

BPC-157

Molecular Weight: 1419.5355 | Sequence: L-Valine, glycyl-L-alpha-glutamyl-L-prolyl-L-prolyl-L- prolylglycyl-L-lysyl-L-prolyl-L-alanyl-L-alpha-aspartyl-L-alpha-aspartyl-L-alanylglycyl-L-leucyl-;glycyl-L-alpha-glutamyl-L-prolyl-L-prolyl-L-prolylglycyllysyl-L-prolyl-L-alanyl-L-alpha-aspartyl- L-alpha-aspartyl-L-alanylglycyl-L-leucyl-L-valine

DESCRIPTION:

Pentadecapeptide BPC 157, composed of 15 amino acids, is a partial sequence of body protection compound (BPC) that is discovered in and isolated from human gastric juice. Experimentally it has been demonstrated to accelerate the healing of many different wounds, including tendon-to-bone healing and superior healing of damaged ligaments. Additionally, BPC 157 has shown to protect organs and aids in the prevention of gastric ulcers. BPC-157 acts systemically in the digestive tract to combat leaky gut, IBS, gastrointestinal cramps, and Crohn's disease.

This peptide has been known to exhibit analgesic characteristics as well. Those who suffer from discomfort due to muscle sprains, tears and damage may benefit from treatment with this peptide. It can also help to aid skin burns at a faster rate by increasing blood flow to damaged tissues.

CLINICAL RESEARCH:

The Promoting effect of Pentadecapeptide BPC 157 on tendon healing involves tendon outgrowth, cell survival, and cell migration

Many growth factors such as epidermal growth factor (EGF), transforming growth factor-(TGF-), and bone morphogenetic proteins (BMPs) have been used to improve the healing of torn tendon in the lab. However, the short duration of these easily digested growth factors hampers their clinical usage. Gastric pentadecapeptide BPC 157 is a partial sequence of human gastric protein BPC, which has been discovered in and isolated from gastric juice. It is highly stable and resistant to hydrolysis or enzyme digestion, even in the gastric juice. Besides, it is easily dissolved in water and needs no carrier for its application.

Experimentally it was demonstrated to enhance the healing of different wounds, such as gastric ulcer, skin, cornea, muscle, colon-colon anastomosis, colocutaneous fistula, and segmental bone defect. It was also found to accelerate the healing of transected rat Achilles tendon (12, 29) and medial collateral ligament of knee. Currently it is in clinical trials for treating inflammatory bowel disease.

Chung-Hsun Chang, Wen-Chung, Tsai Miao-Sui Lin, Ya-Hui Hsu, and Jong-Hwei Su Pang

Cerebrolysin

Purity: >99%

DESCRIPTION:

Cerebrolysin (synonym FPE 1070) is a nootropic drug which consists of low-molecular peptides which possesses neuroprotective and neurotrophic repair properties. The active fragment of Cerebrolysin is made of proteins with very low molecular masses that do not exceed 10.000 daltons. This means they can penetrate the blood-brain (or blood-SCF) barrier and reach neurons directly, making the drug able to show organo-specific combined effects towards the brain. Cerebrolysin has been proven to have

neurotrophic action similar to nerve growth factors, which cause peripheral and central neuronal stimulation. It improves efficiency within the brain's aerobic metabolic processes and improves intracellular peptide synthesis. The neuroprotective properties of this nootropic agent help to shield neurons from lactic acidosis, to prevent the formation of free radicals, and have been studied in Parkinson's, Alzheimer's, MS, ALS, TBI, and stroke.

CLINICAL RESEARCH:

Cerebrolysin in Alzheimer's disease: a randomized, double-blind, placebo-controlled trial with a neurotrophic agent

Cerebrolysin (Cere) is a compound with neurotrophic activity. It has been shown to be effective in the treatment of Alzheimer's disease (AD) in earlier trials. In this multicenter, randomized, double-blind, placebo-controlled, parallel-group study, patients were injected intravenously with placebo or 30mL Cere five days per week for four weeks. Effects on cognition and global function were evaluated with the Alzheimer Disease Assessment Scale – Cognitive Subscale (ADAS-Cog) and the Clinician Interview based Impression of Change with Caregiver Input scale (CIBIC+) 4, 12, 24 weeks after the beginning of the injections. 192 patients were enrolled, 95 were randomized to placebo, and 97 to Cere. At baseline, there was a significant difference between groups for age, age of onset of dementia, and the number of patients with hallucinations. At week 12 there was a significant difference on the CIBIC + ($p=0.033$) in favor of Cere. The number of CIBIC+ responders (score < 4), was significantly higher ($p=0.007$), with 68 (76%) in the Cere group and 51 (57%) in the placebo group. Trends were noted in the Disability Assessment in Dementia scale and the Cornell Depression Scale. Adverse events were recorded in 73% of placebo and 64% of Cere patients. Most common adverse events were headaches, dizziness, weight loss and anxiety. Conclusions: Cere treatment was well tolerated and resulted in significant improvements in the global score two months after the end of active treatment.

M. Panisset, S. Gauthier, H. Moessler, M. Windisch

iRGD

Purity: >98% (HPLC on request) | Molecular Formula:
C35H58N14O13S2 Molecular Weight: 947.07g/mol |
Sequence: Cys-Arg-Gly-Asp-Lys-Gly-Pro-Asp-Cys

DESCRIPTION:

iRGD is a cyclic peptide that binds to integrins that are expressed on tumor endothelial cells.

Upon binding, a protease cleavage event is activated. When this event is activated the peptide is then able to bind neuropilin-1, activating an endocytotic/exocytotic transport pathway. As a result of this, it is able to hone to tumor cells and make them permeable to transport of many types of cancer therapies. This makes traditional cancer therapies target cells

PROTOCOL:

better and makes the therapy less toxic. One study showed that doxorubicin, liposomal doxorubicin, Herceptin trastuzumab or Abraxane nab-paclitaxel had greater drug accumulation in the tumor by up to 40-fold than mice injected with one of the drugs alone. They equaled greater reductions in tumor growth. In all, the drug- peptide combination was as effective as threefold higher doses of drug alone.

CLINICAL RESEARCH:

Co-administration of a Tumor-Penetrating Peptide Enhances the Efficacy of Cancer Drugs

Poor penetration of anti-cancer drugs into tumors can be an important factor limiting their efficacy. Studying mouse tumor models, we show that a previously characterized tumor-penetrating peptide, iRGD (CRGDK/RGPD/EC), increased vascular and tissue permeability in a tumor- specific and neuropilin-1-dependent manner, allowing co-administered drugs to penetrate into extravascular tumor tissue. Importantly, this effect did not require the drugs to be chemically conjugated to the peptide. Systemic

injection with iRGD improved the therapeutic index of drugs of various compositions including a small molecule (doxorubicin), nanoparticles (nab-paclitaxel and doxorubicin liposomes), and a monoclonal antibody (trastuzumab). Thus, co-administration of iRGD may be a valuable way to enhance the efficacy of anti-cancer drugs while reducing their side effects, a primary goal of cancer therapy research.

Sugahara, Kazuki N et al. "Coadministration of a tumor-penetrating peptide enhances the efficacy of cancer drugs." Science (New York, N.Y.) vol. 328,5981 (2010)

DHH-B

Purity: >98% (HPLC on request) | Molecular
Formula: C₂₄H₃₁NO₄ Molecular Weight:
397.51 g/mol | Sequence: Non- peptide

DESCRIPTION:

DHH-B, dihydrohonokiol-B, is a natural supplement which has anxiolytic-effects. Treatment with DHH-B does not cause any significant changes in motor activity or muscle relaxation. Benzodiazepines are some of the most commonly prescribed medications in the United States. These anxiolytics have many well-known side effects including motor function and more. That being said, this product has the potential to help people transition from benzodiazepines to DHH-B or act as an alternative to benzodiazepines.

CLINICAL RESEARCH:

Comparative assessment of the anxiolytic-like activities of honokiol and derivatives

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Ami-machi, Inashiki-gun, Ibaraki 300-1192, Japan Department of Biochemistry, The University of Texas Health Science Center at San Antonio, San Antonio, TX, USA

Honokiol has previously been shown to be an effective anxiolytic-like agent in mice when administered for 7 days at 0.2 mg/kg/day prior to evaluation in an elevated plus-maze, while 20 mg/kg is required for efficacy as a single oral dose. The aim of this study was to find analogs of honokiol that are more effective for acute administration. Among the eight analogs evaluated, one partially reduced

derivative of honokiol [30-(2-propenyl)-5-propyl-(1,10-biphenyl)-2,40-diol] exhibited significant anxiolytic-like activity at 0.04 mg/kg.

Following oral administration of 1 mg/kg of this analog, anxiolytic-like activity was clearly evident at 1 h, peaked at 3 h, and remained significant for longer than 4 h after treatment. Combined administration of the derivative with diazepam led to enhanced anxiolytic-like efficacy. Moreover, as with diazepam, the anxiolytic-like effect of the analog was reduced by flumazenil. In contrast, bicuculline, a GABA_A antagonist, had no effect on the activity of the derivative. Taken together, these results suggest that this analog of honokiol acts at the benzodiazepine recognition site of the GABA_A ± benzodiazepine receptor complex.

Hisashi Kuribara^a, Eiko Kishia, Masayuki Kimura^b, Susan T. Weintraub^c, Yuji Maruyama^{a,*}

Dihexa

Dihexa is a peptide variant derived from angiotensin IV which has been found to potently improve cognitive function in animal models of disease such as Alzheimer's. Angiotensin IV is a derivative of the potent vasoconstrictor angiotensin II and has been shown to enhance acquisition, consolidation, and recall of learning and memory in animal models when administered centrally or peripherally. In an assay of neurotrophic activity, Dihexa was found to be seven orders of magnitude more potent than BDNF. It could possibly help in the repair of the brain and nerves in neurological disease.

CLINICAL RESEARCH:

The Procognitive and Synaptogenic Effects of Angiotensin IV- Derived Peptides Are Dependent on Activation of the Hepatocyte Growth Factor / c-Met System

A subset of angiotensin IV (AngIV)-related molecules are known to possess procognitive/antidementia properties and have been considered as templates for potential therapeutics. However, this potential has not been realized because of two factors: 1) a lack of blood- brain barrier- penetrant analogs, and 2) the absence of a validated mechanism of action. The pharmacokinetic barrier has recently been overcome with the synthesis of the orally active, blood-brain barrier-permeable analog N-hexanoic-tyrosine-isoleucine-(6) aminohexanoic amide (dihexa). Therefore, the goal of this study was to elucidate the mechanism that underlies dihexa's procognitive activity. Here, we demonstrate that dihexa binds with high affinity

to hepatocyte growth factor (HGF) and both dihexa and its parent compound Norleucine 1-AngIV (Nle1-AngIV) induce c-Met phosphorylation in the presence of subthreshold concentrations of HGF and augment HGF- dependent cell scattering. Further, dihexa and Nle1-AngIV induce hippocampal synaptogenesis and synaptogenesis similar to HGF itself. These actions were inhibited by an HGF antagonist and a short hairpin RNA directed at c-Met. Most importantly, the procognitive/antidementia capacity of orally delivered dihexa was blocked by an HGF antagonist delivered intracerebroventricularly as measured using the Morris water maze task of spatial learning.

Benoist, Caroline C et al. "The procognitive and synaptogenic effects of angiotensin IV-derived peptides are dependent on activation of the hepatocyte growth factor/c-met system." The Journal of pharmacology and experimental therapeutics vol. 351,2 (2014): 390-402.

DSIP

Purity: >98% (HPLC on request) | Molecular
Formula: C₃₅H₄₈N₁₀O₁₅ Molecular Weight: 848.81
| Sequence: Trp-Ala-Gly-Gly-Asp-Ala-Ser-Gly-Glu

DESCRIPTION:

DSIP is a well-known neuromodulator and natural somnogenic nonapeptide with many other physiological functions. It is typically found in the brain and easily passes the blood-brain barrier. It is mainly prescribed for the treatment of pain conditions, alcohol and opioid withdrawal, CRH and stress-related symptoms, low testosterone (via stimulation of LH), and even sometimes as an antioxidant and anti-oncogenic protein. It has been discovered and heavily studied for over 40 years, yet, the mechanism of action is still complex and not well understood. The results of studies of DSIP and its analogues over a period of 30 years since its discovery enable one to state with confidence that DSIP is a unique member of the family of peptide neuromodulators. It exhibits a pronounced stress protective action and decreases stress-induced metabolic and functional disorders in human and animal organisms exposed to a variety of stresses. Some of the effects of the peptide are accomplished through the modulating action on central regulatory processes, owing to the systemic antioxidant action, the modulating influence on the activity of GABAergic, glutamatergic, and other neuronal systems. It also works on the expression of early response genes in brain structures, and on the activity of biosynthetic and proteolytic processes. DSIP has traditionally been dosed as an IV infusion, however, it can be given subcutaneously as well. Traditional doses have been 100mcg.

CLINICAL RESEARCH:

DSIP-more than a sleep peptide?

In several species DSIP at low doses has been shown to promote sleep. Although its physiological role remains to be clarified, DSIP illustrates several concepts applicable to other brain peptides. These include the bell-shaped dose-response curve, central effects after peripheral administration, a delayed and prolonged time course, and

some penetration of the blood-brain barrier in essentially intact form. Concepts applicable to one neuropeptide, therefore, appear to be applicable to others. In this article Abba Kastin and colleagues review the known effects of DSIP and argue that more work needs to be carried out before it can be labelled functionally.

J. Kastin, Abba & A. Olson, Gayle & V. Schally, Andrew & H. Coy, David. (1980). DSIP — more than a sleep peptide?. Trends in Neurosciences - TRENDS NEUROSCI. 3. 163-165.

Epitalon

Purity: >98% (HPLC on request) | Molecular
Formula: C₁₆H₂₄N₄O₁₀ Molecular Weight: 432.4
g/mol | Sequence: H-Ala-Glu-Asp-Gly-O

DESCRIPTION:

Epithalon (also known as Epitalon or Epithalone) is the synthetic version of the polypeptide Epithalamin which is naturally produced in humans. The pineal peptide preparation is secreted in the epithalamium-epiphyseal region of the brain. Its more prominent tasks are: to regulate metabolism in the epiphysis, increase the sensitivity of hypothalamus to its natural hormonal influences, normalize the function of the anterior pituitary, regulate the levels of gonadotropins and melatonin in the body.

Epithalamin increases a person's resistance to emotional stress and also acts as an antioxidant.

It is a bio-regulator for the endocrine system, especially for the pineal gland, and has been shown to lengthen telomeres in human cells. The mechanisms in Epitalon are a lot more complex than just activating telomerase. It reduces lipid oxidation and ROS, along with normalizing T cell function. It seems to normalize cholesterol and uric acid, along with prolactin levels. It has shown promise in restoring pancreatic hormone function. Additionally, it restored and normalized melatonin levels in older patients who have lost some pineal function due to aging.

CLINICAL RESEARCH:

Peptide Geroprotector from the Pituitary Gland Inhibits Rapid Aging of Elderly People: Results of 15-Year Follow-Up

The paper presents the results of randomized comparative study of the efficiency of peptide geroprotector from the pituitary gland in elderly patients with rapidly aging cardiovascular system. Over three years 39 coronary patients received, in addition to basic therapy, regular courses of epithalamin (peptide drug), while 40 coronary patients (control group) received basic therapy alone. Long-term treatment with epithalamin (6 courses over 3

years) decelerated aging of the cardiovascular system, prevented age-associated impairment of physical endurance, normalized circadian rhythm of melatonin production and carbohydrate and lipid metabolism. A significantly lower mortality in the group of patients treated with epithalamin in parallel with basic therapy also indicated a geroprotective effect of the peptide preparation from the pineal gland.

O. V. Korkushko, V. Kh. Khavinson*, V. B. Shatilo, and I. A. Antonyk-Sheglova Translated from Byulleten' Eksperimental'noi Biologii i Meditsiny, Vol. 151, No. 3, pp. 343-347, March, 2011.

GHK-Cu

**Purity: >98% (HPLC on request) | Molecular
Formula: C₂₈H₅₂CuN₁₂O₈ Molecular Weight:
748.346 g/mol | Sequence: Non-Peptide**

DESCRIPTION:

GHK-Cu is a naturally occurring copper complex that was first identified in human plasma, but has hence been found in multiple locations such as saliva and urine. Copper peptides are small,

naturally occurring protein fragments that have high affinity for copper ions, which are critical to normal body function. GHK-Cu has a variety of roles in the human body including, but not limited to, promoting activation of wound healing, attracting immune cells, antioxidant and anti-inflammatory effects, stimulating collagen and glycosaminoglycan synthesis in skin fibroblasts, and promoting blood vessel growth. There has been evidence that has shown that it acts as a

feedback signal that is generated after tissue injury. First, it seems to act as a potent protector of tissue and anti-inflammatory agent that controls the oxidative damage that occurs post-tissue injury. Further, it then plays a big role in signaling tissue remodeling which removes damaged/scarred tissue and generates new, healthy tissue. However, these positive effects decline with age because the concentration of GHK-Cu in the body decreases with age. Thus, there is an increase in inflammation, cancerous activity, and tissue destruction. Clinically, it is mostly used to decrease fine lines and wrinkles and to improve hair regrowth.

CLINICAL RESEARCH:

GHK Peptide as a Natural Modulator of Multiple Cellular Pathways in Skin Regeneration

GHK (glycyl-L-histidyl-L-lysine) is present in human plasma, saliva, and urine but declines with age. It is proposed that GHK functions as a complex with copper 2+ which accelerates wound healing and skin repair. GHK stimulates both synthesis and breakdown of collagen and glycosaminoglycans and modulates the activity of both metalloproteinases and their inhibitors. It stimulates collagen, dermatan sulfate, chondroitin sulfate, and the small proteoglycan, decorin. It also restores replicative vitality to fibroblasts after radiation therapy. The molecule attracts immune and endothelial cells to the site of an injury. It accelerates wound-healing of the skin, hair follicles, gastrointestinal tract, boney tissue, and foot pads

of dogs. It also induces systemic wound healing in rats, mice, and pigs. In cosmetic products, it has been found to tighten loose skin and improve elasticity, skin density, and firmness, reduce fine lines and wrinkles, reduce photodamage, and hyperpigmentation, and increase keratinocyte proliferation. GHK has been proposed as a therapeutic agent for skin inflammation, chronic obstructive pulmonary disease, and metastatic colon cancer. It is capable of up and down regulating at least 4,000 human genes, essentially resetting DNA to a healthier state. The present review revisits GHK's role in skin regeneration in the light of recent discoveries.

GHK Peptide as a Natural Modulator of Multiple Cellular Pathways in Skin Regeneration

Pickart, Loren & Vasquez-Soltero, Jessica & Margolina, Anna. (2015). GHK Peptide as a Natural Modulator of Multiple Cellular Pathways in Skin Regeneration. BioMed Research International.

KPV

Purity: >99% (confirmed by HPLC) | Molecular Formula:
Ac-C16H32N4O6-NH2 Molecular Weight: 378.47 g/mol |
Sequence: Lys-Pro-Val

DESCRIPTION:

KPV (Lysine-Proline-Valine) is a C-terminal tripeptide fragment of α -melanocyte stimulating hormone (α -MSH). α -MSH stimulates the production and release of melanin by melanocytes in skin and hair, acting through melanocortin 1 receptor. Several studies have previously shown that KPV has decreased inflammation and tumorigenesis in the body. The KPV anti-inflammatory effect is PepT1-mediated in intestinal epithelial and immune cells. PepT1 is an oligopeptide transporter that is overexpressed in the colonic epithelial cells of chronic ulcerative colitis, which can deliver KPV into cytosol in the intestine.

The tripeptide, KPV has significant antimicrobial and

CLINICAL RESEARCH:

anti-inflammatory properties especially in those with psoriasis. Psoriasis is a chronic autoimmune condition which causes the rapid build-up of skin cells and is usually treated using hydrocortisone. In people with psoriasis, KPV has shown to limit symptoms of the condition including itchiness, dryness, redness, peeling, and more. Therefore, KPV could be used

for an extended period of time without risking the unwanted complications of long term steroid therapy. KPV is a promising, therapeutic treatment for inflammatory bowel disease (IBD), colon cancer, and inflammatory skin disorders, in particular, psoriasis.

Alpha-Melanocyte-Stimulating Hormone and Related Tripeptides: Biochemistry, Anti Inflammatory and Protective Effects in Vitro and in Vivo, and Future Perspectives for the Treatment of Immune-Mediated Inflammatory Diseases

Alpha-MSH is a tridecapeptide derived from proopiomelanocortin. Many studies over the last few years have provided evidence That Alpha -MSH has potent protective and antiinflammatory effects. These effects can be elicited via centrally expressed melanocortin receptors that orchestrate descending neuro-genic antiinflammatory pathways. Alpha-MSH can also exert antiinflammatory and protective effects on cells of the immune system and on peripheral nonimmune cell types expressing melanocortin receptors. At the molecular level, Alpha-MSH affects various pathways implicated in regulation of inflammation and protection, i.e., nuclear factor-B activation, expression of adhesion molecules and chemokine receptors, produc- tion of proinflammatory

cytokines and mediators, IL-10 synthesis, T cell proliferation and activity, inflammatory cell migration, expression of antioxidative enzymes, and apoptosis. The antiinflammatory effects of -MSH have

been validated in animal models of experimentally induced fever; irritant and allergic contact dermatitis, vasculitis, and fibrosis; ocular, gastrointestinal, brain, and allergic airway inflammation; and arthritis, but also in models of organ injury. One obstacle limiting the use of alpha-MSH in inflammatory disorders is its pigmentary effect. Due to its preserved antiinflammatory effect but lack of pigmentary action, the C-terminal tripeptide of -MSH, KPV, has been delineated as an alternative for antiinflammatory therapy. KdPT, a derivative of KPV corresponding to amino acids 193–195 of IL-1, is also emerging as a tripeptide with antiinflammatory effects. The physicochemical properties and expected low costs of production render both agents suitable for the future treatment of immune-mediated inflammatory skin and bowel disease, fibrosis, allergic and inflammatory lung disease, ocular inflammation, and arthritis.

Endocr Rev. 2008 Aug;29(5):581-602. doi: 10.1210/er.2007-0027. Epub 2008 Jul 8. Brzoska T1, Luger TA, Maaser C, Abels C, Böhm M.

Pentosan Polysulfate

Purity: >98% (HPLC on request) | Molecular Formula:
(C₅H₆Na₂O₁₀S₂)_n Molecular Weight: 602.473 g/mol |
Sequence: Non- peptide

DESCRIPTION:

Pentosan polysulfate is a semi-synthetic polysulfated xylan used for the relief of Osteoarthritis. The mechanism of PPS action in osteoarthritis is multifactorial, with both stimulation of cartilage matrix synthesis and prevention of cartilage breakdown. There are also systemic effects on blood lipid and fibrinolysis

that may help clear the subchondral circulation.

In one study, after a series of four to six intra- articular PPS injections into knees of human volunteers, there was a significant increase in the size of the synovial fluid hyaluronan without causing any inflammation or bleeding into the joint cavity.

CLINICAL RESEARCH:

Intra-articular injection pentosanpolysulphate results in increased hyaluronan molecular weight in joint fluid.

The influence of an oversulphated glycosaminoglycan, pentosanpolysulphate, on hyaluronan metabolism of the synovial lining cell was studied in vivo in human volunteers. Significant increases in the mean degree of polymerisation of the hyaluronan chains were observed

after a series of four to six intra-articular injections of this glycosaminoglycan. No increases in hyaluronan synthesis rates were observed. Repeated administration of the drug did not cause any inflammation or bleeding in the joint cavity.

Clin Exp Rheumatol. 1992 May-Jun;10(3):249-54.

PNC-27

PNC-27 is a membrane active anticancer peptide that has been found to kill cancer cells by inducing membranoylsis via cellular necrosis. It has been designed to bind tightly to the p53-binding pocket on the mdm2 protein, a negative regulator of the P53 tumor suppressor. Almost all cancers have a mechanism to decrease the functionality of P53 which can stop cellular replication. P53 is usually not expressed in high degrees in normal cells. Through blocking its inhibition via mdm2 protein modulators, we can make sure P53 is expressed. Thus, cancer cells can be selectively targeted for necrosis and death. This complex works in cancer cell membranes.

Together, PNC-27 and Mdm2 result in trans-membrane pore formation which results in cancer cell death. This is evident in literature including studies on P53-null K562 in leukemia cells, melanoma, pancreatic cancer, breast cancer, epithelial ovarian cancer, and additional cancers. Essentially, the peptide has been found to be cytotoxic to human cancer cells while having no effect on healthy cells and is functional almost across all cancer cell types.

CLINICAL RESEARCH:

Anticancer peptide PNC-27 adopts an HDM-2-binding conformation and kills cancer cells by binding to HDM-2 in their membranes.

The anticancer peptide PNC-27, which contains an HDM-2-binding domain corresponding to residues 12-26 of p53 and a transmembrane-penetrating domain, has been found to kill cancer cells (but not normal cells) by inducing membranolysis. We find that our previously determined 3D structure of the p53 residues of PNC-27 is directly superimposable on the structure for the same residues bound to HDM-2, suggesting that the peptide may target HDM-2 in the membranes of cancer cells. We now find significant levels of HDM-2 in the membranes of a variety of cancer cells but not in the membranes of several

untransformed cell lines. In colocalization experiments, we find that PNC-27 binds to cell membrane-bound HDM-

2. We further transfected a plasmid expressing full-length HDM-2 with a membrane-localization signal into untransformed MCF-10-2A cells not susceptible to PNC- 27 and found that these cells expressing full-length HDM- 2 on their cell surface became susceptible to PNC-27. We conclude that PNC-27 targets HDM-2 in the membranes of cancer cells, allowing it to induce membranolysis of these cells selectively.

RG3, Methylcobalamin, NAD+

Purity: >99.5% | Molecular Formula: C₄₂H₇₂O₁₃ Molecular Weight: 85.025 g/mol | Sequence: Non-Peptide Molecular Formula: C₆₃H₉₁CoN₁₃O₁₄P Molecular Weight: 1344.4 g/mol | Sequence: Non-Peptide Molecular Formula: C₂₁H₂₇N₇O₁₄P₂

Molecular Weight: 663.43 g/mol | Sequence: Non-Peptide

DESCRIPTION:

RG3 is a Panax ginseng that has been used in oriental countries for its pharmacologic effects, such as antidiabetic, neurological, and anti-inflammatory activities. Neuroinflammation is associated with activation of the central nervous system (CNS) glia with significant cytokine and chemokine production, infiltration of immune cells, edema, increased blood-brain barrier (BBB) permeability and breakdown.

Ginsenoside 20(S) RG3 is one of the many active ingredients of ginseng saponins. RG3 is a ginseng known for aiding chronic inflammation. Specifically, RG3 has been shown to reduce chronic neurodegenerative inflammation, the proinflammatory cytokine, interleukin-6 (IL-6) and interleukin-1 β (IL-1 β), and tumor necrosis factor- α (TNF- α). Methylcobalamin and NAD⁺ are combined with RG3 to enhance its effects. Target treatments for RG3/Methylcobalamin/NAD⁺ include aging, traumatic brain injury (TBI), Alzheimer's, diabetes, atherosclerosis, and hypertrophic scar formation. RG3 also has promising views for treatment in ovarian cancer, prostate cancer, and other cancers as well.

CLINICAL RESEARCH:

Suppressive Effect of Ginsenoside Rg3 against Lipopolysaccharide- Induced Depression-Like Behavior and Neuroinflammation in Mice

Ginsenoside Rg3 (Rg3), a major active ingredient enriched in red ginseng, possess well-confirmed

immunoregulatory effects. Immune disturbance is a common trigger and aggravating factor in depression. The aim of this study was to explore the effects on Rg3 on

lipopolysaccharides (LPS)-induced depression-like behavior in mice and the involvement of immune regulation. Pretreatment with Rg3 (i.g., 20 and 40 mg/ kg) effectively ameliorated LPS (i.p., 0.83 mg/kg) induced body weight loss, anorexia, and immobility time in both the tail suspension test and the forced swimming test. Rg3 attenuated the disturbed turnover of tryptophan and serotonin in the hippocampus, accompanied by decreased

mRNA expression of cytokines and indoleamine-2, 3- dioxygenase (IDO). These central benefits were partially linked to the regulation of microglia activation and nuclear factor kappa B (NF- κ B) pathway. In addition, Rg3 significantly reduces LPS-induced elevation of interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α) in plasma, and restored the systemic balance of tryptophan-ky- nurenine metabolism. Taken together, our results demonstrated the Rg3 was effective in ameliorating depressive-like behavior induced by immune activation, adding new evidence to support its health benefits by immunoregulation.

Kang, An & Xie, Tong & Zhu, Dong & Shan, Jinjun & di, liuqing & Zheng, Xiao. (2017).
Suppressive Effect of Ginsenoside Rg3 against Lipopolysaccharide-Induced Depression-Like
Behavior and Neuroinflammation in Mice. Journal of Agricultural and Food Chemistry. 65.

Selank

**Purity: >98% (HPLC on request) | Molecular
Formula : C₃₃H₅₇N₁₁O₉ Molecular Weight:
751.89 g·mol⁻¹ | Sequence: Thr-Lys-Pro-Arg-Pro-
Gly-Pro**

DESCRIPTION:

Selank is another ACTH/MSH-like peptide of the melanocortin class most closely related to the analog tufstin. While traditionally prescribed for anxiety and depression, it has been known to be effective in many other treatments related to immune modulation, anticoagulation, PTSD, ADHD, and metabolic syndromes. Selank has pronounced anxiolytic activity and acts as a stable neuropsychotropic, antidepressant, and anti-stress drug that relieves aggression and fear reaction in different animal species. Selank also has a nootropic action, which positively influences the formation of memory and learning processes, and marked immunomodulatory activity. Clinical studies have shown that the effect of selank is similar to that of tranquilizers at low doses, but is not accompanied by the unwanted side effects of benzodiazepine tranquilizers such as amnesia, withdrawal, or

dependence. Experiments have also demonstrated the effectiveness of Selank in preventing the accumulation of body fat (i.e., weight gain) with simultaneous activation of the functional state of the anticoagulation system in development of the metabolic syndrome. Furthermore, decreased blood glucose levels have been observed with chronic treatment of this peptide. The peptide Selank, like the drug SemaX, induces anticoagulant and hyperglycemia effects possibly due to the presence of the same amino acid sequence, Pro-Gly-Pro, in its structure. Thus, Selank can be used as a broad-spectrum therapeutic agent for the treatment of metabolic syndrome.

Often prescribed for: Anxiolytic, Immune improvement, gastric protection, as a preventative weight gain/metabolic syndrome, and with opioid and alcohol withdrawal/ dependence.

CLINICAL RESEARCH:

P-1114 - Rapid and Slow Response During Treatment of Generalized Anxiety Disorder with Peptide Anxiolytic Selank

Results: 40% of patients were rapid responders (RR) and characterized by abrupt reduction of whole set of symptoms in first 1-3 Days. At the Day 3 Hamilton Anxiety Rating Scale (HARS) mean total score [SD] reduced from 20.3[11.9] to 7.0[2.9] ($p < 0.01$). 60% of patients responded gradually (conventional responders - CR). Clinically significant changes of mean HARS total

score from 16.1[7.2] to 6.2[4.7] were achieved at Day 14, $p < 0.01$. In contrast to CR, RR demonstrated obvious EEG-reaction after single dose (900 µg) with increase of beta-rhythm, decrease of theta- and low frequencies of alpha-rhythm (all $p < 0.05$). Initially RR and CR significantly differed by the score of asthenic and cognitive symptoms ($p < 0.05$).

Syuniyakov, Timur & S Teleshova, E & G Neznamov, G & Bochkarev, Vitaly. (2012). P-1114-Rapid and slow response during treatment of generalized anxiety disorder with peptide anxiolytic selank. European Psychiatry. 27.

SemaX

It is well known that ACTH/MSH-like peptides (melanocortins) exert pleiotropic non-hormonal actions among their larger activities.

Melanocortins affect learning processes and exploratory behavior, regeneration and development, nociceptive and inflammatory processes, accelerate nerve regeneration and improve neuromuscular performance. Together these classes of peptides control many behaviors such as regulating attention, processes of learning, and memory formation as a result of their pronounced effect on CNS functions.

Heptapeptide SEMAX (MEHFP GP) is the analogue of ACTH (4-10) that has prolonged neurotropic activity and thus is a good candidate for medical therapy. Currently this peptide is successfully used in treatment of patients with pathologies related to brain circulation dysfunction and with different intellectual- amnesic problems of the CNS. Doctors have

prescribed it for many conditions like anxiety, memory improvement, ischemic events, stroke, nerve regeneration, ADHD, opioid withdrawal, and even chronic diseases such as ALS, Parkinson's, and Alzheimer's. Some doctors use it as a preventative measure to protect against chronic disease and to acutely help improve memory and learning processes. It also has a marked antithrombotic and fibrinolytic effect and a gastric protective effect. It has also been suggested in literature that due to its effect on carboxypeptidase it can also increase physical performance and adaptation capacities in exposure to high intensity exercise. At its higher doses, .5mg/kg can even be analgesic.

Often prescribed for: Anti-Thrombosis, ADHD/ Learning, Gastric protection, Physical exertion improvement pain, Metal toxicities.

CLINICAL RESEARCH:

The Nootropic and Analgesic Effects of Semax Given via Different Routes

The heptapeptide Semax (MEHFPGP) is an analog of the fragment ACTH(4-10) with long-lasting actions. The aim of the present work was to study the effects of Semax on learning ability and pain sensitivity in white rats given different doses via the intraperitoneal and intranasal routes. The nootropic effects of Semax were studied in a test based on the acquisition of a conditioned passive avoidance reaction to pain stimulation. Pain sensitivity was assessed

in a hindpaw compression test. The results showed that i.p. Semax had nootropic and analgesic actions. Dose-response characteristics were different for these different effects.

Intranasal Semax was more effective in improving learning in animals than i.p. Semax but had no effect on pain sensitivity. Our results provide evidence that different mechanisms and brain structures are involved in mediating the nootropic and analgesic effects of Semax.

D.M, Manchenko & N.Yu, Glazova & Levitskaya, Natalia & L.A, Andreeva & , Kamenskii A.A & N.F, Myasoedov. (2012). The Nootropic and Analgesic Effects of Semax Given via Different Routes. Neuroscience and Behavioral Physiology. 42. 264-270.

Thymosin Alpha-1

Purity: >98% (HPLC on request) | Molecular Formula: C₁₂₉H₂₁₅N₃₃O₅₅

Molecular Weight: 3108.28 | Sequence: Ac-Ser-Asp-Ala-Ala-Val-Asp-Thr-Ser-Ser-Glu-Ile-Thr-Thr-Lys-Asp-Leu-Lys-GluLysLys-Glu-Val-Val-Glu-Glu-Ala-Glu-Asn-OH

DESCRIPTION:

Thymosin α -1 is a major component of Thymosin Fraction 5 and is responsible for restoring and modulating immune function, particularly cell mediated immune function. Recent studies showed that Thymosin Alpha-1 molecule increased major histocompatibility complex (MHC) class-1 and Toll-like receptor expression as well as cytokine production, suggesting its immunoregulatory role.

It is an FDA approved medication under the trade name zadaxin after it received orphan drug

approval status. It is widely used and studied in multiple types of cancer and viral illnesses. Some physicians are using thymosin for chronic fatigue and Lyme disease as well as autoimmune function as well.

TA 1 is thought to modulate the immune system by augmenting T-cell function. TA1 may affect thymocytes by stimulating their differentiation or by converting them to active T cells. TA1 is rapidly absorbed, achieving peak serum concentrations within two hours.

CLINICAL RESEARCH:

Thymosin Alpha 1: Biological activities, applications and engineering production

Thymosin alpha 1 (T α 1), a 28-amino acid peptide, was first described and characterized from calf thymuses in 1977. This peptide can enhance T-cell, dendritic cell (DC) and antibody responses, modulate cytokines and chemokines production and block steroid-induced apoptosis of thymocytes. Due to its pleiotropic biological activities, T α 1 has gained increasing interest in recent years and has been used for the treatment of various diseases in clinic. Accordingly, there is an increasing need for the

production of this peptide. So far, T α 1 used in clinic is synthesized using solid phase peptide synthesis. Here, we summarize the genetic engineering methods to produce T α 1 using prokaryotic or eukaryotic expression systems. The effectiveness of these biological products in increasing the secretion of cytokines and in promoting lymphocyte proliferation were investigated in vitro studies. This opens the possibility for biotechnological production of T α 1 for the research and clinical applications.

Li, Juan Jenny et al. "Thymosin alpha 1: Biological activities, applications and genetic engineering production." *Peptides* 31 (2010): 2151-2158.

Other studies :

[PLoS One](#). 2013 Aug 19;8(8):e72242. doi: 10.1371/journal.pone.0072242. eCollection 2013.

A tumor-penetrating peptide modification enhances the antitumor activity of thymosin alpha 1.

Author information

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Abstract

A serious limitation of numerous antitumor drugs is the incapacity to penetrate solid tumors. However, addition of an RGD fragment to peptide drugs might solve this problem. In this study, we explored whether the introduction of a permeability-enhancing sequence, such as iRGD (CRGDK/RGPD/EC) fragments, would enhance the activity of thymosin alpha 1 (Tα1). The modified Tα1 (Tα1-iRGD) was successfully expressed and purified, and the in vitro assay showed that Tα1-iRGD presented a similar activity as Tα1 in promoting proliferation of mouse splenocytes. Meanwhile, cell adhesion analysis revealed that Tα1-iRGD exhibited more specific and greater binding with tumor cells compared with Tα1. Furthermore, the iRGD fragment evidently enhanced the basal ability of Tα1 to inhibit proliferation of cancer cells in vitro, particularly of mouse melanoma cell line B16F10 and human lung cancer cell line H460. Our findings indicated that the addition of an iRGD fragment increased the anti-proliferative activity of Tα1 against cancer cells by improving the ability of Tα1 to penetrate the tumor cells. This study highlighted the important roles of an iRGD sequence in the therapeutic strategy of Tα1-iRGD. Thus, Tα1-iRGD could be a novel drug candidate for cancer treatment.

Ann N Y Acad Sci. 2012 Oct;1269:26-33. doi: 10.1111/j.1749-6632.2012.06697.x.

Thymosin α1 and cancer: action on immune effector and tumor target cells.

Garaci E¹, Pica F, Serafino A, Balestrieri E, Matteucci C, Moroni G, Sorrentino R, Zonfrillo M, Pierimarchi P, Sinibaldi-Vallebona P.

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Abstract

Since it was first identified, thymosin alpha 1 (Tα1) has been characterized to have pleiotropic effects on several pathological conditions, in particular as a modulator of immune response and inflammation. Several properties exerted by Tα1 may be attributable to a direct action on lymphoid cells. Tα1 has been shown to exert an immune modulatory activity on both T cell and natural killer cell maturation and to have an effect on functions of mature lymphocytes, including stimulating cytokine production and cytotoxic T lymphocyte-mediated cytotoxic responses. In previous studies we have shown that Tα1 increases the expression of major histocompatibility complex class I surface molecules in murine and human tumor cell lines and in primary cultures of human

macrophages. In the present paper, we describe preliminary data indicating that T α 1 is also capable of increasing the expression of tumor antigens in both experimental and human tumor cell lines. This effect, which is exerted at the level of the target tumor cells, represents an additional factor increasing the antitumor activity of T α 1.

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[Ann N Y Acad Sci.](#) 2007 Sep;1112:326-38. Epub 2007 May 10.

Thymosin alpha1: an endogenous regulator of inflammation, immunity, and tolerance.

[Romani L¹](#), [Bistoni F](#), [Montagnoli C](#), [Gaziano R](#), [Bozza S](#), [Bonifazi P](#), [Zelante T](#), [Moretti S](#), [Rasi G](#), [Garaci E](#), [Puccetti P](#).

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Abstract

Thymosin alpha1 (Talpha1), first described and characterized by Allan Goldstein in 1972, is used worldwide for the treatment of some immunodeficiencies, malignancies, and infections. Although Talpha1 has shown a variety of effects on cells and pathways of the immune system, its central role in modulating dendritic cell (DC) function has only recently been appreciated. As DCs have the ability to sense infection and tissue stress and to translate collectively this information into an appropriate immune response, an action on DCs would predict a central role for Talpha1 in inducing different forms of immunity and tolerance. Recent results have shown that Talpha1: (a) primed DCs for antifungal Th1 resistance through Toll-like receptor (TLR)/MyD88-dependent signaling and this translated in vivo in protection against aspergillosis; (b) activated plasmacytoid DCs (pDC) via the TLR9/MyD88-dependent viral recognition, thus leading to the activation of interferon regulatory factor 7 and the promotion of the IFN-alpha/IFN-gamma-dependent effector pathway, which resulted in vivo in protection against primary murine cytomegalovirus infection; (c) induced indoleamine 2,3-dioxygenase activity in DCs, thus affecting tolerization toward self as well as microbial non-self-antigens, and this resulted in vivo in transplantation tolerance and protection from inflammatory allergy. Talpha1 is produced in vivo by cleavage of prothymosin alpha in diverse mammalian tissues. Our data qualify Talpha1 as an endogenous regulator of immune homeostasis and suggest that instructive immunotherapy with Talpha1, via DCs and tryptophan catabolism, could be at work to control inflammation, immunity, and tolerance in a variety of clinical settings.

Thymosin Beta

Purity: >98% (HPLC on request) | **Molecular Formula :** C₂₁₂H₃₅₀N₅₆O₇₈S

Molecular Weight: 4963.506 g/mol | **Sequence:** Ac-Ser-Asp-Lys-Pro-Asp-Met-Ala-Glu-Ile-Glu-Lys-Phe-Asp-Lys-Ser-Lys-Leu-Lys-Lys-Thr-Glu-Thr-Gin-Glu-Lys-Asn-Pro-Leu-Pro-Ser-Lys-Glu-Thy-Ile-Glu-Gin-Glu-Lys-Gin-Ala-Gly-Glu-Ser

DESCRIPTION:

Thymosin is a hormone secreted from the thymus. Its primary function is to stimulate the production of T cells, which are an important part of the immune system. Thymosin also assists in the development of B cells to plasma cells to produce antibodies. The predominant form of Thymosin, Thymosin Beta 4, is a member of a highly conserved family of actin monomer-sequestering proteins. In addition to its role as a major actin-sequestering molecule, Thymosin Beta 4 plays a role in tissue repair. Tβ4 has been found to play an important role in protection, regeneration and remodeling of injured or damaged tissues. The gene for Tβ4 has also been found to be one of the first to be upregulated after injuries. Thymosin Beta 4 is currently being trialed as a potential therapy for HIV, AIDS, and Influenza. Thymosin Beta 4 is most often prescribed for acute injury, surgical repair and for senior athletes. It has most recently been shown to help regrow hair in addition to PRP.

CLINICAL RESEARCH:

Differential expression of the human thymosin-beta 4 gene in lymphocytes, macrophages, and granulocytes.

A cDNA clone encoding human thymosin-beta 4 was isolated from a cDNA library prepared from peripheral blood leukocytes of a patient with acute lymphocytic leukemia. This clone contained the entire coding sequence of 43 amino acid residues of thymosin-beta 4 and had an initiation codon and two termination codons. The amino acid and nucleotide sequences in the coding region were well conserved between rat and human. Nine of 132 nucleotides were different in the coding sequences (93% homology), but the deduced amino acid sequences were identical. No signal peptide was found in the deduced protein sequence. Human thymosin-beta 4 mRNA, approximately 830 nucleotides in length, was about 30 nucleotides larger than rat thymosin-beta 4 mRNA. Expression of the human thymosin-beta 4 gene in various

primary myeloid and lymphoid malignant cells and in a few human hemopoietic cell lines was studied. Northern

blot analyses of different neoplastic B lymphocytes revealed that steady state levels of thymosin-beta 4 mRNA varied as a function of differentiation stage. Thymosin-beta 4 mRNA levels were decreased in myeloma cells as are class II human leukocyte antigen, Fc receptor, and complement receptor, suggesting a relationship between thymosin-beta 4 and the immune response. Thymosin-beta 4 mRNA was more highly expressed in mature granulocytes than in immature blastic cells. Treatment of THP-1 cells, a human monocytic cell line, with recombinant human interferon- lambda reduced the levels of thymosin-beta 4 mRNA. Its level decreased after differentiation of THP-1 cells into Ia⁺ macrophages, but increased after differentiation of HL-60 cells into Ia⁻ macrophages. The pattern of thymosin-beta 4 gene expression suggests that it may play a fundamental role in the host defense mechanism.

H Gondo, J Kudo, J W White, C Barr, P Selvanayagam, G F Saunders The Journal of Immunology December 1, 1987, 139 (11) 3840-3848;

Zinc Thymulin

**Purity: >98% (HPLC on request) | Molecular
Formula: C₃₃H₅₄N₁₂O₁₅ Molecular Weight: 858.85
g/mol | Sequence: Non-Peptide**

DESCRIPTION:

Thymulin is a nonapeptide produced by two distinct epithelial populations in the thymus first described by Bach in 1977. It requires zinc for biological activity. The hormone is involved in

T-cell differentiation and enhancement of T and NK cell actions. Thymulin has neuroendocrine effects as well. It follows a circadian rhythm and physiologically elevated ACTH levels correlate positively with thymulin plasma levels and vice versa. A recent study was done on Zinc Thymulin to test its efficacy in the treatment of hair loss. The study indicated that topical treatment with zinc thymulin significantly increased hair growth over 6 months; further, there were no systemic or local side effects from the treatment. The zinc thymulin metallo-peptide optionally also improves endogenous hair pigmentation. For example, by stimulating melanogenesis in grey or greying hair.

CLINICAL RESEARCH:

An Analysis of the Safety and Efficacy of Topical Zinc-Thymulin to treat Androgenetic Alopecia

To assess the safety and efficacy of the metallopeptide zinc-thymulin (ZT) for treating androgenetic alopecia (AGA). Previous in vitro studies have described that different thymic peptides can both increase and decrease anagen (thymulin and thymosin beta-4, respectively). Zinc is an essential element and serum zinc deficiency can cause hair loss.

Eighteen consecutive adult subjects were recruited, 17 males and 1 female, age range 35-90 years(mean 55.4, SD 13.3) with a diagnosis of AGA, Norwood classification 2-7, and hair loss duration range of 3-40 years (mean 15.8, SD 9.6). The trial duration for each subject ranged from

4-10 months. The test compound ZT was synthesized by standard Fmoc peptide protocols and administered in water based topical spray to the scalp. Baseline and after treatment images for hair growth were graded by two blinded assessors using two validated scales: 1. numerical visual analog scale (VAS) for global assessment 2. hair growth

index (HGI) of images under higher magnification for percentage changes of vellus, intermediate and terminal hair.

ZT demonstrated no adverse systemic effects or local side effects of redness or scalp irritation in any subject over a total of 3,300 treatment days. Three subjects who were concurrently using minoxidil (N=2) and minoxidil / finasteride (N=1) did not report any drug interaction with ZT. VAS hair assessment improvement was significant in subjects who completed 6 months of treatment ($P=0.045$, t-test). HGI assessment showed a significant increase in the number of newly observed intermediate hairs in previous "absent hair" regions ($P<0.0001$) with an average increase of vellus type (32%) and intermediate type (23%) hairs at 6 months. Melanogenesis was observed in several subjects.

Topical applications of ZT demonstrated safety and established efficacy for initiating and maintaining anagen to treat male pattern baldness when applied for >6 months.