



BPC-157 - Investigating the Peptide's Role in Cellular and Tissue Repair

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History

BPC-157, also known as PL 14736, PL-10, Bepecin, or PLD 116 is a 15 amino acid peptide with the sequence (three letter code): Gly-Glu-Pro-Pro-Gly-Lys-Pro-Ala-Asp-Asp-Ala-Gly-Leu-Val. It was first isolated from stomach tissue in 1991 by a group led by P. Sikiric at the university of Zagreb, Croatia. Due to its reported beneficial effects on wound healing, the peptide has sparked further experiments and has continuously been experimented with to this day.

The peptide is banned by the World Anti-Doping Agency in 2022 under the S0 category of non-exempt substances.

Animal Studies

Injury and healing

The observation that stomach wounds could be treated with

BPC-157 and its origin from gastric tissue led to experiments exploring the effect of BPC-157 on the stomach. Initial work explored dosing of the drug and under which circumstances healing was most effective.¹ NSAIDs like ibuprofen or naproxen are known to cause stomach ulcerations in some patients and BPC-157 is likely to help in such cases, as evident by animal experiments.² BPC-157 was able to reduce the number of ulcerations and lesions in blood vessels and organs from alcohol application in rats.³

Another approach focused on the potential superficial wound healing. For example, it was found that BPC-157, either injected, dissolved in drinking water or applied as a topical cream, was able to accelerate the wound healing process and leads to better results compared to untreated animals.⁴ A similar study, which investigated burn-

healing and gastric lesions in mice has confirmed these findings.⁵ Better healing of traumatic brain injury was also reported in mice who received 10 ng/kg BPC-157 per injection after the injury.⁶

Similarly, a further study on the topic of wound healing examined rats with skin wounds and abdominal surgery wounds. It also observed the capacity of the animals to form new blood vessels was increased. BPC-157 had a positive effect on tissue regeneration, showing an accelerated formation of extracellular matrix and cells.⁷ Increased healing capacity was also demonstrated in cecum⁸ and other parts of the gastrointestinal system after artificial injury.⁹

The application of corticosteroids (cortisol derivatives) to wounds is known to impair the healing of wounds. A study on mice with burn injuries showed that BPC-157 consistently improved healing

and counteracted the corticosteroid induced impairment of the healing process. The peptide was also observed to inhibit the corticosteroid induced suppression of the immune system.¹⁰

Fistulas in the GI tract can occur due to a blockage in the NO-system, which seems to be one of the main systems affected by BCP-157. Rats with esophageal fistulas, which would have been lethal without treatment, showed accelerated healing and increased survival if treated with BCP-157, either given orally or by injection. L-arginine, a precursor of NO, did also improve the clinical conditions of the rats, although to a lesser extent, while N(ω)-nitro-L-arginine methyl ester (L-NAME), a blocker of NO synthesis, clearly worsened the condition of the rats, even if L-arginine was present. Interestingly, BCP-157 was able to counteract L-NAME, indicating a different route of NO generation.¹¹ This relationship was observed again in further studies.¹²

BPC-157 was shown to promote healing demonstrating particular angiogenic/angiomodulatory potential. A direct effect on the formation of new blood vessels in cell culture could not be observed. The effect seems to be connected to an increased production of vascular endothelial growth factor (VEGF), which indicates the accelerated healing of wounds caused by BCP-157 by the upregulation of this molecule.¹³ In total, there is a lot of evidence that BCP-157 is able to promote the growth of blood vessels.¹⁴

Effects on the Nervous System

Besides the effects on wound healing, there are number of studies that show there is a direct effect of BCP-157 on the nervous system. The exact nature of this effect is not clear, but it seems BCP-157 attenuates neurophysiological pathways to return to normal function in unusual circumstances.

Serotonin syndrome is a dangerous condition occasionally seen in patients which receive high doses of serotonin increasing medication. Symptoms include tachycardia, sweating, fever, tremor and seizures. Rats who have received serotonin in high doses showed reduced clinical symptoms from serotonin syndrome if they had previously received a 10 pg/kg injection of BCP-157.¹⁵ There is also a study that has highlighted a potential use of BCP-157 on preventing long-term damage to the nervous system induced by amphetamines.¹⁶

Mice treated with 2 drugs that lead to the development of Parkinson's symptoms, MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) and reserpine showed typical behaviour of these compounds. In both cases BCP-157 inhibited the development of symptoms evoked by these drugs and could reverse them if it was given with a delay. It did also inhibit the formation of stomach lesions usually observed in animals treated with MPTP. These results indicate that BCP-157 has an antagonistic effect to these two drugs, which both can damage certain neuron populations in the brain.¹⁷ Similarly, BCP-157

drastically reduced the side effects of other neuroleptic drugs haloperidol, fluphenazin, sulpirid and clozapine, which all leads to a blockade of D2-receptors, a subtype of the dopamine receptor. Together, these findings indicate that pentadecapeptide BPC-157 interacts with the dopamine system, both centrally and peripherally.¹⁸

Digitalis, a drug sometimes prescribed to patients suffering from heart failure, causes cardiac arrhythmia if overdosed. It changes the flow of electrolytes within the heart muscle cells which can potentially lead to life-threatening changes in heart muscle activity. BPC-157 did partially restore normal electrical activity of the heart in mice with digitalis poisoning at doses of 50 μ g. Fatal outcome was either avoided (50 μ g), reduced (10 μ g), or only delayed (10 ng). The beneficial effect of BPC-157 was attributed to its interaction with the nitric oxide (NO) system.¹⁹ In general, BCP-157 seems to protect the heart conduction system from toxic damage and recover electrolyte disbalances.²⁰ The effect of potassium chloride on the heart muscle, which usually induces life threatening arrhythmia, was also diminished by BCP-157.²¹

A study in 2010 focused on the healing of rat nerve fibers and the influence of BPC-157. If BPC-157 (10 μ g, 10 ng/kg) was applied shortly after injury either intraperitoneally, intragastrically or locally, the animals exhibited faster regeneration (an increased density and size of regenerative fibers, uniform target orientation of regenerative fibers, and higher

proportion of neural vs. connective tissue). The function of the lost nerve was also regained quicker compared to the control group.²²

Rats who received BCP-157 were also reported to have a reduced symptom burden if the superior sagittal sinus, a large venous blood vessel in the brain, was occluded. The authors assumed that this was due to the blood vessel dilating effect of BCP-157, which permits more blood to bypass the blocked site.²³

Clinical Trials

A clinical study in 2016 with 42 healthy volunteers investigating safety and pharmacokinetics was completed. However, no results from this study were published. (NCT02637284)

Conclusion

There are numerous studies on the effects of BCP-157 on injuries of lesions of different type and severity. Together, these studies suggest that BCP-157 promotes wound healing via increased oxygen supply through new blood vessels and dilation of existing vessels through the release of nitric oxide. There is also experimental evidence that points toward a stimulating effect of fibroblast mediated healing of wounds. The exact mechanism by which BCP-157 exerts these effects are unknown, but it is likely that VEGF and NO play a role as a mediator. Hence BCP-157 may be useful to treat internal injuries by oral update or surface injuries by the application of BCP-157 containing crèmes and lotions.

Even though there are a lot of published papers about the positive effects of BCP-157, the overwhelming majority of these data stem from the same group of researchers. Hence, it would be of great value to confirm these results by independent groups. Also, data from clinical trials is not available and almost all data is from rats or mice, a minority is observed in cell culture.

No toxicological data is reported but is likely practically not existent for oral or topical use.

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