechanism that remains incompletely characterized.

Growth hormone receptor crosstalk

Several published studies report that BPC-157 increases growth hormone receptor expression in tendon and ligament fibroblasts, with downstream implications for collagen synthesis. The mechanism is reported to be transcriptional rather than acting through the GH/GHR ligand-receptor binding event; growth hormone levels themselves are not consistently affected by BPC-157 administration. The functional implication is enhanced anabolic response in connective tissue without the systemic consequences of GH elevation.

Dopaminergic system effects

In neurological models, BPC-157 attenuates the dopaminergic disturbances associated with neuroleptic-induced catalepsy, MPTP-induced Parkinsonian phenotype, and amphetamine-induced stereotypy. The mechanism is not direct dopamine receptor binding; rather, the peptide appears to normalize dopaminergic tone through a mechanism that may involve serotonergic modulation, GABAergic effects, or restoration of vascular integrity in the basal ganglia.

Limits of the mechanistic model

The mechanistic literature is consistent in its broad strokes (VEGFR2 upregulation, eNOS facilitation, GH receptor enhancement, dopaminergic normalization) but lacks a unified molecular target. There is no well-characterized direct binding partner for BPC-157. The compound's reported activities span tissue and pathway effects that are not obviously connected through a single receptor. This is a real limitation of the model and a genuine open question; investigators should not treat the mechanistic claims as fully resolved.

Pharmacokinetics

Routes of administration

The published preclinical literature includes intraperitoneal, intramuscular, subcutaneous, intravenous, oral (gavage), and topical (cream, eye drop) administration in rodent models. The wide range of routes is unusual for a peptide and is attributed to the parent compound's evolutionary role as a gastric-juice-derived protective factor. Oral bioavailability has been reported in the range of 8 to 14 percent across studies, depending on vehicle, fasting state, and assay method. Subcutaneous and intramuscular administration produce predictable absorption with peak plasma concentrations within 30 to 60 minutes.

Plasma half-life and tissue distribution

Plasma half-life following intravenous administration in rodents is reported in the range of 60 to 90 minutes. Tissue distribution is broad; the peptide is detectable in skeletal muscle, gastrointestinal mucosa, liver, kidney, and brain following systemic administration. The brain-to-plasma ratio is reported as approximately 0.10 in the rodent literature, consistent with limited but non-negligible blood-brain barrier penetration.

Metabolism and excretion

BPC-157 is hydrolyzed by serum and tissue peptidases, primarily at the C-terminal Leu-Val and the N-terminal Gly-Glu sites. The proline-rich central segment confers unusual resistance to proteolytic degradation relative to comparably sized peptides. Major metabolites are inactive in published behavioral and angiogenic assays. The compound is not a known inducer or inhibitor of major CYP isoforms at expected exposure ranges.

Reported research dose ranges

The published preclinical literature reports rodent doses ranging from 1 microgram per kilogram to 1 milligram per kilogram by various routes, with the bulk of mechanistic studies clustering around 10 micrograms per kilogram intraperitoneally or subcutaneously, daily. Allometric scaling to human equivalent doses (dividing rodent doses by approximately 6 to 7 to account for body surface area) places the equivalent human exposure in the range of 0.14 to 1.4 micrograms per kilogram, or approximately 10 to 100 micrograms per dose for a 70 kg subject. The Phase 1 safety study used doses up to 1 milligram intravenously, an order of magnitude above the allometrically scaled efficacy range.

The dose range commonly cited in research-grade vendor literature (200 to 500 micrograms per research subject per day, divided into one to two administrations) is broadly consistent with the upper end of the allometrically scaled range. Dose-response data in the published literature do not extend cleanly to humans, and investigators should treat published research-grade dose ranges as approximate guidance rather than validated dosing.

Sourcing and quality verification

Synthesis route

BPC-157 is produced by solid-phase peptide synthesis using Fmoc chemistry. The proline-rich central segment is the synthetic bottleneck; coupling efficiency at the third proline is the most common point of failure, producing truncated 12 or 13 residue impurities that lack activity. High-quality batches require optimized coupling conditions (extended reaction times, double couplings at the proline positions, or pseudoproline dipeptide substitutions) to achieve total purity above 99 percent.

The lot of record for the current Kodiak inventory (lot 20260211) was synthesized by the supplier of record and shipped to Kodiak biolabs in lyophilized acetate salt form. The vendor COA reports purity of 99.4 percent by HPLC with identity confirmation by mass spectrometry.

Common adulterants and impurities

The research-grade BPC-157 supply chain has documented patterns of substandard product. Reported issues include:

1. Truncated peptides arising from incomplete coupling at the proline-rich segment, primarily 12-mer and 13-mer fragments missing one or two of the central prolines. These fragments are biologically inactive.
2. Acetylation at the N-terminal glycine, producing a peptide of correct mass plus 42 daltons that may show altered activity.
3. Glutamic-aspartic acid racemization at positions 2, 10, and 11 under prolonged synthesis at elevated temperature.
4. Excess acetate or trifluoroacetate counterions inflating apparent mass by 5 to 12 percent depending on salt form.
5. Endotoxin contamination from non-pyrogen-controlled synthesis, particularly relevant for in vivo work.

Independent verification by HPLC and mass spectrometry on every batch is essential. The vendor COA is necessary but not sufficient; a rigorous sourcing model includes a third-party lab that can detect adulterations the vendor lab might miss. Kodiak biolabs is in the process of establishing this third-party verification through Janoshik Analytical; as of this revision, only the vendor COA is available, and that limitation is acknowledged on every product page.

Analytical standards

Reverse-phase HPLC on a C18 column with gradient elution from aqueous TFA (0.1 percent) to acetonitrile, monitoring at 215 nm and 280 nm, is the standard purity assay. Identity confirmation by LC-MS with electrospray ionization yields a protonated molecular ion (M+H) at 1420.6 m/z for the free acid or as the sodium adduct at 1442.6 m/z. The acceptance criteria applied by the vendor lab and replicated in the planned Janoshik verification are: total purity above 98.0 percent at both wavelengths, identity confirmation within 0.5 ppm of theoretical mass, and absence of major impurity peaks above 0.5 percent of the parent peak.

Reconstitution and handling

Solvent system

BPC-157 dissolves readily in water, bacteriostatic water, and 0.9 percent saline. The standard reconstitution protocol uses bacteriostatic water (0.9 percent benzyl alcohol preservative) for any solution intended to be stored beyond a single use. For acute in vitro experiments where preservative is undesired, use sterile water for injection or PBS.

DMSO is not the appropriate vehicle. The peptide does not require organic co-solvent for solubility, and DMSO at the concentrations sometimes used for poorly soluble compounds (10 percent or more) introduces vehicle effects in cellular and in vivo assays that confound dose-response interpretation.

Reconstitution protocol

Add the calculated volume of solvent slowly along the side wall of the vial. Avoid injecting the solvent stream directly onto the lyophilized powder; the impact disrupts the dry cake unevenly. Allow the vial to rest for 60 to 90 seconds at room temperature, then gently swirl until the powder is fully dissolved. A 5 mg vial reconstituted in 2 mL produces a 2.5 mg/mL solution that is fully clear within 90 seconds at typical laboratory temperature. Visual inspection should confirm a clear solution without particulates; turbidity at this concentration indicates either a manufacturing defect or substantial degradation.

Storage stability

Lyophilized BPC-157 in the unopened vial: stable at minus 20 degrees Celsius for at least 24 months under the conditions documented in the lot expiration date. Reconstituted solutions: stable at 2 to 8 degrees Celsius for 30 days minimum, with published stability extending to 60 days. Aliquot working solutions to avoid freeze-thaw cycles; the published peptide stability data are not generated through repeated thawing of the same vial. Reconstituted solutions should not be stored at room temperature beyond 24 hours.

Stack interaction considerations

Combination with TB-500 is the most commonly cited stack in the research literature, on the rationale that TB-500 contributes actin-binding and migration effects while BPC-157 contributes vascular and matrix effects. The mechanistic case for synergy is plausible but not formally documented in controlled comparison studies; investigators should not assume that the two compounds are simply additive.

Combination with growth hormone secretagogues (Ipamorelin, CJC-1295) is reported in the research-grade literature on the basis that growth hormone receptor upregulation by BPC-157 may potentiate the anabolic effects of GH-axis stimulation. The mechanistic case is again plausible but not formally established.

Pharmacokinetic interactions with CYP-substrate compounds are not expected at standard research dose ranges due to the peptide's minimal hepatic metabolism. There is no published evidence of receptor-level interactions with conventional small-molecule pharmacotherapy.

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