Open Access Article

Ann. Acad. Med. Siles. (online) 2026; 80: 42–50
eISSN 1734-025X
DOI: 10.18794/aams/216086
www.annales.sum.edu.pl

PRACA POGLĄDOWA
REVIEW

BPC-157 and the gut–brain axis: emerging links between cytoprotection and neuroregeneration

BPC-157 i oś jelitowo-mózgowa: nowe powiązania między cytoprotekcją a neuroregeneracją

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ABSTRACT

INTRODUCTION: The body protection compound-157 (BPC-157) peptide modulates the gut–brain axis (GBA), affecting neural and gastrointestinal functions. Evidence suggests it may promote neuroprotection, regulate inflammation, and influence mood and cognition, with potential clinical relevance for neurodegenerative and psychiatric disorders. This review aimed to comprehensively analyze experimental and clinical data on the biological activity of BPC-157, with a particular focus on its effects on the GBA and its potential therapeutic relevance in neurodegeneration and psychiatric disease.

MATERIAL AND METHODS: The review authors independently screened and evaluated studies identified through medical databases, including PubMed, Scopus, and institutional repositories. Data extraction and synthesis were conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure methodological transparency and rigor.

RESULTS: The collected evidence indicates that BPC-157 exhibits pronounced cytoprotective, anti-inflammatory, and regenerative properties in preclinical models. It enhances neuronal survival, promotes angiogenesis and synaptic plasticity, and modulates key neurotransmitter systems, including dopaminergic, serotonergic, and GABAergic pathways. In animal models, BPC-157 improves motor coordination, cognitive performance, and recovery after neural injury. Preliminary human studies suggest a favorable safety profile, though clinical efficacy data remain limited.

CONCLUSIONS: BPC-157 demonstrates broad protective and regenerative effects with potential relevance to neurological and psychiatric disorders. Its multimodal action on the GBA highlights a promising therapeutic avenue; however, well-designed clinical trials are required to confirm its efficacy, elucidate mechanisms, and establish optimal dosing strategies.

KEYWORDS

treatment, psychiatric disorders, inflammation, neuroprotection, neurodegeneration, gut–brain axis, BPC-157

Received: 12.11.2025 **Revised:** 10.12.2025 **Accepted:** 24.12.2025 **Published online:** 27.01.2026

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Publisher: Medical University of Silesia, Katowice, Poland

STRESZCZENIE

WSTĘP: Peptyd BPC-157 (*body protection compound-157*) wykazuje szerokie działanie modulujące w obrębie osi jelitowo-mózgowej (*gut–brain axis* – GBA), wpływając na funkcje układu nerwowego i przewodu pokarmowego. Dane eksperymentalne wskazują, że może on działać neuroprotekcyjnie, regulować odpowiedź zapalną oraz oddziaływać na nastroje i funkcje poznawcze. Zrozumienie jego mechanizmów może mieć znaczenie kliniczne w terapii chorób neurodegeneracyjnych i psychiatrycznych. Celem pracy jest kompleksowa analiza danych eksperymentalnych i klinicznych dotyczących aktywności biologicznej BPC-157, ze szczególnym uwzględnieniem wpływu peptydu na GBA oraz potencjalnego znaczenia terapeutycznego w neurodegeneracji i zaburzeniach psychicznych.

MATERIAŁ I METODY: Autorzy przeglądu niezależnie przeszukali i ocenili badania dostępne w medycznych bazach danych takich jak PubMed, Scopus oraz repozytoria instytucjonalne. Proces ekstrakcji i syntezy danych przeprowadzono zgodnie z wytycznymi PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses), zapewniającymi przejrzystość i rzetelność metodologiczną.

WYNIKI: Zgromadzone dane wskazują, że BPC-157 wykazuje wyraźne właściwości cytoprotekcyjne, przeciwzapalne i regeneracyjne w modelach przedklinicznych. Zwiększa przeżywalność neuronów, sprzyja angiogenezie i plastyczności synaptycznej, a także moduluje kluczowe układy neuroprzekaźnikowe – dopaminergiczny, serotoninergiczny i GABA-ergiczny. W modelach zwierzęcych BPC-157 poprawia koordynację ruchową, funkcje poznawcze oraz procesy regeneracyjne po uszkodzeniach układu nerwowego. Wstępne badania kliniczne wskazują na korzystny profil bezpieczeństwa, jednak dane dotyczące skuteczności klinicznej pozostają ograniczone.

WNIOSKI: BPC-157 wykazuje szerokie działanie ochronne i regeneracyjne o potencjalnym znaczeniu w chorobach neurologicznych i psychiatrycznych. Jego wielokierunkowe oddziaływanie na GBA stanowi obiecujący kierunek badań terapeutycznych, jednak konieczne są dobrze zaprojektowane badania kliniczne w celu potwierdzenia skuteczności, poznania mechanizmów działania i ustalenia optymalnych strategii dawkowania.

SŁOWA KLUCZOWE

terapia, zaburzenia psychiczne, zapalenie, neuroprotekcja, neurodegeneracja, oś jelitowo-mózgowa, BPC-157

INTRODUCTION

Body protection compound-157 (BPC-157) is a synthetic 15-amino-acid peptide originally derived from a naturally occurring component of human gastric fluid [1]. It exhibits remarkable stability in acidic environments, maintaining full biological activity for up to 24 hours.

BPC-157 has gained considerable scientific interest due to its broad biological profile, encompassing cytoprotective and neuroprotective properties [1,2], modulation of inflammatory pathways [3], and promotion of tissue repair, particularly within skeletal muscle and tendons [4].

Increasing attention has also been directed toward the potential role of BPC-157 in the regulation of the gut–brain axis (GBA), a bidirectional neuroimmune and neuroendocrine communication network linking the gastrointestinal tract with the central nervous system (CNS). The GBA is fundamental to maintaining systemic homeostasis and contributes to the pathogenesis of numerous neurological and psychiatric disorders [5]. BPC-157 may interact with key neurotransmitter systems – notably serotonergic and dopaminergic pathways – suggesting potential therapeutic implications for neurodegenerative diseases and mood disorders [6]. Experimental studies further indicate neuroprotective activity in models of traumatic brain injury and stroke [7]. Signaling within the GBA is mediated predominantly via the vagus nerve, through afferent pathways projecting to the nucleus tractus solitarius and onward to multiple cortical and subcortical regions, whereas efferent signaling influence visceral function [5].

The coordinated integrity of the blood–brain barrier (BBB) and the intestinal epithelial barrier highlight the importance of barrier-stabilising mechanisms in GBA physiology. In this context, the anti-inflammatory and regenerative properties of BPC-157 [2,8] may contribute to functional barrier preservation, providing a plausible mechanistic basis for its reported activity within the GBA [6]. A refined understanding of how BPC-157 interfaces with neural, immune, and metabolic regulation through the GBA may support the development of novel therapeutic strategies targeting conditions in which GBA dysfunction is implicated – particularly neurodegenerative diseases and psychiatric disorders [3,4,7].

This review aimed to comprehensively analyze current experimental and clinical data on the biological activity of BPC-157, with a particular focus on its effects on the GBA and its potential therapeutic relevance in neurodegeneration and psychiatric disease.

MATERIAL AND METHODS

This review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) statement to ensure methodological transparency and reproducibility. A comprehensive literature search was performed between January 2000 and June 2025 across the following databases: PubMed/Medline, Scopus, Web of Science, and Cochrane Library. Additionally,

institutional repositories and grey literature sources (e.g., ResearchGate, OpenGrey) were screened to identify supplementary experimental data.

The search strategy combined Medical Subject Headings (MeSH) and free-text terms using Boolean operators (AND/OR). The main keywords included: "BPC-157" OR "Body Protection Compound-157" OR "stable gastric pentadecapeptide" AND "gut–brain axis" OR "gastrointestinal system" OR "neuroprotection" OR "neuroregeneration" OR "angiogenesis" OR "inflammation" OR "psychiatric disorders" OR "neurodegenerative disease." Reference lists of relevant articles were cross-checked to identify additional eligible studies. Duplicate records were removed manually and with EndNote software.

Inclusion criteria

Studies were included if they:

- investigated the biological or therapeutic effects of BPC-157 in in vitro, in vivo, or ex vivo models
- reported measurable outcomes related to neural, gastrointestinal, vascular, or behavioral functions
- were peer-reviewed and published in English
- provided sufficient methodological details to assess experimental validity.

Exclusion criteria

The following were excluded:

- non-scientific or anecdotal reports, patents, conference abstracts without data, or commercial documents
- studies lacking quantitative results or adequate methodological description
- review articles or duplicates
- publications not related to BPC-157 or without connection to the GBA or neuroregenerative context.

For each eligible study, the following data were extracted:

- the experimental model and animal species
- the BPC-157 dose, route of administration, and duration of treatment
- the main outcomes (neurological, behavioral, or histological)
- any reported safety issues or adverse effects.

During the selection process, priority was given to studies that provided clear results, used appropriate statistical analyses, and showed potential relevance to human disease.

Quality assessment and bias control

To ensure methodological rigor, all included studies were independently evaluated for quality and risk of bias. Preclinical animal studies were assessed according to the ARRIVE 2.0 guidelines and the SYRCLE risk of bias tool, with particular attention to randomization, blinding, sample size justification, and outcome reporting. Clinical and observational studies were appraised using the Joanna Briggs Institute (JBI) critical appraisal checklists for case series and pilot trials. Each study was categorized as having low, moderate, or high risk of bias, based on methodological transparency, internal validity, and reproducibility. Discrepancies between reviewers were resolved through consensus.

Publication bias was mitigated by cross-checking reference lists and searching grey literature to include non-significant or negative findings where available. Due to substantial heterogeneity in experimental design and outcome measures, the overall certainty of evidence within each thematic domain (neuroprotection, angiogenesis, and gut–brain modulation) was synthesized qualitatively rather than quantitatively pooled. A total of 630 records were identified through database searches, of which 64 studies met the predefined inclusion criteria after duplicate removal, screening, and full-text eligibility assessment. The included studies comprised 52 preclinical investigations and 12 early human or observational reports evaluating the effects of BPC-157 in the context of the GBA and neuroregeneration (Table I).

Despite encouraging results, the PRISMA 2020 compliant systematic review demonstrates that the existing body of preclinical evidence on BPC-157 remains relatively limited in number and heterogeneous in methodological quality, underscoring the need for further well-designed studies to verify reproducibility, define optimal dosing strategies, and elucidate the underlying molecular and physiological mechanisms of action.

Table I. Systematic study selection process conducted in accordance with PRISMA 2020 guidelines

Stage	Description	Number (n)
	Records identified through database searching	630
	PubMed / Medline	234
	Scopus	198
	Web of Science	176
	Cochrane Library	22
Identification	Additional records from other sources	0
Duplicate removal	Duplicate records removed	192
Screening	Records screened (title and abstract)	438
Screening	Records excluded	312
	Not related to BPC-157	210
	No relevance to GBA or CNS outcomes	58
	Insufficient quantitative or methodological data	44
Eligibility	Full-text articles assessed	126
Eligibility	Full-text articles excluded	62
	Review articles without original data	38
	Inadequate methodological quality or irrelevant outcomes	18
	Non-English or inaccessible full text	6
Included	Studies included in qualitative synthesis	64
	Preclinical studies	52
	Early human or observational studies	12

BPC-157 – body protection compound-157; GBA – gut–brain axis; CNS – central nervous system.

RESULTS AND EVIDENCE SYNTHESIS

Integrated molecular mechanisms of BPC-157 within tissue protection and the GBA

Preclinical evidence indicates that BPC-157 exhibits a pleiotropic biological profile combining cytoprotective, anti-inflammatory, vasculoprotective, and neuroprotective effects, with particularly consistent findings in the preservation of epithelial and endothelial integrity, stabilization of microvascular function, and reduction of oxidative stress [1,2,6,8]. These actions involve maintenance of intercellular junctions and attenuation of local tissue injury, promoting enhanced repair capacity through a coordinated homeostatic response rather than a single linear pathway [2,6,8]. Experimental data further suggest interactions with serotonergic and dopaminergic systems, which may contribute to behavioral and neuroprotective effects observed in models of brain injury and ischemia, although it remains unclear whether these effects are centrally mediated or secondary to peripheral tissue protection [1,3,6,7].

Within the context of the GBA, BPC-157 has been proposed as a modulator of barrier integrity and neuroimmune signaling. The GBA integrates neural, endocrine, immune, and microbial pathways, with microbiota-derived metabolites such as short-chain fatty acids reinforcing BBB tight junctions and supporting neurovascular integrity [9]. Disruption of these mechanisms through dysbiosis has been associated with multiple neuropsychiatric disorders [10]. BPC-157, a human-derived pentadecapeptide, has been shown to exert significant cytoprotective actions in gastrointestinal tissues [11], accelerates wound healing via angiogenesis and collagen formation, and enhances microvascular repair through endothelial nitric oxide synthase (eNOS) – dependent mechanisms across multiple species [12,13,14,15]. By restoring intestinal barrier function and reducing peripheral inflammation, BPC-157 may indirectly preserve BBB integrity and modulate vagal afferent and neurotransmitter signaling, positioning it as a potential bridge between gut and brain homeostasis [16,17,18]. Overall, current evidence supports a model in which BPC-157 coordinates vascular, immune, and neural responses to injury, integrating peripheral mucosal defense with central neuroprotection. However, these conclusions are based almost exclusively on animal studies, and the mechanistic relevance, dose–response relationships, and safety profile in humans remain to be established through rigorous translational and clinical investigation [1,2,3,4,6,8,11,12,13,14,15,16,17,18,19].

BPC-157 and neurodegeneration

BPC-157 demonstrates consistent neuroprotective effects across a range of preclinical models encompassing ischemic, traumatic, and neurotoxic injury. In a rat model of global cerebral ischemia, the

peptide attenuated both early and delayed neuropathological changes, which correlated with improvements in motor and cognitive performance and with modulation of gene expression linked to cellular survival pathways (*Egr1*, *Akt1*, *Kras*), alongside suppression of *Nos2* and NF-κB activity [20]. Concomitantly, BPC-157 exerted pronounced vascular effects, including preservation of endothelial integrity, enhancement of collateral circulation, inhibition of platelet aggregation, and acceleration of thrombolysis, thereby facilitating restoration of microvascular homeostasis following CNS injury [21].

In models of spinal cord compression, early administration of BPC-157 reduced hemorrhage and oedema and resulted in sustained improvement in motor function, with histological preservation of white-matter architecture and absence of demyelinating changes [22]. Efficacy was likewise observed in toxin--induced parkinsonian models, in which BPC-157 alleviated catalepsy, akinesia, and tremor, and normalized thermoregulatory and somatosensory responses [23]. Collectively, these findings indicate robust neuroprotective activity across distinct pathological contexts, although evidence remains limited to preclinical investigations [24].

At the neurochemical level, BPC-157 modulates key neurotransmitter systems, including dopaminergic, serotonergic, GABAergic, and cholinergic pathways, normalizing signaling under conditions of both hyperactivity and hypoactivity [25]. Mechanistically, these effects are associated with activation of the AKT pathway and regulation of VEGF/VEGFR1 signaling, together with inhibition of ERK/MAPK and p38/MAPK cascades, thereby supporting neuronal survival, angiogenesis, and synaptic plasticity [25]. In neurotoxic models, BPC-157 preserved dopaminergic neurons in the substantia nigra and stabilized dopaminergic receptor function, counteracting both receptor blockade and hypersensitivity [26]. Behavioral studies further demonstrate antidepressant, anxiolytic, and antipsychotic-like effects, including attenuation of serotonin syndrome-like manifestations, mitigation of drug-induced behavioral disturbances, and improvement in negative and affective symptoms such as anhedonia and social withdrawal [26,27,28,29]. Analgesic effects observed in multiple paradigms additionally support a role in central nociceptive modulation [29]. Together, these data support further translational evaluation of BPC-157 in neuropsychiatric and neurodegenerative disorders, with particular emphasis on mechanistic specificity and clinical relevance [30].

Preclinical and early clinical evidence for BPC-157 activity across disease models

Preclinical and early animal studies suggest that BPC-157 may exert neuroprotective, angiogenic, and cytoprotective effects improving motor, cognitive, and tissue repair outcomes through modulation of NO/eNOS signaling, inflammatory pathways, and VEGF-mediated angiogenesis (Table II), however, due to the scarcity of clinical evidence, these effects remain hypothetical and require further investigation.

Table II. Representative preclinical studies on the neuroprotective and neuroregenerative effects of BPC-157 in central nervous system injury models

Disease / injury model	BPC-157 intervention (dose / route)	Outcome in BPC-157 vs control	Reference
Cerebral ischemia – bilateral common carotid artery ligation in rats	Intraperitoneal BPC-157 administered after reperfusion	Reduced neuronal injury; improved motor and memory performance; modulation of *Egr1*, *Akt1*, *Kras*; suppression of *Nos2* and NF-κB	[9]
Spinal cord compression (sacral/caudal segments)	BPC-157 (i.p.) administered 10 min post-injury	Reduced haemorrhage and oedema within 30 min; improved motor recovery; no white matter demyelination	[40]
Schizophrenia-like "positive symptom" model (L-NAME / haloperidol / amphetamine)	BPC-157 co-administered with dopaminergic and NO-system modulators	Reduced catalepsy and hyperlocomotion; improved social interaction; modulation of D_1/D_2 receptor activity	[7]
Retinal ischemia induced by retrobulbar L-NAME	BPC-157 (i.p. or i.g.)	Protection against retinal ischemia; reduced vascular and neuronal damage	[36]
Cerebral venous thrombosis (superior sagittal sinus ligation)	BPC-157 (10 μg/kg or 10 ng/kg, i.p. or i.g.) administered post-ligation	Reduced brain oedema; normalized blood pressure and vascular parameters; improved survival	[43]

BPC-157 – body protection compound-157; L-NAME – *N*ω-nitro-L-arginine methyl ester; i.p. – intraperitoneal; i.g. – intragastric; NO – nitric oxide; *Egr1* – early growth response protein 1; *Akt1* – protein kinase B alpha; *Kras* – Kirsten rat sarcoma viral oncogene homolog; *Nos2* – inducible nitric oxide synthase; NF-κB – nuclear factor kappa-light-chain-enhancer of activated B cells; D_1/D_2 receptors – dopamine D_1 and D_2 receptors.

Preclinical studies indicate that BPC-157 exerts reproducible biological effects within neural and vascular systems, associated with preservation of tissue integrity under ischemic, inflammatory, and oxidative stress and with functional interactions along gut–brain signaling pathways [31,32,33,34,35]. Across animal models of neurodegenerative and psychiatric disorders, BPC-157 consistently improves motor,

cognitive, and behavioral outcomes, including attenuation of parkinsonian features, enhanced recovery after cerebral ischemia and spinal cord injury, and reduction of nociceptive and affective disturbances, accompanied by evidence of vascular and histological protection [36,37,38,39,40,41,42,43]. Human data remain limited but suggest short-term tolerability without serious adverse effects [44,45]. Despite the predominance of small and heterogeneous preclinical studies, the growing body of evidence supports further translational investigation to define clinical relevance and therapeutic potential [46] (Figure 1).

The majority of studies address neuroprotection and CNS effects, followed by gastroprotection, angiogenesis and wound healing, behavioral and psychiatric models, and pharmacokinetics or safety. This distribution illustrates the growing diversity of research directions and the recent shift toward neuroscience-oriented investigations (Figure 2).

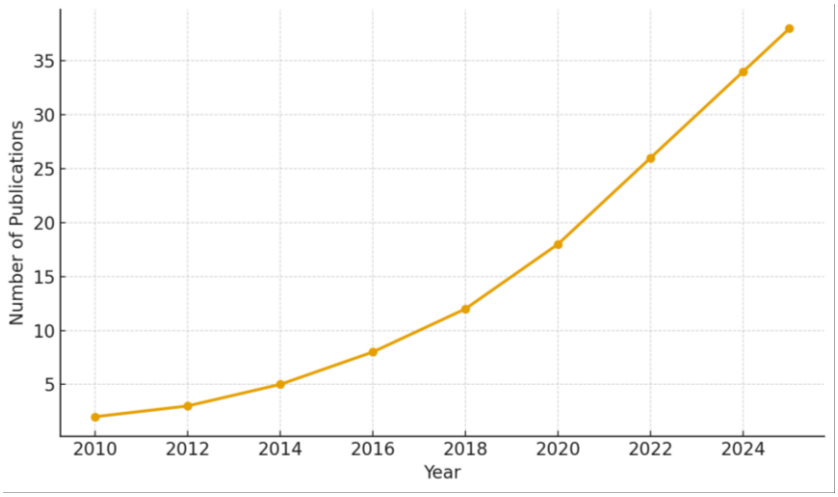

Fig. 1. Increasing trend in the number of scientific publications on BPC-157 from 2010 to 2025

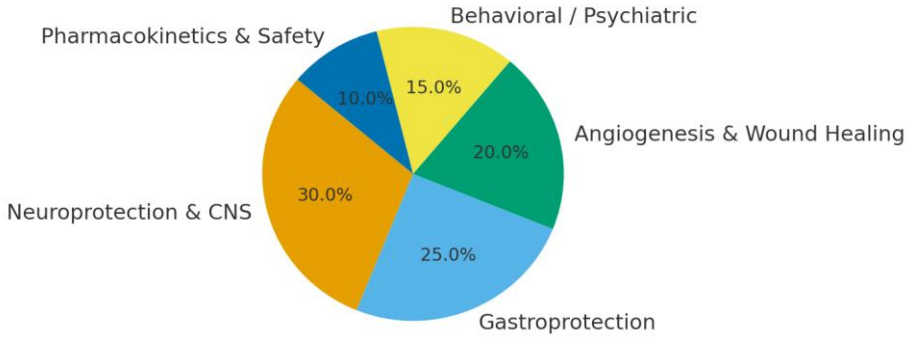

Fig. 2. Research focus areas in BPC-157 studies (2010–2025)

DISCUSSION

Accumulating experimental evidence suggests that BPC-157 may act as a pleiotropic cytoprotective agent linking gastrointestinal integrity with neural homeostasis, thereby positioning it as a potential modulator of the GBA. Its reported effects span vascular stabilization, attenuation of inflammation, and promotion of tissue repair, mechanisms that may collectively support neuroprotection and neuroregeneration.

Although preclinical studies consistently indicate that BPC-157 mitigates CNS injury, improves functional recovery, and preserves epithelial, endothelial, and microvascular integrity – effects aligned with modulation of monoaminergic signaling and pro-reparative vascular responses – the translation of these findings into human physiology remains limited by the scarcity and methodological weakness of available clinical data (Table II, Figure 2).

The available human evidence is confined to small pilot interventions and observational case series, without randomization, blinding, or predefined clinical

endpoints. Consequently, no reliable conclusions can be drawn regarding efficacy, dose response relationships, mechanism specificity, or long-term safety. This disparity likely reflects unresolved translational challenges, including incomplete pharmacokinetic characterization, uncertain oral bioavailability, heterogeneity of dosing regimens, and the absence of biomarkers enabling confirmation of target engagement in humans.

Two principal strands dominate the literature. The first consists of preclinical experimental studies – largely in rat models – demonstrating cytoprotective, vasculoprotective, and regenerative effects across musculoskeletal, gastrointestinal, and neurovascular systems. Reproducible benefits, such as accelerated muscle healing after quadriceps reinsertion [47] and improved integrity of intestinal anastomoses in surgical models [48], support the internal consistency of peripheral tissue effects. Mechanistic investigations further implicate vascular and metabolic pathways involved in ischemia-reperfusion injury and tissue repair [49]. The second strand comprises narrative and systematic reviews that synthesize these findings while highlighting substantial risks, including non-certified compound use and lack of regulatory approval. Importantly, both strands converge on the conclusion that current evidence is insufficient to justify clinical application and that well-designed randomized trials are required [50].

Within the preclinical domain, the most coherent and reproducible signal arises from neurovascular injury models. In cerebral and hippocampal ischemia, BPC-157 consistently reduces functional deficits and modulates gene expression linked to cellular stress and inflammation (e.g., suppression of *Nos2* and NF-κB), while in spinal cord injury models it improves motor recovery and limits oedema and tissue damage [51]. Studies addressing vascular occlusion further support a role in microvascular stabilization and perfusion recovery [52]. However, across these models, mechanistic attribution remains largely inferential, as few studies employ pathway-specific inhibition or genetic strategies to establish causality. Behavioral and pain-related studies suggest neuromodulatory effects, including dose-dependent analgesia and attenuation of anxiety, depression, and psychosis-like phenotypes, with proposed involvement of dopaminergic, serotonergic, GABAergic, and NMDA systems [53]. Nevertheless, these findings show greater variability across experimental paradigms and are particularly sensitive to methodological factors, limiting their immediate translational relevance. Recent methodological advances have started to fill important gaps related to the absorption, distribution, and detection of BPC-157. Preclinical ADME (Absorption, Distribution, Metabolism, and Excretion) studies and isotope-based analytical methods now allow reliable identification of BPC-157 and its metabolites in biological samples, creating the basis for future pharmacokinetic and pharmacodynamic studies [54]. Human safety data remain limited but do not indicate relevant short-term adverse effects after intravenous or intra-articular administration [55,56]. However, these observations are insufficient to evaluate long-term safety or clinical efficacy. Regulatory factors further limit clinical translation. BPC-157 is classified by the World Anti-Doping Agency as a prohibited and non-approved substance, highlighting the gap between its commercial availability and the lack of regulatory approval for medical use [57]. Potential safety concerns therefore require careful consideration, particularly in relation to its pro-angiogenic effects, possible tumor-promoting activity, and unpredictable CNS effects linked to neurotransmitter modulation [31]. Available observational data and experimental screening approaches cannot replace properly designed phase I and II clinical trials [32,33]. Although the preclinical evidence base for BPC-157 is substantial and internally consistent with respect to cytoprotection, vascular repair, and neuroregeneration, decisive clinical validation is lacking. Progress will depend on rigorously designed, adequately powered randomized trials with predefined endpoints, robust pharmacokinetic and bioavailability studies, comprehensive safety evaluation, and independent replication of key findings [58]. Until such evidence is available, BPC-157 should be regarded as an experimental compound with mechanistic interest but unproven clinical utility.

CONCLUSIONS

Preclinical data indicate that BPC-157 acts as a pleiotropic cytoprotective and neuroregenerative peptide integrating inflammatory, vascular, and neurotransmitter pathways. By modulating NO/eNOS and VEGF-mediated signaling and stabilizing epithelial and endothelial barriers, it supports tissue repair across gastrointestinal and neural systems.

Human evidence remains limited to small, uncontrolled studies confirming short-term safety but not efficacy. Robust, randomized clinical trials with validated pharmacokinetic profiling are essential to define dosing, bioavailability, and long-term safety.

Until such data emerge, BPC-157 should be viewed as a promising yet unproven therapeutic candidate bridging gastrointestinal cytoprotection and neuroregeneration.

Authors' contribution

Study design – M. Waluga, B. Pietrzyk
Data collection – M. Waluga, B. Pietrzyk
Manuscript preparation – B. Pietrzyk, M. Waluga
Literature research – B. Pietrzyk, M. Waluga
Final approval of the version to be published – B. Pietrzyk

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