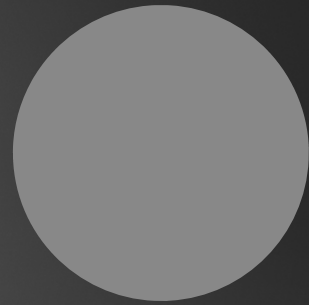


# BPC -157

BODY PROTECTION COMPOUND  
DOES THIS PEPTIDE PROMOTE HEALING MAGIC?  
NO TOXICITY?  
NO SIDE EFFECTS?



PEPTIDES

## Learning Objectives

- ▶ Define BPC-157 and its qualities
- ▶ Identify physiological systems where BPC-157 has been show to have regenerative effects



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## BPC-157

- ▶ Biologically active Peptide fragment is a sequence of 15 amino acids
- ▶ Isolated from Gastric Juice
- ▶ Can be obtained high pressure liquid chromatography purification
- ▶ Highly stable , resistant to hydrolysis and enzyme digestion
- ▶ Can be dissolved in water and given orally
- ▶ No carrier molecule required
- ▶ Can be administered sub q, intramuscular, intranasal

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## BPC 157

- ▶ This peptide has significant anti-inflammatory modulating effects
- ▶ Peptide promotes tissue healing through signaling pathways
- ▶ Peptide up regulates gene transcription to influence these healing factors
- ▶ This peptide has no primary effect ,it is all about the **signaling!!!!**

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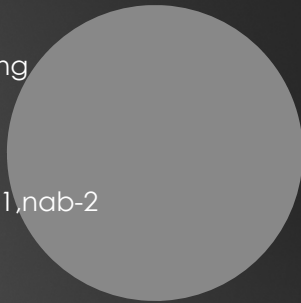
## BPC-157 Influence

- ▶ Repair Tendon
- ▶ Repair Muscle
- ▶ Repair intestine
- ▶ Repair bone
- ▶ Repair teeth
- ▶ Repair brain
- ▶ Repair the cornea
- ▶ Up regulates GH receptors?



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## BPC 157

- ▶ Can modulate Angiogenesis in muscle and tendon healing
  - ▶ Can protect the endothelium
  - ▶ Influence the NO system
  - ▶ Response to vessel injury stimulates gene expression-EGR-1,nab-2
- 

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## Muscle and Tendon healing

- ▶ Similar process
- ▶ Muscle set up to heal better than tendon
- ▶ Muscle-Increased Vascular network, metabolic active tissue, satellite cells, stem cells
- ▶ Tendon- hypovascular, hypocellular and hyponeural
- ▶ Both under regulation of VEGF, FGF, TGF- $\beta$ , TNF, and NO



PEPTIDES

# BPC 157

L. BRCIC<sup>1</sup>, I. BRCIC<sup>2</sup>, M. STARESINIC<sup>3</sup>, T. NOVINCAK<sup>3</sup>, P. SIKIRIC<sup>3</sup>, S. SEIWERTH<sup>1</sup>

MODULATORY EFFECT OF GASTRIC PENTADECAPEPTIDE BPC 157  
ON ANGIOGENESIS IN MUSCLE AND TENDON HEALING

<sup>1</sup>Institute of Pathology, University of Zagreb Medical School, Zagreb, Croatia; <sup>2</sup>Clinical Department of Pathology and Cytology,

University Hospital Center Zagreb, Zagreb, Croatia; <sup>3</sup>Department of Pharmacology, University of Zagreb Medical School,

Zagreb, Croatia

PEPTIDES

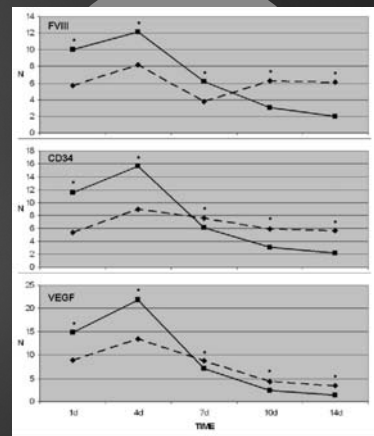
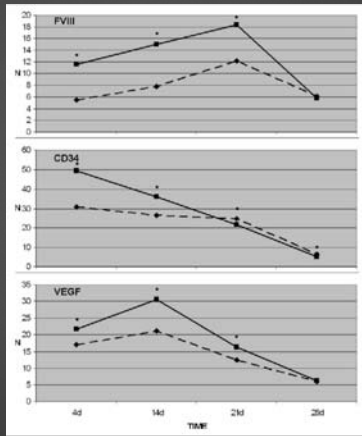
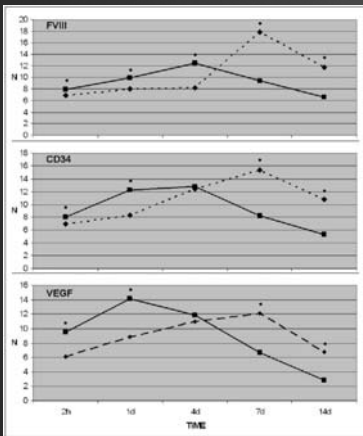


## BPC 157 Bricic

- ▶ Showed that BPC 157 has ability to up regulate VEGF in muscle tendon healing
- ▶ In vivo and in vitro

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# BPC 157 Crush and Transection



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## BPC-157 Angiogenesis

- ▶ Charts provide evidence of BPC 157 influence on increased angiogenesis on crushed muscle, transected muscle and transected tendon
- ▶ Present on endothelial cells
- ▶ Followed with endothelial cell antigens FVIII( platelet adhesion and aggregation)
- ▶ CD34( leukocyte adhesion and endothelial cell migration)
- ▶ VEGF presentation( primary angiogenesis)( mitogen for vascular endothelial cells)

PEPTIDES

## BPC 157 Cell culture vs in-vivo

- ▶ Showed no direct effect of BPC 157
- ▶ But in-vivo model showed modulating effect( signaling) of pro-angiogenic factors and better healing , faster healing and more adequate healing environment.

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## BPC -157 other factors on injured tissue

- ▶ Decrease inflammatory response
- ▶ Decrease leukotriene B4
- ▶ Decrease thromboxane B2
- ▶ Decrease myeloperoxidase



PEPTIDES

## BPC -157 further evidence

- ▶ Ivetic Tkalcevic V, Cuzic S, Brajsa K, et al. Enhancement by PL 14736 of granulation and collagen organization in healing wounds and the potential role of egr-1 expression. Eur J Pharmacol 2007; 570: 212-221.

Looked at BPC 157 in comparison to PDGF-BB in diabetic mice and tissue granulation. BPC stimulates mRNA-EGR-1- same effects VEGF on cells

PEPTIDES

## BPC 157 influence on GH receptors

- ▶ Chang, Chung-Hsun, et al. "Pentadecapeptide BPC 157 enhances the growth hormone receptor expression in tendon fibroblasts." *Molecules* 19.11 (2014): 19066-19077.
- ▶ Rat study evaluating fibroblast proliferation showed an increased gene expression up regulation of the GH receptors in the tendon fibroblast.

PEPTIDES

## Tendon healing

- ▶ Inflammation
- ▶ Regeneration
- ▶ Remodeling



PEPTIDES



## Tendon Healing-Regeneration

- ▶ Tendon fibroblast migration and proliferation at site of injury
- ▶ Extracellular matrix formation of glycoproteins and types of collagens (tendons type I and Type III)
- ▶ Healing produces weak repair

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## Tendon healing –Growth Factors

- ▶ Insulin derived growth factor
- ▶ Platelet derived growth factor
- ▶ Transforming Growth Factor- Beta
- ▶ Basic fibroblast growth factor
- ▶ Vascular endothelial Growth factor
- ▶ Growth Hormone



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## BPC 157 increasing GH expression

- ▶ GH promotes cell regeneration and proliferation
- ▶ Increase secretion of collagens
- ▶ Direct activation of tyrosine kinase
- ▶ Indirect effect by induction of IGF-1



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## BPC-157 GH receptor mechanism

- ▶ Effect of BPC 157 on rGH receptor increased with time
- ▶ The present study, for the first time, demonstrated that the expressions of growth hormone receptor at both the mRNA and protein levels in tendon fibroblasts were increased by BPC 157
- ▶ GH increased JAK2 proteins( JAK-STAT signaling pathway) in treated fibroblast with BPC 157

PEPTIDES

## BPC 157 Medial Collateral Ligament

- ▶ Cerovecki, Tomislav, et al. "Pentadecapeptide BPC 157 (PL 14736) improves ligament healing in the rat." *Journal of orthopaedic research* 28.9 (2010): 1155-1161.
- ▶ Study validated not just microscopic regeneration but also functional recovery making this clinically relevant

PEPTIDES

## BPC -157 collateral Ligament

- ▶ Microscopic and macroscopic evaluation showed outcome close to non injured ligament
- ▶ Granulation tissue faster and better organization of collagen( more longitudinal)
- ▶ Initially more of type I collagen
- ▶ Inflammatory cells initially reduced more abundant fibrin and thicker
- ▶ BPC 157 is more active than recombinant human platelet-derived growth factor homodimer of B-chains (PDGF-BB) in stimulating early collagen organization and expression of the egr-1 gene<sup>12</sup> and its repressor nab2.

PEPTIDES

## BPC -157 Medial collateral - Relevance

- ▶ BPC 157 ligament healing may be clinically relevant (i.e., no knee joint contracture, no obvious valgus instability, preserved muscle motor function and walking pattern), thus, the significant knee joint failure counteracted (as important proof of the activity that is lacking in the standard peptide)

PEPTIDES

## BPC 157 tendon-bone healing

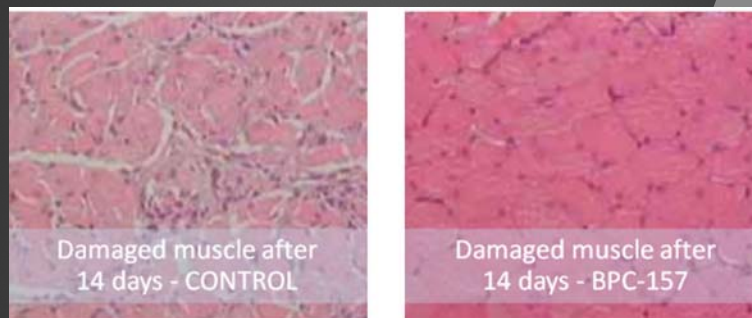
- ▶ Krivic, Andrija, et al. "Achilles Detachment in Rat and Stable Gastric Pentadecapeptide BPC 157: Promoted Tendon-to-Bone Healing and Opposed Corticosteroid Aggravation." *Journal of orthopaedic research* 24.5 (2006): 982-989

PEPTIDES



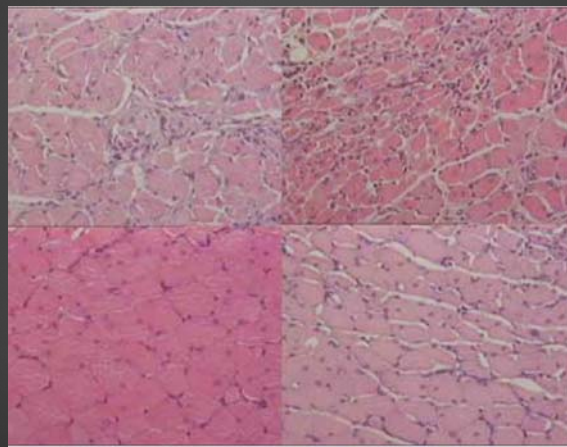
## BPC -157 Steroid damage

Pevec, Danira, et al. "Impact of pentadecapeptide BPC 157 on muscle healing impaired by systemic corticosteroid application." *Medical Science Monitor* 16.3 (2010): BR81-BR88.



PEPTIDES

# Corticosteroid and BPC-157



PEPTIDES

## Steroid damage to muscle cell

- ▶ corticosteroid course: early transient recovery, a sparing effect on the local muscle tissue with inhibition of the inflammatory response, followed by unwanted atrophy and failed collagen synthesis by inhibition of the inflammatory response in the long term.
- ▶ BPC 157 can effectively counteract steroid effects to achieve normal healing

PEPTIDES

## Steroids muscle effect

- ▶ Steroids affect NO system alter the expression of inducible NITROUS OXIDE SYNTHETASE and GTP-cyclohydrolase I (GTP-CH1) rate limiting enzyme in production of i-nos cofactor
- ▶ So expression of I-NOS and GTP suppressed by glucocorticoid
- ▶ BPC 157 modulates NO system, strong angiogenic effect, protects endothelium and counter acts endothelin over expression. ( cause of scar tissue)

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## BPC 157 Bone healing

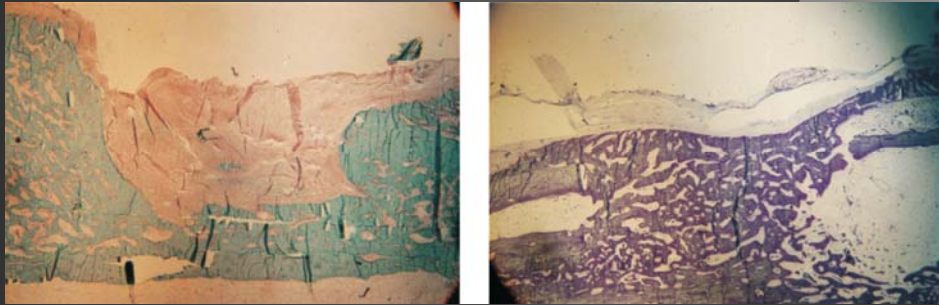
- ▶ Osteogenic Effect of a Gastric Pentadecapeptide, BPC-157, on the Healing of Segmental Bone Defect in Rabbits: A Comparison with Bone Marrow and Autologous Cortical Bone Implantation

B. ŠEBEČIĆ,<sup>1</sup> V. NIKOLIĆ,<sup>2</sup> P. SIKIRIĆ,<sup>2</sup> S. SEIWERTH,<sup>2</sup> T. ŠOŠA,<sup>1</sup> L. PATRLJ,<sup>1</sup> Ž. GRABAREVIĆ,<sup>2</sup> R. RUCMAN,<sup>2</sup> M. PETEK,<sup>2</sup> P. KONJEVODA,<sup>2</sup> S. JADRIJEVIĆ,<sup>1</sup> D. PEROVIĆ,<sup>2</sup> and M. ŠLAJ<sup>2</sup>

Department of Surgery, Clinical Hospital "Merkur," and Departments of Pharmacology and Pathology and Anatomy, Medical and Veterinary Faculty, University of Zagreb, Zagreb, Croatia

PEPTIDES

# BPC 157 Bone healing



PEPTIDES

## BPC 157 Bone Healing

- ▶ Pentadecapeptide could protect endothelium and modulate the release of nitric oxide (NO) and it has angiogenic properties and would promote new vessels formation, an activity regularly impaired markedly in nonunion healing.
- ▶ Cells of bone periosteal, endosteal, and medullary canal have healing abilities it is possible there is some signaling from BPC-157.
- ▶ Gastrectomy causes osteoporosis, fractures . Non responsive to calcium or vitamin d supplementation

PEPTIDES

## BPC 157 Bone healing

- ▶ **Intra-muscular** administration of pentadecapeptide BPC-157 produced results comparable with percutaneous injection of autologous bone marrow, or autologous bone grafting (whereas its effectiveness could be seen also after local administration)
- ▶ Systemic as effective as local administration
- ▶ **Adherence to normal physiology** -no evidence for extracortical new bone formation, bony hypertrophy or ectopic bone formation was noted

PEPTIDES



## BPC-157 Ileoileal Anastomosis

- ▶ Stable Gastric Pentadecapeptide BPC 157 in Trials for Inflammatory Bowel Disease (PL-10, PLD-116, PL14736, Pliva, Croatia) Heals Ileoileal Anastomosis in the Rat

Tihomir Vuksic, Ivan Zoricic, Luka Brcic, Marko Sever, Robert Klicek, Bozo Radic, Vedran Cesarec, Lidija Berkopic, Neike Keller, Alenka Boban Blagacic, Neven Kokic, Ivan Jelic, Juraj Geber, Tomislav Anic, Sven Seiwerth, and Predrag Sikiric

Departments of Pharmacology and Pathology, Medical Faculty, University of Zagreb, Salata 11, POB 916, 10000 Zagreb, Croatia

PEPTIDES

## BPC 157 Bowel Healing

- ▶ improved wound/ intestinal anastomosis healing, adhesion prevention, collagen deposition, and anastomotic strength
- ▶ Advanced tensile strength (as a direct reflection of the successful repair process, while the loss of anastomotic strength characterizes the degradation of collagen)
- ▶ improved functional, biomechanical, macroscopic, and microscopic findings
- ▶ Clinical trials with Inflammatory Bowel Disease. Show no toxicity, no Gene alteration

PEPTIDES

## BPC 157 NSAID damage control

- ▶ Current Pharmaceutical Design, 2013, 19, 76-83
- ▶ Toxicity by NSAIDs. Counteraction by Stable Gastric Pentadecapeptide BPC 157

Predrag Sikiric\*, Sven Seiwert, Rudolf Rucman, Branko Turkovic, Dinko Stancic Rokotov, Luka Brcic, Marko Sever, Robert Klicek, Bozo Radic, Domagoj Drmic, Spomenko Ilic, Danijela Kolenc, Gorana Aralica, Hana Safic, Jelena Suran, Davor Rak, Senka Dzidic, Hrvoje Vrcic and Bozidar Sebecic

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PEPTIDES

## BPC 157 NSAID control

- ▶ Cytoprotective
- ▶ Counter action of prolonged bleeding time and thrombocytopenia
- ▶ Stomach – counter acts NSAID lesions
- ▶ Small Intestine- Counter acts NSAIDS effect on lesions and pyloric Sphincter( very important for healing of Duodenal ulcers)
- ▶ Large Intestine- protect against intestinal lesions-They also reestablished mucosal integrity (i.e., abolished or reduced gastric and intestinal lesions)
- ▶ Liver- protects against Hepatotoxicity- BPC 157 counteraction of paracetamol-, diclofenac- and ibuprofen-hepatotoxicity

PEPTIDES

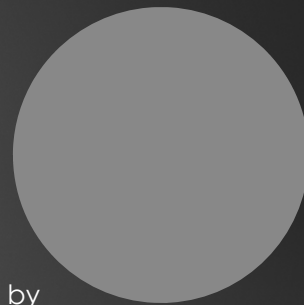
## BPC 157 NSAIDS

- ▶ Encephalopathy- throughout the paracetamol-, diclofenac- and ibuprofen-intoxication course ,BPC 157 eventually counteracted all NSAID-encephalopathies
- ▶ All three had different sites and mechanisms of action in the brain
- ▶ Paracetamol- inhibit brain cyclooxygenase , hyperammonemia and convulsions
- ▶ Diclofenac-brain edema, cyanosis, cerebral cortex and cerebellum,damaged red neurons, purkinjje cell damage
- ▶ Ibuprofen- Brain edema, cerebellum white matter more than grey

PEPTIDES

## BPC-157 thrombus protection and dissolution

- ▶ Cytoprotection- endothelium protection
- ▶ Acts against active thrombus
- ▶ Counter acts bleeding time and thrombocytopenia
- ▶ Works both sides of the equation
- ▶ Possible because of wound healing abilities
- ▶ Fibrin mesh, platelet plug, vascular constriction- followed by dissolution of clot



PEPTIDES

## BPC 157 Periodontitis

- ▶ Keremi, B., et al. "Antiinflammatory effect of BPC 157 on experimental periodontitis in rats." *Journal of physiology and pharmacology* 60.7 (2009): 115-122
- ▶ periodontitis induced by LPS and by bacterial infection also clearly resulted in alveolar bone destruction increased inflammation
- ▶ BPC 157 can reverse these changes of bone loss and gingival resorption

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## BPC 157 Corneal Abrasion

- ▶ Avascular Tissue
- ▶ BPC 157 also heals hypovascular, hypocellular, and hypo-neural tissues
- ▶ This beneficial effect of BPC 157 could be essential for the maintenance and renewal of normal tissue in the anterior eye and the prevention of undesirable immune or angiogenic reactions. The counteraction of neovascularization likely indicates that the effects of BPC 157 contribute to the balance between competing proangiogenic and antiangiogenic mediators, characterizing corneal avascularity as “**angiogenic privilege**”, which is essential for corneal wound healing.

PEPTIDES

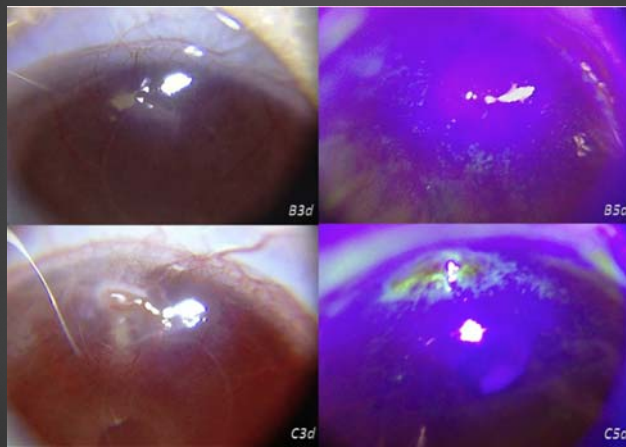


## BPC 157 Corneal Abrasion

- ▶ Spontaneous corneal healing- Aqueous cells remained present, as did edema, fibrin, and granulation tissue; the increase in granulocytes and mononuclear cells was confirmed by histology
- ▶ BPC 157 had rapid beneficial effects on the epithelium, lowering granulocyte and mononuclear cell levels and thereby decreasing aqueous cells, granulation tissue, edema, and fibrin formation.

PEPTIDES

# BPC 157 Corneal Abrasion



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3 day to 5 day healing with and without BPC 157

## BPC 157 Gut-Brain Axis

- ▶ Curr Neuropharmacol. 2016;14(8):857-865.

Brain-gut Axis and Pentadecapeptide BPC 157: Theoretical and Practical Implications.

Sikiric P1, Seiwert S, Rucman R, Kolenc D, Vuletic LB, Drmic D, Grgic T, Strbe S, Zukanovic G, Crvenkovic D, Madzarac G, Rukavina I, Sucic M, Baric M, Starcevic N, Krstonijevic Z, Bencic ML, Filipcic I, Rokotov DS, Vlainic J.

- ▶ Works on serotonergic and Dopamine systems

PEPTIDES

## BPC 157 gut-Brain Axis

- ▶ Induces release of serotonin in Nigrostriatal area of brain
- ▶ Beneficial effects in over stimulated or damaged dopaminergic, serotonergic, GABAergic and opioid system.
- ▶ Not just neuroprotective but also protects somatosensory Neurons
- ▶ strongly improves nerve regeneration after peripheral nerve transection
- ▶ counteracts autotomy

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## BPC -157 Gut- Brain Axis

- ▶ Literature supported evidence of beneficial effects over:
- ▶ akinesia , catalepsy ,
- ▶ somatosensory disorientation , tremor , seizures,
- ▶ stereotypies (both acute and chronic) , hypothermia ,
- ▶ , hyperthermia, serotonin syndrome , acute and
- ▶ chronic alcohol intoxication , climbing and helpless
- ▶ behavior , morphine-induced analgesia , diazepam
- ▶ tolerance and dependence , muscle weakness and
- ▶ function failure , dopamine vesicle depletion ,
- ▶ amphetamine given acutely and chronically ,
- ▶ amphetamine tolerance , amphetamine supersensitivity
- ▶ , morphine and naloxone , picrotoxin and isoniazid
- ▶ convulsions , cuprizone effects, a neurotoxin
- ▶ mimicking multiple sclerosis brain lesions and presentation



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## BPC 157 Gut –Brain Axis

- ▶ BPC 157 attenuated the course of traumatic brain injury, postponed deleterious outcome and
- ▶ counteracted the primary injury with respect to the secondary injury process
- ▶ Beneficial effects on neuronal necrosis, demyelination, cyst formation

after spinal cord injury and rescue of tail function

- ▶ Counters side effects of neuroleptics, catalepsy and akinesia and the accompany of gastric lesions. Continues with Parkinson's agents

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## BPC 157 Gut Brain Axis

- ▶ BPC 157 has a modulatory effect on dopamine system, and it could be used in both acute and chronic amphetamine disturbances



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## BPC 157 Gut Brain Axis

- ▶ anti-depressant activity of BPC 157
- ▶ BPC 157 may have a particular interaction with serotonergic system in a similar way like it does with dopaminergic system
- ▶ BPC 157 acts by favoring the homeostasis of the GABAergic system, as well as by upregulating the GABAergic neurotransmission, and having a mechanism(s) of action



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## BPC 157 Mechanism Recap

- ▶ Upregulation of the gene early growth response-1 (egr-1) and co repressor nerve growth factor1-A binding protein 2(naB-2)- effects cytokine and growth factor production ( extracellular increased collagen and new blood vessels.
- ▶ Activating cellular focal adhesion kinase(FAK-paxillin signal pathway)
- ▶ Increase the expression of growth hormone receptor, Janus Kinase-(JAK-2)- downstream signal pathway of GHr

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## BPC 157 Conclusion

- ▶ The mechanism of action of BPC 157 is not clear yet. It was shown to have multiple sites of action. BPC reduces the release of inflammatory mediators (i.e., myeloperoxidase, leukotriene B4, tromboxane B2) ,interacts with prostaglandin-dependent pathways ,has a direct protective and proliferative effect on target cells and modulates the release of nitric oxide .In addition, it has been claimed to promote new vessel formation ,upregulation of the growth factors, as well as influencing other local factors .

PEPTIDES

## BPC-157 references

- ▶ Enhancement by PL 14736 of granulation and collagen organization in healing wounds and the potential role of egr-1 expression Article in European Journal of Pharmacology 570(1-3):212-21 · October 2007
- ▶ Modulatory effect of gastric pentadecapeptide BPC 157 on angiogenesis in muscle and tendon healing :Article in Journal of physiology and pharmacology: an official journal of the Polish Physiological Society · December 2009
- ▶ Molecules 2014, 19, 19066-19077; Article Pentadecapeptide BPC 157 Enhances the Growth Hormone Receptor Expression in Tendon Fibroblasts Chung-Hsun Chang 1,2, Wen-Chung Tsai 3, Ya-Hui Hsu 1 and Jong-Hwei Su Pang 1,\*

PEPTIDES

## BPC 157 References

- ▶ Pentadecapeptide BPC 157 (PL 14736) Improves Ligament Healing in the Rat Tomislav Cerovecki,<sup>1</sup> Ivan Bojanic,<sup>2</sup> Luka Brcic,<sup>3</sup> Bozo Radic,<sup>4</sup> Ivan Vukoja,<sup>4</sup> Sven Seiwert,<sup>3</sup> Predrag Sikiric<sup>4</sup>

<sup>1</sup>University Hospital of Traumatology, Zagreb, Croatia, <sup>2</sup>Department of Orthopaedic Surgery, Clinical Hospital Center Zagreb, Medical Faculty University of Zagreb, Zagreb, Croatia, <sup>3</sup>Department of Pathology, Medical Faculty University of Zagreb, Zagreb, Croatia, <sup>4</sup>Department of Pharmacology, Medical Faculty University of Zagreb, Zagreb, Croatia

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([www.interscience.wiley.com](http://www.interscience.wiley.com)). DOI 10.1002/jor.21107

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- ▶ Pevec, Danira, et al. "Impact of pentadecapeptide BPC 157 on muscle healing impaired by systemic corticosteroid application." *Medical Science Monitor* 16.3 (2010): BR81-BR88
- ▶ Šebečić, Božidar, et al. "Osteogenic effect of a gastric pentadecapeptide, BPC-157, on the healing of segmental bone defect in rabbits: a comparison with bone marrow and autologous cortical bone implantation." *Bone* 24.3 (1999): 195-202
- ▶ Vuksic, Tihomir, et al. "Stable gastric pentadecapeptide BPC 157 in trials for inflammatory bowel disease (PL-10, PLD-116, PL14736, Pliva, Croatia) heals ileoileal anastomosis in the rat." *Surgery today* 37.9 (2007): 768-777

PEPTIDES

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- ▶ Pregled bibliografske jedinice broj: 192824

Zbornik radova

Autori: Veljača, Marija; Krnić, Žarka; Brajša, Karmen; Mildner, Boris; Pavić-Sladoljev, Dubravka; Ševeljević-Jaran, D.; Kolega, M.; Erceg, Damir; Krznarić, Željko

Naslov: The development of PL 14736 for treatment of inflammatory bowel disease  
Zbornik: Advanced in GI pharmacology

Dio CC časopisa: NE

Skup: IUPHAR GI: Advances in GI pharmacology. From acid secretion to mucosal protection

Mjesto i datum: Honolulu, Hawaii, 13.-15.07.2002.

PEPTIDES

## BPC 157 references

- ▶ Current Pharmaceutical Design, 2013, 19, 76-83

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PEPTIDES

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- ▶ Keremi, B., et al. "Antiinflammatory effect of BPC 157 on experimental periodontitis in rats." *Journal of physiology and pharmacology* 60.7 (2009): 115-122
- ▶ Enhancement by PL 14736 of granulation and collagen organization in healing wounds and the potential role of egr-1 expression Article in *European Journal of Pharmacology* 570(1-3):212-21 · October 2007
- ▶ Perforating corneal injury in rat and pentadecapeptide BPC 157 Article in *Experimental Eye Research* · April 2015 DOI: 10.1016/j.exer.2015.04.016 · Source: PubMed

PEPTIDES



## BPC 157 References

- ▶ Brain-gut Axis and Pentadecapeptide BPC 157: Theoretical and Practical Implications

Predrag Sikiric<sup>1,\*</sup>, Sven Seiwert<sup>1</sup>, Rudolf Rucman<sup>1</sup>, Danijela Kolenc<sup>1</sup>, Lovorka Batelja Vuletic<sup>1</sup>, Domagoj Drmic<sup>1</sup>, Tihomir Grgic<sup>1</sup>, Sanja Strbe<sup>1</sup>, Goran Zukanovic<sup>1</sup>, Dalibor Crvenkovic<sup>1</sup>, Goran Madzarac<sup>1</sup>, Iva Rukavina<sup>1</sup>, Mario Sucic<sup>1</sup>, Marko Baric<sup>1</sup>, Neven Starcevic<sup>1</sup>, Zoran Krstonijevic<sup>1</sup>, Martina Lovric Bencic<sup>1</sup>, Igor Filipcic<sup>1</sup>, Dinko Stancic Rokotov<sup>1</sup> and Josipa Vlainic<sup>2</sup>

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PEPTIDES