Pentadeca Arginate and BPC-157: Medical Evidence

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Abstract

Pentadeca arginate and BPC-157 are gaining attention in the medical field for their regenerative and anti-inflammatory properties. Peptides like BPC-157, originally derived from gastric juice, have demonstrated potential in reducing inflammation and supporting tissue repair, while pentadeca arginate, a newer synthetic peptide, is designed to enhance these effects. Both compounds hold promise across various applications, from treating injuries to promoting tissue repair and supporting gut health. However, clinical studies on the use of pentadeca arginate and BPC-157 remain limited.

The primary goal of this white paper is to evaluate existing research on these peptides, offering insight into their mechanisms of action and therapeutic potential. By summarizing the benefits, safety profiles, and emerging applications of pentadeca arginate and BPC-157, this whitepaper provides a comprehensive view of their role in modern regenerative medicine. It further underscores the need for additional research to explore the long-term efficacy and safety of these peptides, supporting their potential integration into contemporary medical treatments.

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Introduction

Pentadeca arginate (PDA) is a synthetic peptide that promotes tissue regeneration and recovery. Derived from Body Protection Compound 157 (BPC-157), a naturally occurring peptide in human gastric juice, PDA retains the same 15 amino acid sequence as BPC-157, enhanced with an arginate salt for increased stability. This modification expands its potential applications, positioning PDA as a promising tool in muscle growth, anti-aging protocols, sports performance, and cellular health.

Both PDA and BPC-157 are emerging therapeutic peptides garnering interest for their role in tissue repair, wound healing, and anti-inflammatory treatments. Although still in the early stages of application, particularly for PDA, these peptides are under investigation as innovative solutions for conditions associated with tissue damage, chronic inflammation, and musculoskeletal injuries. Research is also exploring off-label uses, such as for injury recovery, neuroprotection, and gut health.

The mechanisms of action associated with pentadeca arginate and BPC-157 suggest a transformative potential for therapeutic approaches within regenerative medicine. This white paper examines current scientific findings on PDA and BPC-157, highlighting their applications and future directions in peptide-centered therapies.

Problem Statement

The role of peptides in inflammation regulation and tissue repair is gaining recognition, with increasing interest in their potential to address a range of health conditions. While pentadeca arginate (PDA) and BPC-157 have shown considerable promise in preclinical studies, further exploration is needed to clarify their mechanisms of action, safety, and long-term efficacy—particularly in human applications. As demand for innovative solutions in regenerative medicine continues to grow, advancing research on PDA and BPC-157 is essential to

understanding their full therapeutic potential and the balance of benefits and risks in modern treatment practices.

Literature Review

This white paper synthesizes a broad spectrum of studies investigating the therapeutic effects of pentadeca arginate (PDA) and BPC-157, with a focus on their applications in tissue repair, inflammation management, and injury recovery. Noteworthy contributions include the research by **J. Vukojević et al.**, who explored the peptide's pleiotropic effects, revealing its ability to mitigate neuronal damage post-stroke and influence behavioral disorders. **M. Tudor et al.** further demonstrated the peptide's efficacy in traumatic brain injury, noting reduced damage and brain edema, along with improved early recovery outcomes.

P. Sikirić et al. contributed to understanding BPC-157's interaction with nitric oxide pathways, showing that it can help maintain blood pressure and protect gastric mucosal integrity. **C.H. Chang et al.** studied the peptide's role in tendon healing, illustrating how it promotes fibroblast survival and migration via the activation of the FAK-paxillin pathway.

In musculoskeletal recovery, **M. Staresinic et al.** and **T. Cerovecki et al.** highlighted BPC-157's potential in tendon and ligament repair, demonstrating consistently accelerated healing processes. Extending its applications further, **R. Kličeк et al.** examined BPC-157's therapeutic potential for inflammatory bowel disease and multiple sclerosis, suggesting a broader range of inflammatory conditions where it may be beneficial. Additionally, **M.J. Hsieh et al.** investigated the peptide's pro-angiogenic properties, revealing increased vessel density and enhanced blood flow in ischemic muscles.

Other notable studies include **A. Krivic et al.** on tendon-to-bone healing, and **A. Zemba Cilic et al.**, who examined BPC-157's effects on neurological disorders such as schizophrenia and its modulation of the nitric oxide system. **D. Gwyer et al.** and **S. Seiwerth et al.** provided comprehensive overviews of the peptide's regenerative properties across various tissues, including the gastrointestinal, neural, and musculoskeletal systems.

Collectively, these studies underscore the potential of pentadeca arginate and BPC-157 as promising agents in regenerative medicine, offering valuable insights into their mechanisms of action and therapeutic potential for treating diverse conditions.

Methodology

The primary goal of this white paper is to assess and investigate the therapeutic effects of pentadeca arginate (PDA) and BPC-157 across a range of physiological and pathological conditions, particularly those associated with injury recovery, tissue repair, and inflammation. The studies reviewed in this white paper examine the effectiveness of these peptides in promoting muscular, neural, and vascular healing within preclinical models and in early-stage human applications.

Additionally, this white paper provides a comprehensive review of BPC-157's impact on various health outcomes, including neural damage, traumatic brain injury, stroke recovery, cardiovascular health, and tendon and ligament repair. We evaluate the mechanisms behind these effects, focusing on BPC-157's interactions with angiogenesis, nitric oxide pathways, and

gene regulation. Understanding these mechanisms provides greater insight into the peptide's role in cytoprotection and tissue regeneration.

The evidence covered in this white paper includes studies using animal models to analyze BPC-157's therapeutic potential across diverse conditions, such as ischemia/reperfusion injury, traumatic injuries, and musculoskeletal disorders. By evaluating these findings, this white paper aims to highlight the peptide's promise for treating physical injuries as well as systemic and chronic conditions, while also addressing potential limitations and areas where further research is warranted.

Results/Findings

J. Vukojević et al. reviewed the pleiotropic beneficial effects of the stable pentadecapeptide BPC-157 and found that this peptide exhibits a direct therapeutic effect in rats following a stroke. For example, BPC-157 may counteract the injuries due to hippocampal ischemia/reperfusion. In the rats subjected to ischemia, this peptide was administered during reperfusion and it counteracted both early and delayed neural damage. Vukojević and the team reported that BPC-157 treatment promoted recovery from severe muscle weakness that appears alongside brain lesions. Other findings of this review included the beneficial effect of BPC-157 on behavioral disorders and schizophrenia-like symptoms. Moreover, this peptide can help treat spinal cord injury.

The abovementioned review relied on a study also conducted by **Vukojević et al,** whose main objective was to investigate yet undescribed therapy effect of the stable gastric pentadecapeptide BPC-157 in hippocampal ischemia/reperfusion injuries following bilateral clamping of the common carotid arteries in rats. They found that in operated rats, at 24 and 72 hours of the reperfusion, the treatment counteracted early and delayed neural hippocampal damage after which the animals achieved full functional recovery. Vukojević and the team concluded that this peptide could be considered as a therapeutic solution for stroke. The researchers also examined changes in messenger RNA (mRNA) expression in the brain one and 24 hours following the injury to determine the potential mechanism of action of this peptide. Treatment with BPC-157 resulted in upregulation of *Egr1, Akt1, Src, Kras, Foxo, Vegfr2, Srf, Nos1,* and *Nos3* and downregulation of *Nos2* and *Nfkb*. Upregulation of *Egr1* and *Vegfr2* indicates that BPC-157 holds vascularization properties, which explains its ability to modulate ischemia/reperfusion injury.

M. Tudor et al. suggest that BPC-157 led to a significant attenuation of damage following traumatic brain injury (TBI), improved early outcomes, and minimal postponed mortality through a 24-hour post-injury period. The traumatic lesions were less intense and consecutive brain edema had significantly improved as well.

P. Sikirić et al. reported that BPC-157 could interfere with the effects of nitric oxide on blood pressure maintenance and gastric mucosal integrity in a specific way, particularly with l-arginine. It has a more superior or particularly different effect than nitric oxide. In gastric mucosa from rat stomach tissue homogenates, BPC-157 (when administered in the same dosage as l-arginine) produced a comparable generation of nitric oxide, but its effect couldn't be inhibited by N(G)-nitro-l-arginine methylester (L-NAME).

C.H. Chang et al. found that BPC-157 promotes the ex vivo outgrowth of tendon fibroblasts from tendon explants, cell survival under stress, as well as the in vitro migration of tendon fibroblasts,

which could be mediated by the FAK-paxilin pathway activation. Their study showed this peptide didn't affect cell proliferation of cultured tendon fibroblasts derived from rat Achilles tendon when evaluated by MTT assay, but the survival of cells treated with BPC-157 improved under the H(2)O(2) stress.

M. Staresinic et al. published a report on the complete transaction of major muscle (quadriceps) and the systemic peptide treatment. They found that stable gastric pentadecapeptide BPC-157 speeds up the healing of transected Achilles tendon. The study also showed that BPC-157 consistently improves healing throughout the 72 days. More specifically, it improves biomechanic properties, function, microscopy/immunochemistry, and macroscopic presentation. Staresinic and the team concluded that posttransection healing consistently improved thereby suggesting the potential role of BPC-157 in treating muscle disorders.

T. Cerovecki et al. successfully used stable gastric pentadecapeptide BPC-157 to improve the healing of acute ligament injury, which is why they concluded it can support the management of injuries within further ligament therapy. Following the medial collateral ligament (MCL) transaction, BPC-157 was effective in rats when administered once a day intraperitoneally or locally as a thin layer at the site of injury. Additionally, BPC-157 was effective when administered per-orally. Rats experienced functional, biochemical, macroscopic, and histological healing improvements.

A. Krivic et al. found that direct tendon-to-bone healing using stable gastric pentadecapeptide BPC-157 without a carrier may successfully exchange the present reconstructive surgical methods. In the study, Krivic and the team noticed that BPC-157 improves healing functionality after Achilles detachment and addresses other parameters including macroscopic, and immunochemistry. Moreover, 6-alpha-methylprednisolone consistently worsens healing, while BPC-157 significantly decreases healing aggravation caused by this compound.

R. Kliček et al. published experimental evidence that advocates the use of BPC-157 in multiple sclerosis and inflammatory bowel disease therapy. In their study, BPC-157 induced an efficient healing of cysteamine colitis and colon-colon anastomosis. Rats that received cuprizone exhibited an exaggerated and accelerated damaging process affecting primarily corpus callosum, laterodorsal thalamus, nucleus reunions, and anterior horn motor neurons. A combination of BPC-157 and cuprizone exhibited less nerve damage, particularly in most affected areas. Additionally, this peptide counteracted cerebellar ataxia and impaired forelimb function.

M.J. Hsieh et al. explored the potential therapeutic effect and pro-angiogenic activity of BPC-157. They reported that this peptide could increase vessel density in vivo and in vitro alike. The peptide is also capable of speeding up the recovery of blood flow in the ischemic muscle of the rat's hind limb. In vitro study on human vascular endothelial cells further confirmed that BPC-157 improved expression of mRNA and protein *VEGFR2*, but not *VEGF-A*. Hsieh and the team concluded that BPC-157 promotes angiogenesis in CAM assay and tube formation assay. It also accelerates the blood flow recovery and vessel number and promotes *VEGFR2* internalization associated with *VEGFR2-Akt-eNOS* activation.

In a study by **A. Duzel et al.**, stable gastric pentadecapeptide BPC-157 exhibited antioxidant activity. More precisely, the peptide therapy attenuated or counteracted the ischemia/reperfusion injury tackled MDA oxidative stress, and normalized nitric oxide tissue values. Duzel and the team concluded the study by confirming that BPC-157 may offer a fundamental treatment

through cytoprotection and endothelium protection that is crucial for quickly restoring blood supply to the ischemically injured area.

S. Gojković et al. found that BPC-157 counteracts Budd Chiari syndrome in rats. The peptide counteracted increased P wave amplitude, tachycardia, and ST-elevation, or right heart failure from acute thrombotic coronary occlusion. Moreover, BPC-157 antagonized portal and caval hypertension and aortal hypotension, and it decreased refractory ascites. Interestingly, the peptide attenuated thrombosis of portal vein tributaries, inferior vena cava, and hepatic and coronary arteries.

A. Zemba Cilic et al. reported that BPC-157 directly inhibited the L-NAME high dose-induced catalepsy and positive-like symptoms of schizophrenia. They found that given alone, BPC-157 or l-arginine, counteracted the amphetamine-, apomorphine-, and MK-801-induced effect, haloperidol-induced catalepsy, and chronic methamphetamine-induced sensitization. Zemba and the team also found that BPC-157 maintains its counteracting effect even in the presence of NOS blockade or nitric oxide system overstimulation.

D. Gwyer et al. published a review explaining that all studies exploring BPC-157 have demonstrated positive and swift healing effects for various types of injuries, traumatic and systemic alike, and for a wide range of soft tissues. That said, most studies have been conducted on animal models and the effectiveness of this peptide on human subjects is yet to be confirmed. Despite these issues, it is still evident that BPC-157 has a huge potential as a therapy to conservatively treat or support recovery in hypovascular and hypervascular soft tissues such as ligaments and tendons.

S. Seiwerth et al. confirmed that this peptide can rapidly increase several genes expression in rat excision skin wounds. This could define healing in tissues present in the gastrointestinal tract, tendons, ligaments, nerves, spinal cord, muscle, bone, cornea, and blood vessels.

Discussion

The experimental evidence and studies evaluated in this white paper offer important insights into the therapeutic potential of pentadeca arginate and BPC-157, mainly in animal models, with implications for human applications. A vast majority of research focuses on BPC-157, due to its ability to support tissue repair, decrease inflammation, and counteract traumatic and ischemic injuries. Since pentadeca arginate is the synthetic form of BPC-157, its therapeutic effects can be drawn from the substantial body of evidence surrounding BPC-157, as both compounds have practically the same biological properties and mechanisms of action.

The reviewed studies consistently showcased that BPC-157 improves outcomes in various conditions, including neural damage after a stroke, traumatic brain injuries, muscle and tendon healing, mental health conditions, and cardiovascular damage. For instance, research by Vukojević et al. revealed that this peptide supports neural recovery following ischemic injuries, and additional studies showed its capability of decreasing brain edema and improving functional recovery associated with traumatic brain injury. These findings shed more light on the multifaceted role of BPC-157 in healing and tissue protection.

That said, although this peptide exhibits outstanding efficacy in animal models, its effects on human subjects remain largely unexplored. While the peptide shows potential to manage conditions such as spinal cord injury, ligament damage, and even multiple sclerosis, as suggested by Sikirić and the team, the lack of clinical data in humans stands as a limitation.

However, the existing body of evidence emphasizes the potential of BPC-157 for promoting angiogenesis, muscle repair, and neuroprotection, all of which are relevant to therapeutic approaches involving pentadeca arginate as well.

The overall findings of this white paper suggest that BPC-157, and by extension pentadeca arginate, could act as a valuable therapy for injuries and conditions affecting hypervascular and hypovascular tissues. Although the body of evidence on this peptide is substantial, there is still a need to carry out more extensive clinical trials in order to investigate the long-term effectiveness and safety of this peptide in human subjects. Further research is particularly necessary on the synthetic form of this peptide i.e. pentadeca arginate. Continuous research of this peptide could ensure it becomes a vital component of tissue healing protocols and regenerative medicine.

Conclusion

Peptide BPC-157 and its synthetic form, pentadeca arginate, play a major role in supporting tissue repair, decreasing inflammation, and promoting recovery from various conditions and injuries. Research shows that BPC-157 has the potential to enhance muscle and tendon healing, improve neuronal recovery, and promote vascular health. For that reason, the peptide could be a useful therapeutic option for trauma-related injuries and chronic conditions.

The evidence suggests that BPC-157 provides multiple benefits, including improvements in recovery from ischemic and traumatic injuries, faster healing of soft tissues, and potential protective effects against conditions such as inflammatory bowel disease and multiple sclerosis. Even though studies yield promising findings, this highlights the need for significant clinical trials in humans. Studies on human subjects would offer a better understanding of the long-term safety and full potential of this peptide. Careful monitoring and continued investigation are essential to fully realize the benefits of BPC-157 and its synthetic form.

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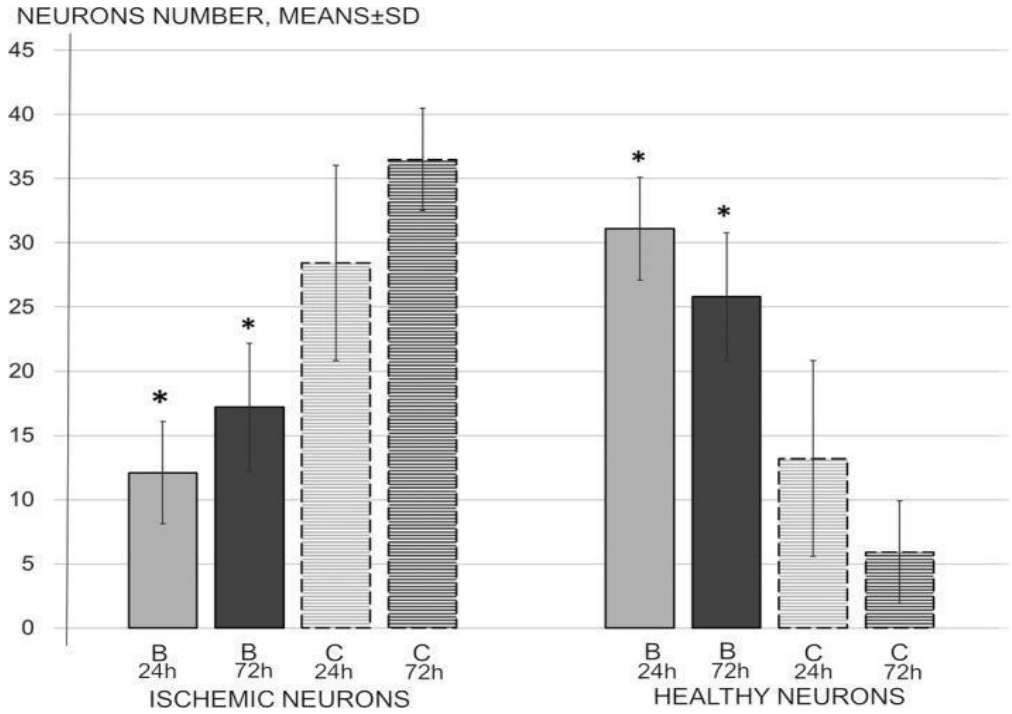
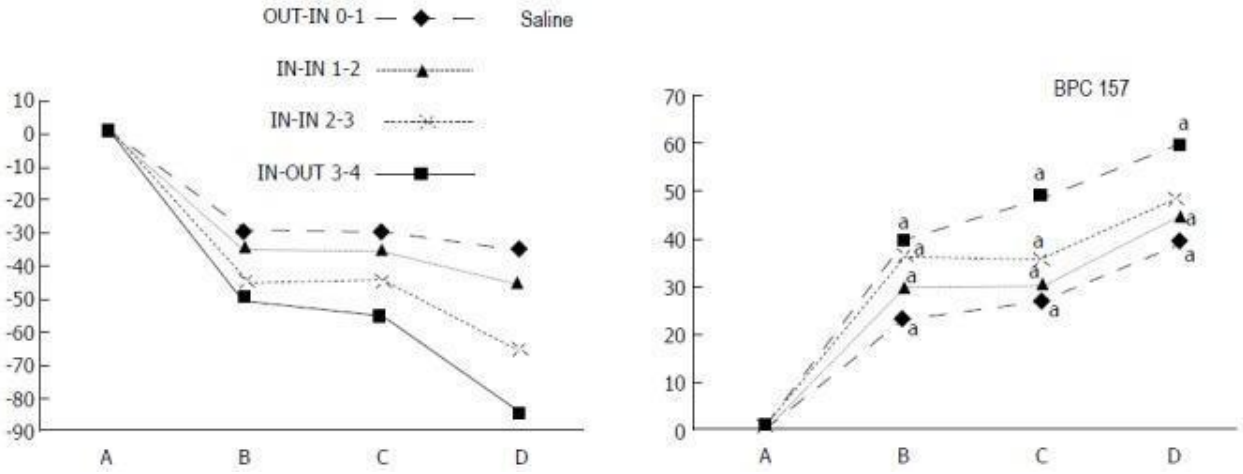
Appendices



Number of ischemic and healthy neurons at 24 and 72 hour reperfusion time.

Vukojević J, Vrdoljak B, Malekinušić D, Siroglavić M, Milavić M, Kolenc D, Boban Blagaić A, Batelja L, Drmić D, Seiverth S, Sikirić P. The effect of pentadecapeptide BPC 157 on hippocampal ischemia/reperfusion injuries in rats. Brain Behav. 2020 Aug;10(8):e01726. doi: 10.1002/brb3.1726. Epub 2020 Jun 18. PMID: 32558293; PMCID: PMC7428500.



Percent of blood vessels present between arcade vessels.

Duzel A, Vlainic J, Antunovic M, Malekinusic D, Vrdoljak B, Samara M, Gojkovic S, Krezic I, Vidovic T, Bilic Z, Knezevic M, Sever M, Lojo N, Kokot A, Kolovrat M, Drmic D, Vukojevic J, Kralj T, Kasnik K, Siroglavic M, Seiwerth S, Sikiric P. Stable gastric pentadecapeptide BPC 157 in the treatment of colitis and ischemia and reperfusion in rats: New insights. World J Gastroenterol.

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Conflicts of Interest

The authors declare that they have no conflicts of interest to disclose.

Contact Information

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