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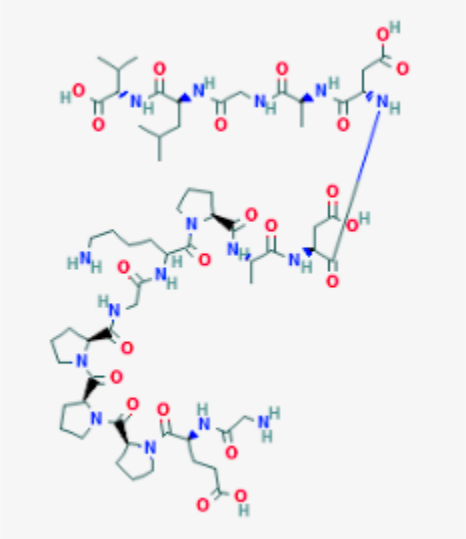
Peptide Primer 3.0

An Introduction to Healing Peptides

Plus: u/BoldMeaures Reddit Archive



INTRODUCTION

When I started looking into peptides, I found that many of the articles, videos, and podcasts on the topic lacked depth or details. In contrast, I found research studies were full of details, but lacked context and were difficult to interpret without a solid foundation of understanding.

I wanted to make something in between. A guide that was accessible to people with no knowledge of peptides, but containing enough detail that they could leave with a firm grasp of what peptides were and how they might be used. More importantly, I wanted to empower readers to decide for themselves if peptides were something they wanted to pursue.

This edition of the Peptide Primer also includes an archive of my Reddit posts, which provide additional information about some of the peptides introduced here.

Disclaimer: The author of this document is not a doctor. This information is not intended to diagnose, treat, cure, or prevent any disease. Readers are responsible for the safety and legality of their decisions. Consult a medical professional before stopping or starting any treatment.

Peptide Primer 3.0

Reddit Archive

BPC-157

TB4/TB500

Peptide experiences of people with EDS/HSD

What is a peptide?

You're probably familiar with amino acids. These simple building blocks are combined in long sequences to form protein structures which provide structural integrity to your body.

Your body also combines amino acids into short sequences as a way of communicating between tissues, and regulating processes in the body. These short sequences are called peptides. You can think of peptides like an email, with the individual amino acids representing specific words. If you string the right words together in the right order and get it to the right address, you can engage specific natural processes in the body.

Have you ever wondered how your body knows to heal a cut? Well, red blood cells contain a peptide called *Thymosin beta 4* (TB4). When red blood cells burst open to clot a wound, they release TB4 and it floats around interacting with nearby cells. The TB4 basically says *hey, we're wounded*. It aids in structural repairs and encourages angiogenesis (blood vessel formation) so that nutrients and oxygen can be delivered where they are needed. In the meantime, it also tells the local cells to resist apoptosis (self destruction), because help is on the way. It encourages neurological healing, and promotes the formation of quality, functional collagen structures, rather than fibrosis (scar tissue).

So now imagine you have a lingering injury that didn't heal properly, or a systemic disease that leads to tissue damage. The healing has stopped, but the wound remains. What if you could use TB4 to tell your body that it's wounded, and encourage it to restart the healing process?

That's the basic premise of peptides. Introduce the appropriate peptides into your body to engage specific natural processes and improve your health.

What's the catch?

Peptides are legitimate medical interventions, and there are doctors who prescribe them. However, many other doctors are unfamiliar with them, or view them as unproven. Some peptides have extensive human testing and FDA approval, others only have rodent studies or theoretical applications. So the catch is that you'll have to grapple with your own standards of evidence and decide what you are comfortable with.

I will say, in regards to safety, that individual needs and tolerances of these compounds could vary substantially. So although I've included some dosage information, **everyone should start with low doses to test tolerance.** Anyone with immune issues or a tendency towards histamine reactions should be especially cautious. Specifically, I've encountered people who reacted strongly to moderate doses of GH secretagogues. This could be due to potency variations or factors that vary between individuals. But it's better to discover these issues at low dosages. You can always add more, but once you inject something.. you can't pull it back out.

Which peptides should I use?

I'm going to highlight some of the most popular peptides in this document, but other options may be more appropriate for your situation. Here's how I've approached finding and using peptides.

1. Learn about your health challenges.

   Ask yourself questions.. What sorts of tissues are involved? What is the underlying mechanism leading to damage? What is your body struggling to do?

2. Compile a broad list of contenders.

   Search the internet for mentions of peptides and your health challenges or goals. Search for mentions of relevant conditions on r/peptides, or search for "peptides" in communities related to your challenges. Anecdotes and opinions of internet strangers are always suspect, but they can be useful in generating ideas.

   If you can, look through the peptides on www.peptidesciences.com, you might find something relevant to your needs that isn't talked about much.

3. Scrutinize your list to find peptides that match your priorities.

   What is important to you.. Human safety data? Anecdotes? Endorsement by doctors? Cost? Method of administration?

How many peptides can I use?

Exercising and eating well can each separately improve your health. But no one advocates for exercising for 6 weeks followed by 6 weeks of healthy eating. It's obvious that combining them together can have a synergistic effect that is even stronger than each separately.

Peptides are similar. Using a peptide like BPC-157 that signals for healing in connective tissue is great, but combining it with other peptides that support robust growth hormone levels or promote healing in different ways can increase the effects.

There are certainly merits to starting peptides alone to determine how you respond. And some situations or priorities might make separate use more appealing. But "stacking" multiple peptides is a common practice. Regardless of how many peptides you use, they will be more effective in combination with other behaviors that support your health, like solid nutrition and generous amounts of sleep.

BPC-157

Origin: This sequence of amino acids was identified within a larger gastric peptide called *Body Protection Compound* which protects the gastrointestinal tract by promoting healing and blood vessel growth.

Effects: BPC-157 is credited with significantly improving wound healing by increasing fibroblast activity. Its effects seem to be especially strong in connective tissue, but benefits have been noted in many tissues and systems.

Some highlights from studies (from World-of-Peptides.com):

- BPC-157 significantly improves healing after the following injuries: skin incisions; deep skin burns; various anastomoses as intestinal wounds; diabetic wounds; various fistulas; various tissue transections, particularly ligament, tendon, muscle and nerve. Healing time of all these injuries is significantly decreased with BPC-157 administration.

- BPC-157 prevents scar tissue buildup after injury, and reduces already existing scar tissue

- BPC-157 modulates the immune system and activates macrophages in the immune system, which leads to increased production of growth factors that fight infections, ultimately strengthening the immune system.

- BPC-157 significantly prolongs survival of rats with carcinoma and melanoma B-16 cancers, from 25 days to 45+ days.

- BPC-157 prevents development of gastric ulcers and heals existing gastric ulcers by reducing the ulcer area and accelerating the rebuilding of glandular epithelium and formation of granulation tissue.

- BPC-157 successfully reduces several models of acute, non-specific inflammation.

- BPC-157 acts against temperature decrease (i.e. water immersion test) and increase (yeast-induced).

- BPC-157 increases pain threshold in carrageenan test in rats.

- BPC-157, given before infection of rats with hepatitis A virus, Lymphatic Choriomeningitis (LCM) virus and herpes virus types 1 and 2, completely prevented all signs of infection and disease.

- BPC-157 given to rats after viral infection delays onset of disease symptoms and decreases death.

There are a few versions of BPC-157. The most common version is *BPC-157 acetate*, and the newest form is *BPC-157 Stable Version.* They both have the same active amino acid sequence, but the "stable version" incorporates the amino acid arginine and is more resistant to breakdown in acidic environments such as the stomach. Because of the incorporation of arginine, I generally refer to BPC-157 Stable Version as *arg-BPC*, or *arg-BPC-157*.

BPC-157 acetate names: BPC-157 acetate, BPC-157, Body Protecting Compound 157, bepecin, Pentadecapeptide 157. There were human trials using BPC-157 under the drug name PL 14736.

BPC-157 Stable Version names: BPC-157 Stable, BPC-157 Stable Version, BPC 157 di-L-arginine salt, Arg-BPC-157, arg-BPC. In studies it may be referred to as "Stable gastric pentadecapeptide BPC 157". BPC-157 Stable is available through Nootroo as BeePC, which is sourced from Diagen, the patent holder. I've been told that the capsules from Tailor Made Health (AKA Infiniwell) are arg-BPC as well.

What's the difference?

The data from the arg-BPC patent shows that two hours in a ph of 2 breaks down both acetate and

arginine versions substantially (2.5% vs 6% remaining). Two hours at ph of 3 breaks down acetate substantially but arginine is largely intact (7.8% vs 93.6% remaining). At ph 4, both do well (81.3% vs 99.5% remaining).

So, if you're using oral BPC-157, arg-BPC may have an advantage in a very acidic stomach. But if you can get to a stomach ph of 4 temporarily, the acetate version might actually do fine.

Does oral administration work systemically?

At first glance, oral BPC-157 doesn't seem like it would improve a shoulder injury because the sequence is too big for significant absorption through the intestine. Despite this apparent barrier, there are people who point to rodent studies and argue that oral BPC-157 helps with peripheral healing. Here's the case for and against oral BPC-157 and peripheral healing.

The case for peripheral healing

- This rodent study shows similar improvements in peripheral healing from injection and oral administration. Both oral and injection groups had improved healing over placebo, and to a similar degree.

- It's possible that BPC-157 could exert some peripheral healing effects through the enteric nervous system or some sort of cascade that promotes healing outside the gut.

- There are anecdotes from people who say oral BPC-157 improved peripheral healing.

The case against peripheral healing

- Rodent study issues..

    - In that study, the BPC-157 was administered immediately to **augment healing**, rather than later to **restart healing** as humans often use it.

    - There were two injection groups in that study, and one of them received an extremely low dose, approximately 2,500x smaller than typically used in humans (by body weight, after species conversion). That group had similar results to the oral group and larger injection group.

      Nobody is taking this one rodent study as "proof" that injecting a 100 nanogram dose of BPC-157 would work just as well as 250 micrograms, but the evidence for that

conclusion is just as strong as for the idea that oral can match the effects of injection.

- Anecdotes strongly favor injection for peripheral healing. In fact, the entire reputation of BPC-157 for healing peripheral injuries is built on injection of BPC-157 acetate.

- The BPC-157 sequence is too long to be absorbed intact, and human enema trials confirmed no meaningful absorption.

- There is evidence that BPC-157 has direct effects on some cells in a dose-dependent manner, which further weakens the argument for matched effects from oral administration.

The verdict

Does oral BPC-157 improve peripheral healing to some degree?
Maybe.

Is it reasonable to expect oral BPC-157 to match the effects of injection, when it comes to peripheral healing?
No.

Oral is convenient, and maybe it will help your shoulder or knee. If you want convenience and the possibility of some help, go for it. But if you want the most proven means of getting the strongest possible improvement in peripheral healing.. that's injection.

When I came to peptides, I had severe widespread connective tissue problems, and I wasn't worried about convenience. **I wanted the best chance for the strongest systemic effects.** So I injected the acetate version, and found it very helpful. I have encountered many people with connective tissue disorders who were confident that injected BPC-157 (acetate or arginine versions) was helpful. I haven't encountered any who were confident that oral BPC-157 helped substantially with peripheral injuries.

I don't think injection is appropriate for everyone. For some people, it makes sense to try oral administration. But regardless, everyone should be allowed to decide what route matches their priorities. I take a firm stance on this because I spent over a year trying to dispel misinformation from the founder of BioPrime Supplements, who lied, doctored evidence, and deliberately misled people on Reddit into believing that it was "proven" that oral administration could match the peripheral healing effects of injection. By portraying oral as "superior" to injection, he denied people the opportunity to decide their own priorities, and he continues to prey on sick people for personal gain. I encountered

many people who'd been badgered into buying something that didn't help them and didn't match their priorities.

What about local injection?

As I mentioned above, there are cell culture studies which indicate that BPC-157 can have a direct effect on fibroblasts. So naturally it's tempting to inject close to the injury so more of the BPC-157 gets in contact with the injured tissue. The counter argument is that once injected, the peptide will quickly slip into the bloodstream and be swept around the body and distributed evenly anyway. That would mean that local injection just needlessly aggravates injured tissues and risks jabbing the needle into a nerve with no benefit.

My stance is that subcutaneous injection into belly fat is a well established approach, and is certainly appropriate for beginners. I got great results from it.

But.. I can't entirely rule out the possibility that some of the peptide could diffuse through the local tissue between cells rather than end up in the bloodstream. And connective tissue generally isn't very well vascularized, so it's not an idea to quickly dismiss. My efforts to sort this out led me to the conclusion that if there is an increased local effect it's likely to be very close to the injection site. For most people, in most cases, I don't think it justifies adventuring around with a needle. But I did it with a few stubborn injuries, and I don't think it's insane. I mean, maybe it's a little insane. Ultimately, I would say most people should stick with belly fat, and shouldn't feel like they are missing out on anything. But as always, I think personal priorities should factor into the decision.

Research summaries: Explanation of BPC-157 Stable, World-of-peptides.com summary of studies, PeptideSciences.com summary, Examine.com research summary, mechanisms and potential side effects from AnabolicDoc

Specific studies (abstracts): BPC-157's effect on healing, BPC 157 cream improves burn-wound healing, BPC 157 modulatory effect on angiogenesis in muscle and tendon healing, BPC 157 and NO-system relation (the authors state that BPC-157 exhibits high safety and a lethal dose has not been found). BPC 157 enhances the growth hormone receptor expression in tendon fibroblasts, Brain-gut Axis and Pentadecapeptide BPC 157: Theoretical and Practical Implications, Therapeutic potential of pro-angiogenic BPC157, BPC 157 and Standard Angiogenic Growth Factors, BPC 157 accelerating musculoskeletal soft tissue healing, BPC 157 in traumatic nerve injury, a collection of BPC-157 studies

Videos: BPC 157 for Gut & Musculoskeletal Healing, Dr Timmermans, BPC-157 effects and delivery

methods (discussion of GI), Dr Moeller, Live Like A Viking summary of effects and reconstitution process, BPC-157 discussion with Ryan Smith from Tailor Made Compounding, Repair and Recovery with Peptide Therapy, Ryan Smith, Tailor Made Compounding

Dosage & delivery methods

1. Subcutaneous injection (most potent systemic effects): How to prepare BPC-157, Subcutaneous injection demo
    a. Dosage: Tailor Made Compounding Catalog (BPC-157: page 8/15) suggests 300mcg 1x/day for 30 days. Many people (myself included) have used 250mcg injections 2x/day with good results. A person could start with 100mcg 1x/day and slowly increase dosage and frequency.
2. Oral dosing: I don't have a demo of oral preparation, but this video discusses dosing.
    a. Dosage: 500mcg capsules 2x/day seems to be common. If using a powder such as BeePC, a person could mix 5mg BPC-157 Stable Version with 10ml bacteriostatic or sterile water in a dropper bottle. That would deliver 500mcg per 1ml (about 20 drops). Or 5mg could be mixed with 5ml, in which case 1/2ml (about 10 drops) would deliver 500mcg. It could also be weighed into capsules. BPC-157 Stable is available through Nootroo as BeePC, which is sourced from Diagen, the patent holder. I've been told that the capsules from Tailor Made Health (AKA Infiniwell) are arg-BPC as well.

Ipamorelin

Note: Ipamorelin is a Growth Hormone Releasing Peptide (GHRP). There are other GHRPs.

Names: Ipamorelin, developmental code name NNC 26-0161.

Origin: Ipamorelin is a short peptide sequence capable of binding to the ghrelin/growth hormone secretagogue receptor, replicating the growth hormone releasing effect of ghrelin without unpleasant side effects. It is one of the most selective growth hormone secretagogues known and doesn't seem to have any effect on ACTH, prolactin, follicle-stimulating hormone, luteinizing hormone, thyroid-stimulating hormone, or cortisol release.

Impact: By injecting Ipamorelin subcutaneously, it induces the pituitary to release stored growth hormone (GH) into the bloodstream. This GH has a variety of effects, which may include increased cellular repair and regeneration, increased collagen production, increased lean muscle mass, improved sleep, increased bone density, decreased body fat, and reduced catabolism. Besides increasing overall

GH, Ipamorelin also releases it in a pulse. As we age, we lose the pulsatile release and our GH trickles out in an ineffective manner. By restoring the pulse of GH it can reach the tissues throughout the body more effectively.

Research summaries: Multiple Effects of Growth Hormone in the Body: Is it Really the Hormone for Growth?, List of Ipamorelin benefits from transformyou.com

Specific studies: Growth hormone stimulates the collagen synthesis in human tendon and skeletal muscle without affecting myofibrillar protein synthesis,

Videos: TMC Ipamorelin and CJC 1295

Delivery & dosage: TMC peptide guide (page 20) recommends 200 mcg subcutaneously 1x/day, 5x/week paired with CJC 1295. Ipamorelin is a GHRP, it should be paired with a GHRH. Some people use 200-300 mcg up to 3x/day, spaced 4+hrs apart.

Some people advocate a lower dose, such as 100 mcg each of Ipamorelin and 100 mcg Mod-GRF. The idea is that going beyond that only increases GH by a small percentage and isn't as cost effective. I don't have a study to point to, but this is addressed in the DatBtrue archive (scroll down if you don't see it). **I'd suggest starting with a very low dose, there are anecdotal reports of allergic reactions.**

Timing: The standard advice is to wait 2-3 hrs after eating, and don't eat for another ½ hr after injection. The reason being that Insulin may interfere with GH, so injecting in a fasted state is suggested for maximum effect. However, when a GHRH and GHRP are used together it may not matter, as suggested by this bovine study. GH release is also blocked by the presence of somatostatin. Again, a GHRH/GHRP combo may overcome this, or it may be worth timing your injections when somatostatin is low, and the body is primed to release GH. This page has a graph of natural GH release. This reasoning would suggest the evening is a good time, shortly before bed. There may also be a good opportunity immediately after waking. The night time release is more likely timed off of darkness, rather than the clock. I put on blue blocking glasses 2 hrs before bed to encourage melatonin production, but it may also reduce my somatostatin and increase the effectiveness of the GH secretagogues. Again, this may all be unnecessary with GHRH/GHRP combos, I don't know for sure.

Mod-GRF (1-29) aka CJC-1295 without DAC

Names: CJC-1295 w/o DAC, CJC-1295 No DAC, Modified GRF (1-29)

Origin: Mod-GRF (1-29) is a slightly modified version of a peptide sequence in Growth Hormone Releasing Hormone (GHRH).

Impact: Mod-GRF increases the number of cells that respond to a GHRP such as Ipamorelin, potentially delivering 5x the pulse compared to Ipamorelin alone. So even if you don't want a huge pulse of GH, using low doses of both together is much more cost effective than either compound separately.

Research summaries: Peptide-guide.com summary of modified-grf-1-29, neobiolab.com current research findings on CJC 1295, Peptidesciences.com/mod-grf-1-29

Videos: TMC Ipamorelin and CJC 1295

Delivery & dosage: The TMC peptide guide (page 11) recommends 200 mcg subcutaneously 1x/day, 5x/week (paired with Ipamorelin). Some guides suggest 100 mcg is adequate, and I personally agree. Again, insulin may diminish the impact of GH, so injecting in a fasted state may produce the strongest effect. The standard advice is to wait 2-3 hrs after eating, and don't eat for 1/2hr after injection.

What the heck is DAC?: Drug Affinity Complex, or DAC, is a chemical complex attached to the peptide sequence which prevents breakdown by the enzyme peptidase and excretion by the liver. This results in a significantly increased half-life. In many peptides, this would be helpful. But when we are intentionally inducing a brief pulse of GH, the DAC isn't appropriate.

CJC-1295 is mod-GRF with DAC attached. So when we say "CJC-1295 without DAC" we're saying "mod-GRF with DAC but actually without DAC". Since this is a roundabout "cheeseburger without cheese" sort of thing I prefer to call it mod-GRF.

A note about growth hormone side effects: A search for "growth hormone side effects" may yield alarming results. It's worth noting that these are generally associated with the injection of HGH at supraphysiological levels, not the use of secretagogues. By using secretagogues we stay within a range our bodies might experience naturally, thereby reducing the risk of side effects. This doesn't mean there couldn't be side effects, consult your doctor.

TB-500 and Thymosin Beta-4

Names: TB-500 (AKA Frag 17-23), Thymosin Beta-4, TB4

Note: Although some sources assert that TB-500 is identical to TB4 (except being a synthesized version), strictly speaking TB-500 is Frag 17-23 of TB4. However, many products sold as TB-500 are full sequence TB4. I have a Reddit post archive on the topic later in this doc.

"A number of active sites on Tβ4 have been identified for some of these activities. Amino acid fragment 1-4 is anti-inflammatory, 1-15 is anti-apoptotic and cytoprotective, and 17-23 is active for cell migration, actin binding, dermal wound healing, angiogenesis, and hair growth." (Source)

To avoid confusion, I will use the term *Frag 17-23* instead of TB-500. And use *TB4* when I mean the full 43 amino acid sequence.

Origin: TB4 is a naturally occurring 43-amino acid peptide present in many human and animal cells. Red blood cells contain TB4, and it is released when they burst open to seal a wound.

Impact: A 2015 meta-analysis showed broad applicability of TB4 in various disease processes, including improvement of tissue regeneration, repair of the heart after heart attack, healing of the brain following stroke, trauma and neurological diseases, kidney and liver diseases, and repair of spinal cord, bone and ligament injuries, as well as reducing consequences of aging and viral infection. The primary mechanisms of action seem to be increasing actin production, increasing angiogenesis, and reducing inflammation. It is often paired with BPC-157. Frag 17-23 is responsible for the actin binding activity which is desirable for muscle healing.

Note: Based on anecdotes, TB4/Frag 17-23 may increase flexibility during use, which may be desirable for some or problematic for others. I experienced reduced spasticity in tight muscles, but not a problematic increase in range of motion.

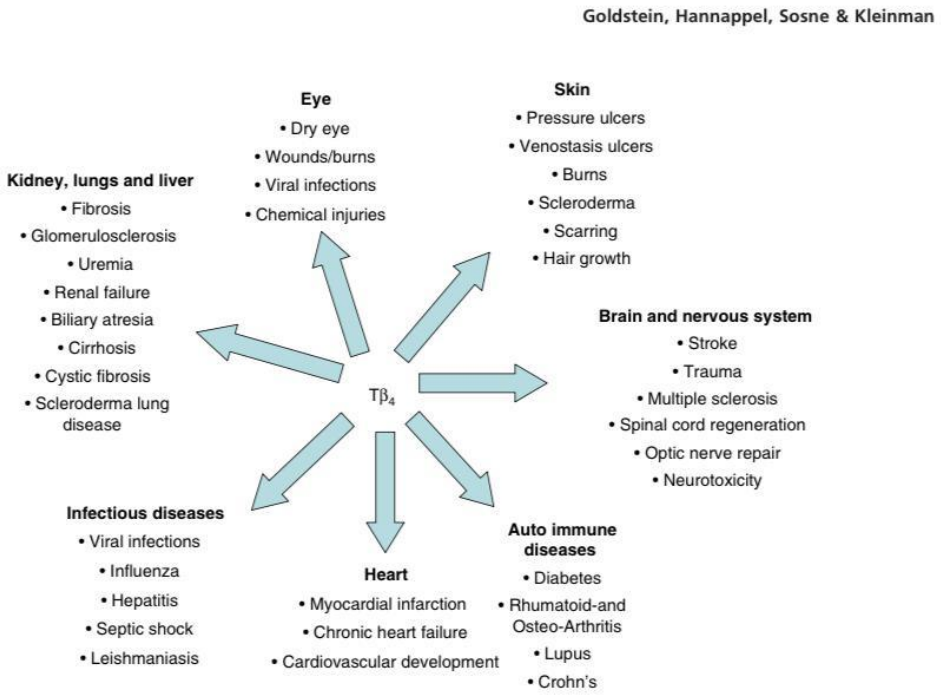
Research summaries: Peptide sciences summary, Peptide-guide.com summary of TB-500,

Individual studies: google drive link

Videos: Jerry Brainium

Delivery & dosage: The TMC peptide guide (page 36) recommends 750 mcg subq daily for 20 days, for a total of 15 mg. A popular dosage protocol is 5 mg 2x/week (such as Monday and Thursday) for 5 weeks, then 5 mg 1x/week for two more weeks. It's unclear what approach is best. My Reddit archive has more dosage info.

Here is an image from Thymosin b4: a multi-functional regenerative peptide. Basic properties and clinical applications.



ARA-290

Names: ARA-290, ARA 290, Cibinetide, PH-BSP

Origin: ARA-290 is a sequence derived from *erythropoietin* (EPO). EPO stimulates red blood cell production, but has also been found to stimulate blood vessel growth, promote cell survival, alter blood pressure, and produce neuroprotective effects in diabetic neuropathy. ARA-290 offers the neuroprotective and pain relieving effects of EPO without stimulating red blood cell production.

Impact: ARA-290 may reduce neuropathic pain and stimulate small fiber nerve repair. It is a potential stimulator of wound repair in chronic diabetes, an immune modulator, and a potential treatment for systemic lupus erythematosus according to some sources. It caught my eye because it may be beneficial for some types of dysautonomia (dysfunction of the autonomic nervous system). I don't have significant dysautonomia symptoms anymore, but it's still an area of interest and the standard treatments are primarily management related.

Research summaries & studies: Peptide sciences summary, Safety and Efficacy of ARA 290 in Sarcoidosis Patients with Symptoms of Small Fiber Neuropathy, ARA 290 Improves Symptoms in Patients with Sarcoidosis-Associated Small Nerve Fiber Loss and Increases Corneal Nerve Fiber Density, ARA 290 Improves Metabolic Control and Neuropathic Symptoms in Patients with Type 2 Diabetes

Videos: Small Fiber Neuropathy and ARA-290 Results (this video has a slow pace but contains good info).

Delivery & dosage: There are no established dosages. One study stated *"The power analysis was based on data collected from a double-blind trial of the safety and efficacy of ARA 290 in patients with sarcoidosis and symptoms of small fiber neuropathy that received 4 mg ARA 290 SC daily for 28 d."*

Another trial included 1mg, 4mg, and 8mg groups.

Note: Epobis is another peptide sequence derived from EPO with similar effects.

Routes to Peptides

So maybe you're intrigued. Here are some options, depending on your comfort level.

1. **The prescription injection route.** This is generally more expensive, but offers confidence that you are using quality medications under the supervision of a doctor.

    a. Ask your current doctor to set up an account with a compounding pharmacy like Tailor Made Compounding that mails products to patients. I didn't go this route, so I don't know what peptides are available. I've heard there are significant restrictions on what can be compounded these days. There may be local compounding pharmacies in your area, or other ways for your doctor to fill the prescription. You may need to direct your doctor towards resources for learning about these medications, as they are unlikely to be familiar with them.
    b. Find a new doctor who prescribes peptides. The International Peptide Society may be able to help you find a physician in your area. There are also clinics which offer online consultations. You could also look for local anti-aging clinics which often prescribe GH secretagogues.

2. **The legally-grey nonprescription injection route.** For those willing to take matters into their own hands, this route is faster and more flexible. Often the products are intended for laboratory use, and will be labeled "not for human consumption".

    Although possession of these compounds isn't illegal* in the United States (from my understanding), injecting or consuming them may be a violation of the purchase agreement. As a result, you may have no recourse if you're unhappy with the results. Here is a list of peptide sources I have heard good things about. I want to be clear: **good businesses go bad quickly**. **It is your responsibility to vet sources to your personal satisfaction.**

*Although GH secretagogues seem to fall into the same category as other peptides, where possession or use isn't illegal, **possession of actual Human Growth Hormone is illegal and may be treated more like anabolic steroids.**

3. **The non-injection (but labeled for human use) route.** Although limited, there are some peptide options which don't require prescriptions and are labeled for human use. Unfortunately, this is an area where unscrupulous people could relieve you of your money. **None of these are endorsements!**

    a. Tailor Made Health has BPC-157 capsules available as dietary supplements. They told me they submitted a GRAS (Generally Regarded As Safe) filing with the FDA.

    b. There are transdermal patches claiming to deliver BPC-157, but I'm very skeptical. The BPC-157 compound is around 1400 Daltons, while the size limit for transdermal delivery seems to be 400-500 Daltons. This may provide local benefits to the skin. I wouldn't expect systemic effects.

    c. A topical option. There are also creams and lotions which include bioactive peptides with beneficial impacts on skin. The effects are generally mild and superficial. Reputable products will list the specific peptides. For example, this one includes Palmitoyl Tripeptide-5 and Palmitoyl Tripeptide-38. A savvy shopper could then check peptidesciences.com to learn about the ingredients, and check other sources as needed. The Ordinary Buffet has peptides, and another version includes GHK-cu.

    d. There are also small peptides such as GHK-Cu, which are available to purchase as cosmetic ingredients. These could be used to boost a peptide cream, or combined with a transdermal carrier like DMSO. Because GHK-Cu is less than 400 Daltons, we can reasonably expect some will be delivered through the skin. DMSO is indiscriminate in what it transports, so be mindful of applying it to skin with cosmetics or sunblock. Also be mindful of getting it on your hands and what you touch afterwards.

    e. Russian bioregulators. The modern approach to peptides is to identify a specific sequence and synthesize it in a lab. But the original approach was to harvest and extract a variety of peptides from the organs of young animals. This method produced a complex of peptides which could then be used to revitalize the same organs and tissues in humans. Although the general concept may be sound, I have doubts about how delicate peptides survive the refining process and can be absorbed orally. You could try breaking the capsules open under your tongue, where the smaller peptides have a chance to reach the bloodstream. Overall, I can't recommend this or completely dismiss it for those who have the money and interest. Sources are surprisingly easy to find. If you're interested in these products check out this bizarre documentary. They start

getting to the point around 9:15, but I suggest watching the whole thing for the full experience.

Supplies

If you're taking the plunge into subcutaneous injection, you'll need some supplies.

1. **Insulin syringes with needles.** 29-30G is a common needle width (higher number = narrower needle). 1 cc/1 ml is a good volume, ½ inch is probably the best needle length. A shorter needle may actually cause more irritation, but this is an area of debate. There are many sources, including local pharmacies. Here is an example. Make sure the syringes include needles, it's not always obvious from the packaging. **These are one time use, so plan on one syringe per injection.** It's fine to pull multiple peptides into a single syringe and inject them all at once.

2. **Alcohol wipes.** It's important to sanitize the vials and skin before each injection. Here is an example.

3. **Bacteriostatic water.** This water is sterile and contains enough alcohol to inhibit bacterial growth. Sterile water doesn't provide the same protection. You may need to shop around due to shortages. **Under no circumstances should you use tap water or store bought distilled water for injection.**

A note about injections: This can be a daunting process at first. It can sting, and local irritation is common. If your hands are shaky, it could bruise. Occasionally it will bleed. These issues will be less common as you become more familiar with the process and develop good technique. Just keep in mind that you wouldn't be surprised if a vaccination stung or bled a little bit, despite being administered by a professional.

Storage

In general, lyophilized (dry powder) peptides should be kept in a freezer and reconstituted peptides should be kept in the refrigerator and away from heat and UV light. Some guides suggest peptides are extremely vulnerable to mechanical damage, to the point where they shouldn't be kept in the door of the fridge because of jostling. Although there's nothing wrong with being gentle, they probably aren't that delicate. Reconstituted peptides won't last forever in the fridge, but they also don't immediately degrade. Peptide Sciences has some very conservative recommendations for storage, explains the possibility of bacterial growth, and discourages multiple freeze-thaw cycles.

In summary:

- Keep powdered peptides in the freezer.

- Reconstitute vials as you need them (not all at once).
- Always use bacteriostatic water to inhibit bacterial growth.
- Keep reconstituted peptides in the fridge, preferably in a box that keeps airborne bacteria off the seals.
- Consistently swab seals with alcohol before use to avoid bacterial growth.
- Don't freak out if you drop your vial or leave it out and it warms up.
- Don't freeze reconstituted peptides, and definitely avoid multiple freeze-thaw cycles with reconstituted peptides.

How to Dose Peptides

So now you have a vial of peptides, a box of syringes, and some bacteriostatic water. The next step is to reconstitute the peptide.

The goal of reconstitution is to dissolve a certain weight of peptide (such as 5 mg) in a volume of bacteriostatic water (such as 2 ml). Then to pull the correct volume of the water into a syringe for injection (such as 10 units), so that it will deliver the desired dose of peptide (such as 250 mcg).

There are 'peptide calculators' I could link you to, but I don't like that approach. If you understand the math you won't need them, and if you don't understand the math you can't trust the results. I've split this into three methods of increasing complexity. Method 1 has the simplest math, but Method 2 has more explanation of the reconstitution steps.

It's important to be able to convert milligrams to micrograms, and units to milliliters. A 'unit' isn't a universal measurement, and is not related to "international units" at all. Within this document we are referring to the **U-100 standard in which there are 100 units in a ml**. If your 1 ml syringe has marks indicating a range from 0-100, you can proceed as written. Similarly, if a ½ ml syringe says it contains 50 units, that's the U-100 standard as well. If you have different markings, you may need to make adjustments.

Conversions:
100 units = 1 ml
1 unit = .01 ml

1 mg = 1,000 mcg
1 mcg = .001 mg

Method 1: Reconstituting with the amount of bacteriostatic water required to deliver the desired dose in 10 units (or any specified number of units).

Most people start by reconstituting with 2 or 3 ml of bacteriostatic water, then do the math to figure out how much to inject. However, the simplest possible approach is to do a little math in the beginning, and reconstitute the peptide with the exact amount of water required so that your desired dose is contained in 10 units, or any other desired volume.

Step 1: Determine the number of doses in your vial. Simply divide the total weight of the peptide in the vial by the desired dosage to get the number of doses in the vial. The only requirement is that they be in the same units of measurement.

Example: A 5 mg vial of BPC-157 to be used in 250 mcg doses. There are 5,000 mcg in the vial, and if we divide that by 250 mcg we see that there are 20 doses in the vial.

Step 2: Now you simply multiply the number of doses by the desired number of units in each dose. I recommend 10 units. The result is the number of units to use for reconstitution. Remember, there are 100 units per ml.

Example: The BPC-157 vial has 20 doses. We multiply 20 doses by 10 units, and get 200 units. We know that 200 units is 2 ml. So if we reconstitute this vial with 2 ml, we can inject 10 units to deliver our desired dose.

Conclusion: So you inject 2ml (two full 1ml syringes) into the vial to reconstitute. And pull 10 units out of the vial to deliver the 250mcg dose.

Method 2: Using 2ml to dissolve 5mg, and a chart to determine units for injection.

This example uses 2ml to dissolve 5mg. This is generally enough bacteriostatic water to dissolve the peptide, and results in 25 mcg per unit. This makes the math easy, as 10 units = 250mcg.

1. Use an alcohol wipe to sanitize the seals. Also sanitize the skin around the injection site.

2. Draw 1 ml of bacteriostatic water into the syringe.

3. Inject the 1ml into the vial of peptides. It may be best to aim for the wall of the vial and be gentle, it may not matter at all. Before withdrawing the needle, pull 1 ml of air into the syringe. This will equalize the pressure.

4. Inject the 1 ml air into the bacteriostatic water vial, equalizing pressure.

5. Repeat steps 2-4. You should now have 2 ml of bacteriostatic water in the peptide vial.

6. Gently roll the vial, or wait for the peptides to dissolve.

7. Use the chart below and draw your desired dosage into the syringe.

8. Here is a video of subcutaneous injection into belly fat.

Number of units	Dosage (when 5mg is dissolved in 2ml)
1 unit	25mcg
2 units	50mcg
3 units	75mcg
4 units	100mcg
5 units	125mcg
6 units	150mcg
7 units	175mcg
8 units	200mcg
9 units	225mcg
10 units	250mcg

Method 3. Using 3 ml to dissolve 5 mg, and a chart to determine units for injection.

I often use 3 ml to dissolve 5 mg. It's always enough to dissolve the peptide, and I prefer working with a little more liquid in each dose. I've included more math to give you the tools to navigate other situations.

I'm going to explain what to do if **your peptide vial is 5 mg** (a measurement of weight equivalent to 5,000 mcg), **your syringes are 1 ml** (volume equivalent to 1cc), and **your desired dosage is 250 mcg** (equal to .25 mg).

1. Wipe all the seals with an alcohol pad, and the area of skin where you'll be injecting.

2. Draw 1 ml of bacteriostatic water into the syringe by pulling it back to the 100 units marking.

3. Gently spray the 1 ml into the vial of peptides, preferably aimed at the wall of the vial.

4. Before removing the syringe, draw 1 ml of air into the syringe. This will restore neutral pressure.

5. Inject the 1 ml of air into the bacteriostatic water container (neutralizing pressure), and repeat steps 2-5 until there are 3 ml in the peptide vial.

6. Get out a calculator. We now have 5 mg dissolved in 3ml. So divide 5 by 3 to get 1.6667. That's how many mg are in each 1 ml. Now we need to figure out what percentage of a ml is necessary to deliver 250 mcg (.250 mg).

   We're going to do that by dividing our desired dose (.25 mg) by the 1.6667 mg in each ml. So .25/1.6667 = .15, or 15%. We know each unit is 1% of a ml, so 15% is 15 units.

7. To double check your math, again divide 5mg by 3ml to get 1.6667, but this time multiply it by .15. The result should be .25, representing the .25mg (250mcg) of peptide in 15 units.

8. Once the peptide is fully dissolved, and you're confident in your math, draw 15 units into the syringe. This will contain 250mcg of the peptide if the vial had 5mg, and was reconstituted with 3ml.

9. Use an alcohol wipe on the injection site if you haven't already. Here is a video of subcutaneous injection into belly fat.

Number of units	**Dosage (when 5mg is dissolved in 3ml)**
3 units	50mcg
6 units	100mcg
9 units	150mcg
12 units	200mcg
15 units	250mcg

What about blends?

Example: You have a vial with a blend of 5 mg Ipamorelin and 5 mg mod-GRF. You've decided to start with 75 mcg of each, but you might work up to 150 mcg doses. We can start by dividing 5,000 mcg (5 mg) by 75 mcg, and it comes out to around 66.7 doses per vial.* If we were to multiply the 66.7 dose by 10 units, we would get 667 units. That seems high, and might not fit in a standard vial. Let's multiply 66.7 by 5 units instead to get 333.5 units.

So, if we take this blend and add 333.5 units (3.34 ml), we can then pull 5 units to deliver 75 mcg of each peptide. If we pull 10 units, that would contain 150 mcg of each.

*You might be tempted to run the math with 10 mg, because there are 5 mg of each. My advice is to focus on one peptide, and remember that the other will be delivered at the same dose. You'll also notice that dividing 10 mg (combined total) by 150 mcg (combined starting dose) equals the same as 5 mg and 75 mcg.

Down the Rabbit Hole

For every tissue, organ, and bodily system there are peptides we know of, and many more which remain unidentified. In this section I will introduce you to a handful of peptides that may be relevant to general health. Most summaries come from Peptide Sciences. Video links will vary greatly in quality.

Google drives with studies: Collection 1, Collection 2

- MK-677. MK677 is another option for increasing Growth Hormone levels, without injection. This isn't a peptide. Let's call it a "research liquid". You drink a small amount and it causes several growth hormone pulses over the next 12-24hrs. It's in the same legal grey area as peptides, so finding a reputable source or a prescription can be a challenge. Here is a study that showed some of the benefits. Keep in mind that muscle growth was mostly seen in the elderly (who have low GH). MK677 is a ghrelin mimetic, and ghrelin is the hormone that makes you feel hungry and causes the sensation many people associate with low blood sugar. In reality, your blood sugar is usually fine, it's just ghrelin making you feel awful. But blood glucose testing is a good way to confirm. Here's a better explanation of MK-677, ghrelin, and blood sugar. MK-677 explanation from More Plates More Dates, Sermorelin & Ibutamoren (MK-677) explanation from Anabolic Doc

- Thymosin Alpha 1 (chronic infection, autoimmune disorders): Thymosin alpha-1 is a naturally occurring peptide fragment that was discovered in 1972. It has since been studied in clinical trials for cystic fibrosis, infection (e.g. tuberculosis, cytomegalovirus), respiratory disorders, chronic hepatitis, and cancer. It is currently approved for use in fighting chronic hepatitis B and C infections in 35 under-developed nations. Immune modulating peptides

- GHK-Cu (connective tissue, anti-aging, immune, etc): GHK-Cu is a naturally occurring peptide first isolated from human blood plasma. It has since been identified in urine and saliva as well. Research into GHK-Cu has found the short peptide to have substantial benefits in wound healing

and immune function. It has anti-aging properties and has been found to suppress free-radical damage, increase protein synthesis, fight bacteria, and increase the health of skin and skin fibroblasts. Here's an interesting article about GHK-Cu and tethered cord syndrome. Note: skin treated with GHK-Cu may be temporarily vulnerable to sunburn due to cell turnover. GHK-Cu discussion with Ryan from TMC, Study summary of GHK-Cu benefits.

- DSIP (sleep, etc): Delta sleep-inducing peptide (DSIP) is a short peptide of natural origin. It gains its name from its ability to cause sleep in rabbits and from the fact that it was first isolated in 1977 from the brains of rats during slow-wave sleep. The peptide, however, has a number of physiologic and endocrine roles that are slowly being uncovered as it gains interest among researchers. Right now, it is known that DSIP can alter corticotropin levels, inhibit somatostatin secretion, limit stress, normalize blood pressure, alter sleep patterns, and alter pain perception. It may also have future applications in cancer treatment, depression, and the prevention of free radical damage. DSIP, Dr John Whitcomb

- LL-37 (immune system, chronic infection): LL-37 is the only known human cathelicidin, which is a large protein family with diverse function. These peptides, which are primarily found in macrophages and polymorphonuclear leukocytes (both types of white blood cell), are important for killing bacteria, but have been found to have other dramatic effects as well. The entire class is often referred to as antimicrobial peptides (AMPs). LL-37 has been found to play important roles in autoimmune disease, cancer, and wound healing. LL-37 and gut health

- Peg-MGF (repair & hypertrophy of muscles, etc): Pegylated Mechano-growth factor (PEG-MGF) is a truncated and slightly altered form of insulin-like growth factor 1 (IGF-1). Research shows that it stimulates myoblast (muscle cell) proliferation and differentiation. It has also been explored in research focused on increasing endurance, boosting the function of the immune system, lowering cholesterol, and reducing total body fat. There is also some evidence to suggest that PEG-MGF improves immune function related to healing and could therefore less the time it takes for wounds to heal. Peptides and Biologics - TMC

- Epithalon/Epitalon (anti-aging, telomeres, immune, sleep, etc): The short-peptide epithalon has been shown to promote proliferation of lymphocytes from the thymus during aging. This is important, as declining expression of lymphocyte interferon gamma is tightly implicated with decreasing immune function in the elderly. It is specifically postulated that epithalon can increase lymphocyte interferon gamma production, thus improving immune function in the elderly. Epitalon and sleep

- Pinealon (misc): Pinealon is a short peptide consisting of just three amino acids. It is one of a handful of synthetic peptides referred to as peptide bioregulators for their ability to interact directly with DNA to alter gene expression levels. Pinealon has been linked to behavior modification and is thought to help protect a number of cell types, including neurons, against the effects of hypoxia. By direct effect on the pineal gland, pinealon may reduce problems with drug metabolism, circadian rhythm disorders, memory, learning, and more.

- Thymalin (inflammation, pain, immune, etc): Thymalin is the synthetic version of thymulin, which was isolated from the thymus in 1977. Thymalin has been shown to play a role in regulating inflammation and pain, has neuroprotective effects, and is important in immune function. Early research revealed that thymalin and other extracts of the thymus and pineal gland can prolong life.

- Semaglutide (primarily used for weight loss): Semaglutide is a derivative of the naturally occurring GLP-1, a peptide known to lower blood sugar levels and enhance insulin secretion. Research shows that Semaglutide may also improve heart, liver, and lung function while helping to slow or prevent the effects of Alzheimer's disease. Semaglutide has been shown to significantly decrease appetite by delaying gastric emptying and reducing intestinal motility. Glucagon-Like Peptide-1 (GLP-1) Analog Shown to Stimulate Insulin and Suppress Glucagon Secretion in a Glucose-Dependent Manner.

- Tirzepatide (weight loss): Tirzepatide is a synthetic derivative of gastric inhibitory polypeptide (GIP) that has simultaneous glucagon-like peptide-1 (GLP-1) functionality as well. This combination allows Tirzepatide to lower blood glucose levels, increase insulin sensitivity, boost feelings of satiety, and accelerate weight loss. Tirzepatide was developed to fight type 2 diabetes, but has additionally been shown to protect the cardiovascular system and act as a potent weight loss agent.

Reddit Posts

BPC-157 human trials

Note: my next post has the full texts.

As some of you may be aware, there have been human clinical trials on BPC-157.

Unfortunately no one seems to have complete access to the results. Nevertheless, I've been putting some effort into determining the extent of human testing and the results.
I wrote this to organize my thoughts and track studies and sources, but some of you may find it interesting.

Title: The development of PL 14736 for treatment of inflammatory bowel disease.
Authors: Veljača, Marija ; Krnić, Žarka ; Brajša, Karmen ; Pavić-Sladoljev, Dubravka ; Mildner, Boris ; Ševeljević-Jaran, Daša ; Kolega, Marko ; Erceg, Damir ; Krznarić, Željko
Date: 2001

"Pl 14736 is a 15 amino acid peptide of a unique sequence, a part of a larger molecule. Pharmacological activity of PL 14 736 has been tested in vitro and in vivo, revealing beneficial activity against experimental tissue damage. Since PL 14736 has shown potent protective and healing properties in the models of upper gastrointestinal tract lesions and in particular in acute and sub-acute models of colitis, this compound was taken to pursue pre-clinical development for IBD indication. In order to fulfill regulatory requirements for the conduct of the phase I study, all non-clinical safety studies were performed with PL 14736." (Source)

Title: The development of PL 14736 for treatment of inflammatory bowel disease
Authors: Veljača, Marija ; Krnić, Žarka ; Brajša, Karmen ; Mildner, Boris ; Pavić-Sladoljev, Dubravka ; Ševeljević-Jaran, D. ; Kolega, M. ; Erceg, Damir ; Krznarić, Željko
Date: 2002

"PL 14736, a 15 amino acid peptide, is a part of a larger protein, first isolated from human gastric juice.

Pharmacological activity of PL14736 has been tested in vitro and in vivo, revealing beneficial activity against experimental tissue damage. Pl 14736 has shown potent protective and healing properties in models of upper GI tract lesions and, in particular, in acute and subacute models of colitis. Hence the pre-clinical development of PL 14736 has been pursued for the treatment of inflammatory bowel disease. In order to fulfill regulatory requirements for the conduct of phase I and phase II clinical testing, adequate non-clinical safety studies were performed with Pl 14736. Acute oral and iv toxicity of Pl 14736 in mice revealed LD50> 2000 mg / kg. repeated four-week iv as well as two-week intracolonic administration to rats and beagle dogs has no significant effect on clinical, gross pathology or histopathology parameters tested, with doses up to 10 and 25 mg / kg, respectively. Safety pharmacology testing in Beagle dogs revealed no cardiovascular or respiratory symptoms. Pl 14736 is neither genotoxic or mutagenic: it did not cause chromosomal aberration in human lymphocyte culture in vitro nor micronuclei formation in polychromatic erythrocytes in mice bone marrow micronucleus test in vivo; Ames test was negative. Following pre-clinical testing, a placebo-controlled phase I tolerability and pharmacokinetics study was conducted in 32 healthy volunteers. Physical examination, observation of clinical signs as well as laboratory testing have revealed no significant adverse effects that could be attributed to single and repeated seven-day treatment with PL 14736 enemas. Based on these encouraging efficacy and safety data, placebo-controlled phase II study with PL 14736 enemas has recently started in order to test the safety and efficacy of two-week treatment in patients suffering from acute to moderate ulcerative colitis." (Source)

Since the title and authors match up, that second entry seems to be a more complete explanation of the same trial.

Title: Safety, tolerability and pharmacokinetics of PL 14736, a novel agent for treatment of ulcerative colitis, in healthy male volunteers.
Authors: Veljača, Marija ; Pavić-Sladoljev, D. ; Mildner, Boris ; Brajša, Karmen ; Krnić, Žarka ; Bubenik, M. ; Stipaničić, S. ; Tabak-Slošić, Maja ; Brnić, L. ; Khan, Z. ; Krznarić, Željko ; Bischoff, A. ; Scroeder, A. ; van Dongen, W.D. ; van Schaik, F.
Date: 2002

"PL 14736, a novel 15 amino acid peptide, has shown beneficial activity in experimental models of gastrointestinal damage. Seven-day intracolonic administration of PL 14736 to rats has significantly reduced the extent of TNBS-induced colonic damage and hastened healing. These results have encouraged the development of the compound for the treatment of patients with ulcerative colitis. In this first study in man, rectal administration of PL 14736 to healthy male volunteers was safe and well tolerated. Based on these data, a randomized, double-blind, placebo-controlled study was started in order to investigate the tolerability and efficacy of Pl 14736 enemas in patients with acute mild to

moderate ulcerative colitis." (Source)

The title is different, and the authors are a bit different. But again it refers to a study that was started to investigate enemas for ulcerative colitis.

This clinical trial was dated 2015 PDF live link and planned to be completed in 2016. However, on the Results Submitted tab it says canceled. It's not clear to me if the trial was canceled before it occurred, or the submission of results was canceled.

Now, to determine if there are other trials, I'll go through the studies that mention trials and match up the dates and names.

This study states that BPC-157 is in clinical trials as a therapy for inflammatory bowel disease, under drug name PL14736.

It states: "BPC 157 was shown as safe in trials for inflammatory bowel disease (PL14736; Pliva, Croatia) (15, 16)."

Citation 15: Veljaca M, Pavic Sladoljev D, Mildner B, Brajsa K, Bubenik M, Stipanicic S, et al. Safety, tolerability and pharmacokinetics of PL 14736, a novel agent for treatment of ulcerative colitis, in healthy male volunteers. Gut. 2003;51 Suppl III:A309.

Citation 16: Ruenzi M, Stolte M, Veljaca M, Oreskovic K, Peterson J, Ulcerative Colitis Study Group. A multicenter, randomized, double blind, placebo controlled phase II study of PL 14736 enema in the treatment of mild-to-moderate ulcerative colitis. Gastroenterology. 2005;128:A584.

Citation 15 seems to be one I already found, but Citation 16 isn't. Google search and other tricks didn't find it, but I found the gastro journal, searched through all the archived pdfs and found it in a supplemental doc.

Title: A Multicenter, Randomized, Double Blind, Placebo-Controlled Phase Ii Study of Pl 14736 Enema in the Treatment of Mild-To-Moderate Ulcerative Colitis
Authors: Michael Ruenzi, Manfred Stolte, Marija Veljaca, Katarina Oreskovic, Janet Peterson, & Ulcerative Colitis Study Group

"Background: PL 14736 is a novel synthetic peptide, which shows antiinflammatory and ulcer healing properties in the gastrointestinal tract. It is under investigation for the treatment of ulcerative colitis (UC)

and this was the first clinical trial of PL 14736 in patients. Methods: A multicenter, randomized, double blind, placebo-controlled study was performed to assess the efficacy, safety and pharmacokinetics of PL 14736 in patients with mild-to-moderate UC. A total of 53 patients were randomized in a 1:1 ratio to receive PL 14736 enema, 80 mg once daily for 2 weeks, or placebo. The primary efficacy end point was a change in Disease Activity Index (DAI) over the treatment period. The DAI was defined as a composite score of clinical, laboratory, endoscopic and pathohistological findings. Blood samples for drug assay were obtained at 4 time points during the study. Results: Forty-six patients completed the study. Five patients, 3 treated with PL 14736 and 2 receiving placebo, were withdrawn due to an adverse event, mainly progression of UC. In addition, one patient from each group was lost for follow-up. Unlike placebo, PL 14736 induced a statistically significant decrease of the DAI at the end of a 2-week treatment period. The mean change of the DAI was -3.2 points (95%CI –5.58, -0.82) in the PL 14736 group and –1.6 (95%CI - 3.86, 0.67) in the placebo group. The estimated difference between groups was 1.6 points (95%CI –4.84, 1.62). The single components of the DAI showed no significant differences between the treatment groups, however, there was a favorable trend for PL 14736, which in contrast to placebo reduced the mean stool frequency, improved stool consistency, and had beneficial effects on histopathological findings. PL 14736 was very well tolerated and safe. There was no difference in the frequency or type of adverse events in comparison with placebo. PL 14736 was not detected in any of plasma samples. Conclusion: PL 14736 enema, at dose of 80 mg daily for 2 weeks, resulted in a statistically significant improvement of the DAI in patients with mild-to-moderate UC. PL 14736 patients had much better response to therapy than placebo patients, justifying further clinical trials in this indication." (Source

Again it's difficult to differentiate between the trials being referred to, but this has a bit more information at least.

This study from 2018/2019 states:

"It is worth noting that there does appear to be a trial administering BPC 157 (rectally administered) in human participants for the treatment and healing of acute to mild ulcerative colitis (Veljaca et al. 2002; Veljaca et al. 2003); however, details on the studies are limited and are not overly informative. Similarly, a pilot study in 2015, a clinical trial (randomised) on 42 healthy human participants, receiving oral (tablet form) dosages of BPC 157 was carried out (Clinicaltrials.gov 2018): 0.25, 0.5, 1 and 2 µg/kg. The details and results for this trial are still pending."

This apparently refers to the trials I found. It seems the authors could not find much more information on the oral trial than I did. However, the dosage scheme appears to be different, so that may have been a new trial started shortly after the first was cancelled.

This study also mentions the trials I found, but is also interesting because it suggests BPC-157 may actually have an anti-proliferative effect on melanoma cell lines. Which is cool.

I also rummaged through the patents to find leads. I also wanted to remind myself of the development timeline to determine which form of BPC-157 was used in the trials.

Patent history

Some of these dates may be off, they vary between countries.

Published 1992 https://patents.google.com/patent/YU176089A/en "A process for the preparation of the compound and the substance BPC bpc" This seems to be about the extraction of BPC from gastric juice, which is cool.

Published in 1998 https://patents.google.com/patent/WO1998052973A1/en "New bpc peptide salts with organo-protective activity, the process for their preparation and their use in therapy" Although it's not clear, this may be the introduction of the acetate version, or a slightly improved salt version.

Published in 2013 https://patents.google.com/patent/SI23928A/en "Pentadecapeptide and its salts and their use in cosmetics and dermatology" The combination of BPC salt and a heavy metal for use in cosmetics and dermatology.

Filed in 2013, published in 2014 (world) US patent date: Dec 26, 2017
https://patents.google.com/patent/WO2014142764A1/en
https://drive.google.com/file/d/1IP6JvXmQsnUZKlmtCZOY1v8Tzxz50dXP/view "New stable pentadecapeptide salts, a process for preparation thereof, a use thereof in the manufacture of pharmaceutical preparations and a use thereof in therapy" This is the new Stable Version with arginine.

So, from this it seems reasonable to expect any studies after 2014 used the stable version, especially if they refer to it as "Stable pentadecapeptide". Studies in 2013 may have used the stable version, but any studies or trials before 2013 likely used acetate or some other salt version since the stable version wasn't patented. That suggests all the trials I found any results for used acetate/salt versions, while the mysterious 2015 oral trial would have used arg-BPC. Again, the patent dates are hard to pin down.

That's as far as I'm taking this for now. It seems that BPC-157 was effective for ulcerative colitis, and well tolerated. It's interesting (though not surprising) that they didn't detect BPC-157 in plasma after the

enema of 80mg. We don't know the timing of the plasma draw, or how deep the enema was, but it certainly doesn't point towards meaningful amounts of absorption into the bloodstream.

BPC-157 human trials pt 2: full text acquired!

Link to full texts

Hi folks,

I've previously posted about BPC-157 human trials, but was only able to find summaries. I also saw indications that professional researchers had been unable to find the full texts, so it seemed unlikely that I would ever get my hands on them. But to my surprise, someone saw my reddit content and sent me the darn things!

The results match up with abstracts and summaries I found previously. The author on the pdf file is Predrag Sikiric, a prominent author of BPC-157 research.

The trials are easy to read, so I'm not going to write a lengthy summary. Enemas were well tolerated in healthy subjects, and seemed helpful for ulcerative colitis. There was a statistically significant improvement with BPC-157, whereas placebo showed smaller and not significant improvement.

They noted a lack of absorption into the bloodstream, despite high doses. There were transient detections of nanogram levels in plasma, but **no indication that BPC-157 is absorbed through the large intestine in significant quantities.**

Study 1: *Enemas in healthy volunteers to establish safety and pharmacokinetics.*
Doses: 0.25 mg/kg, 0.5 mg/kg, 1 mg/kg and 2 mg/kg. Administered for 7 days.

Conclusion: *Single and repeated intracolonic doses of PL 14736 to healthy male volunteers were very well tolerated. No difference to placebo dosing was observed for any of the safety parameters measured. Owing to the fact that most PL 14736 plasma concentration profiles were below the assay LLQ at all time points, it seems that very little PL 14736 is absorbed into the systemic circulation following rectal administration.*

Study 2: *Enemas for treatment of distal ulcerative colitis.*

Doses: 80mg/day for 14 days

Conclusion: *Clinical symptoms, mainly stool frequency and stool consistency, but also 'blood in stool' and abdominal pain, began to improve already with the first days of dosing and showed an ongoing positive trend during the second week of treatment. This positive trend in the subjective, patient-derived parameters was confirmed after 14 days of treatment by the histopathological scoring, which showed an improvement after treatment with PL 14736, but remained constant after placebo dosing.*

These results are of special importance in the light of the PL 14736 plasma concentrations, which were always below the LLQ, thus ***possibly indicating that the substance acts locally and not via systemic absorption****.*

The comparison between the two treatment groups failed to be statistically significant.
This may be due to the low number of patients on the one side, but possibly also due to the short treatment duration.

BPC-157 detection and half-life

Hi folks,

In the process of cataloging BPC-157 research I came across some interesting tidbits. Including this study: *Detection and in vitro metabolism of the confiscated peptides BPC 157 and MGF R23H.*

I believe the full text is on sci-hub or libgen if you care to dig it up.

The TLDR is that a lab put BPC-157 in human plasma and found that there was a prominent metabolite that was stable in urine and could theoretically be used as a urine test to detect the use of BPC-157. However, there are several more steps before this could become a real, validated test. So I don't think anyone is actually being tested for BPC-157 currently.

But that's not the part I found interesting. They reported the rate of degradation in plasma!

BPC-157 was moderately stable in plasma with 36% ± 0.6% of the peptide remaining after 60 minutes.

I'm pretty sure this puts the plasma half-life at around 40 minutes. There might be in vivo factors not present here that accelerate degradation. This is probably the acetate version, but we don't know if arg-BPC is any more resistant to breakdown in plasma.

BPC-157 research list and summaries

Have you ever started a project that turned out to be monstrously complex, but it was too late to back out so you slogged through hours of tedious work just to make something no one asked for?

Well anyway, here's a list of 245 BPC-157 research articles.

I started by making a spreadsheet from the PubMed search results, then went through all the Sci-hub/LibGen results to add the unique entries there. Then ResearchGate, etc. And for each one I tried to track down the full text, and noted what was available on the web. Then I pinned down (or guessed) the missing publication years so I could make a chronological list.

And of course I also searched for the developmental code names like PL 14736.

I found full texts for ~157 entries, which gave me a chuckle. The best I could do was abstracts for ~78. Then I started looking in the reference sections and added 10 to the list that I couldn't find any other info for besides the title. I'm sure I could find a lot more titles this way, but there's not much payoff and it's a massive pain.

There could be duplicates, but mostly in the sense that a single trial led to multiple articles with different titles. I can't promise there aren't any errors, but I'm pretty confident in the data overall.

Why did I do this?

There are a few reasons. First, I got sick of seeing the same 12 studies getting tossed around over and over. And there are people who want to look at the research, but it's a big mess and they get discouraged. This project gives them a map so they can find what they want.

For example, here's the most recent reviews explaining the state of BPC-157 research in some different areas!

- Effect of Pentadecapeptide BPC 157 on Gastrointestinal Tract is a good summary of GI

applications for BPC-157. Includes sections on individual organs.

- Stable Gastric Pentadecapeptide BPC 157 and Wound Healing is cumbersome to read, but has some interesting info on wound healing, such as changes to gene expression.
- Pentadecapeptide BPC 157 and the central nervous system is a good read on the CNS applications of BPC-157. However, most of the trials involve administering BPC-157 along with some noxious agent, and noting how well it mitigated damage. Most people considering BPC-157 for CNS issues are looking to repair damage, not prevent it. So the applicability of these studies is questionable. Also, some models of neurological conditions are absurdly crude, such as restraint stress or drowning as a model of depression.
- Gastric pentadecapeptide body protection compound BPC 157 and its role in accelerating musculoskeletal soft tissue healing is a decent summary of the musculoskeletal research. Like the CNS research, there are limitations which the authors don't acknowledge. All the trials involve administering BPC-157 immediately after an injury, whereas most people don't begin treatment until their injury fails to heal properly. So the applicability of these trials is questionable.

So yeah, stuff like that.

The other reason, and maybe this deserves its own post, is that I have never come across an intervention trial that didn't show positive results from BPC-157. And I wanted to figure out if that was a reflection of the research in general, or just the selection I had seen.

I'm not sure if I've read everything listed here, but certainly the majority. I still haven't found any intervention trials that didn't find positive results. There are some trials that simply observed the effects of BPC-157 without assigning a positive value to the outcome. But if they did something horrible to an animal and gave half of them BPC-157 to see if it helped, I've seen nothing but positive outcomes.

This is not ideal. If you test a compound in a sufficiently wide range of situations, you should get some neutral or even negative results. You should find situations in which it doesn't help.

So it seems like there is a publication bias. For whatever reason, we are only seeing the tests BPC-157 passed. This is a common problem in all areas of research. It's not a conspiracy or anything nefarious. Null results are boring, and there are several reasons they might not get published. The people conducting these trials are probably familiar with BPC-157, and may choose setups they think will demonstrate the effectiveness of BPC-157. Or they might run informal trials to test ideas before a more formal trial for publication.

The consequence of this is that we need to be skeptical of individual trials, and lean more on trends. For example, there are some trials where oral administration improved musculoskeletal healing, but the vast majority used injection. The trend clearly favors injection for that application.

But we also need to be careful about generalizing results. All these intervention trials start the treatment immediately after injury, while the healing response is already strong. Whereas humans typically start BPC-157 after an injury has failed to heal. That's not to say BPC-157 won't help after an injury has failed to heal. But for example, the dosage used or MOA might play a bigger role in typical human use.

I don't have any grand conclusion. Just.. exercise a little restraint. And if someone says a study is "proof" of a certain effect, check to see if they're trying to sell you something.

I don't have any more time to throw at this currently, but there are other potential outcomes to this project. If I identified all the trials vs reviews, and did a bit of work locally, I could potentially run highly specific searches on the full text of all BPC-157 trials simultaneously. Or at least the ones with searchable text.. some are basically pictures of text. So I could generate a list of all the trials that mention dopamine or cancer or kidneys, for example. I don't need that capability, but there are some topics where people would appreciate a list of studies to read. That's in the realm of possibility.

If I were to throw a bunch more time at this I could mine data on species, dosage, MOA, etc. It would be cool to have that info in a spreadsheet. And there are specific topics that interest me.. like some animal trials don't show any dose-response relationship across a wide range of doses. But if you look at cell culture studies there does seem to be one. What's up with that? Maybe the way interventions are conducted doesn't illustrate the dose-response relationship. And there are a dozen other topics where a summary of the relevant research would be cool. But unless I start a Patreon and quit one of my jobs, I don't see that level of analysis happening any time soon.

Before anyone complains that I'm not sharing a massive Google drive with all these documents.. it's not that simple. There are a bunch of barriers on my end and I don't want to deal with them for what amounts to a minor convenience for you. These files are out there. Go find them if you want to read them. There are a handful of gems from my private collection that weren't available publicly, but I'm in the process of posting them.

BPC-157 research upload and highlights

I recently cataloged a massive amount of BPC-157 research. I wanted to share some files from my collection that aren't available online.

Files:

- (6) General Pharmacology, (7) Pharmacokenitics, (8) Toxicokinetics <-- (all one file)
- (9) Toxicology
- (10) Clinical Experience (Human Trials). Addressed in a separate post here.

Widespread production of BPC-157 sequence?

The most interesting tidbit is that early research suggested the BPC-157 sequence is produced in a wide range of human tissues. This kinda makes sense, because it certainly has effects on a wide range of tissues. But this idea hasn't been mentioned in any subsequent research that I've seen. It's a shame this hasn't been investigated further, but we just have to file it under "big if true".

Short version: *Subsequently, BPC 157 was found to be present in all tissue tested in humans, both adults and fetuses (Distribution pattern of BPC*
during human development, Pliva, 1993-1995). Therefore, it seems that BPC 157 has a general presentation, and should be responsible for function of a variety of the tissues.

Long version: *Distribution pattern of BPC during human development, Pliva, 1993-1995 study used human BPC oligonucleotide probes and a specific BPC 157 polyclonal antibody to analyze BPC 157 expression and synthesis in human fetal and adult tissues. Northern blot hybridization revealed two mRNA species of 3 and 1.8 kb. Higher mRNA size was more pronounced in adult, while equal quantities of both mRNA species were detected in fetal tissues. High levels of BPC mRNA were found in adult gastrointestinal epithelium. By in situ hybridization and immunostaining BPC 157 was found in gastrointestinal mucosa, lung bronchial epithelium, epidermal layer of the skin and kidney glomeruli. These data suggest that although BPC has been isolated from gastric juice and probably primarily acts in the gastrointestinal system, it may have additional regulatory roles in the function of human lung, kidney and skin.*
Tissue specific BPC mRNA transcripts.BPC expression was analyzed in several fetal and adult human tissues by Northern hybridization. Hybridization with oligo 1 probe revealed two mRNA species of about 3 and 1.8 kb in both fetal and adult human tissues. In adult tissues BPC expression was observed in the lung and gut, whereas kidney, and skin did not give detectable signals. The higher mRNA size was

abundant in adult tissues while two lower mRNA species of approximately 1.8 and 1.2 kb were scarcely expressed. In fetal tissues of 12-14 weeks of gestation the intensity of expression was less abundant, with 3.0 and 1.8 kb RNA species equally pronounced. The liver was positive in one of fetal RNA preparations but could not be repeated in others including adult tissues RNA blots. The highest levels of BPC mRNA were found in the adult gastrointestinal structures.

Distribution of radioactive BPC-157

They made BPC-157 with radioactive amino acids, and gave it to rats through various methods. Then they observed that the radioactivity spread throughout the rats. This isn't very exciting because **this is exactly what you'd expect if the BPC-157 was digested into constituent amino acids.** This is just a basic pharmacokenitics study. I wanted to address it because I could see people misinterpreting this as being absorbed intact, and we can't tell that from the data.

The test article is rapidly absorbed from the gastrointestinal tract. Between 0.5 and 16 h after administration, plasma levels of radioactivity remain almost unvariable at a concentration of about 10 µg/ml. Elimination from circulation between 24 and 168 h occurs according to a halflife of about 68 h.

Also..

The obtained results indicate that the test article is rapidly distributed in body water and tissues after intravenous administration.

BPC-157 has no affinity for dopamine or serotonin receptors

BPC-157 has been shown to elicit changes in dopamine systems, but it doesn't seem to actually have affinity for the receptors. This isn't surprising, but worth noting.

The interaction of PL 14736 with adrenergic a- and ß- 1 and 2 receptors, with cholinergic muscarinic mr, m2- and m3-, with histamine Hr and H2-receptors, with serotonin 5-HT1 and 5-HT2, with dopamine D1- and D2, and with A1 and A2- adenosine receptors was investigated.

PL 14736 did not display any pharmacological affinity for any of the receptor systems studied. In fact, it did not interact with any of the sites that recognize and bind the radioligands that are considered by all as the best markers (for their affinity, selectivity and high specific activity) for the respective systems.

TB4/TB500 human trials and research summary

Hi folks,

As a follow-up to my research into BPC-157 human trials, I've been exploring some similar questions surrounding TB-500.

I'll divide this into 4 sections.

1. What is TB-500, and how is it different from TB4?
2. What is the status of human testing, and what has testing revealed?
3. What does the research say about cancer and TB4?
4. Why is it generally injected less frequently than BPC-157, but at substantially higher doses?

Summary of findings:

Many people believe TB-500 is a synthetic version of TB4, but the evidence suggests it is a portion of the sequence, Fragment 17-23. Rather than contradict public perception, some sources sell TB4 and call it TB-500, while others sell Frag 17-23 as TB-500. Therefore, the name 'TB-500' has become a source of confusion. Rather than get bogged down in what 'real TB-500' is, we can simply refer to TB4 or Frag 17-23 specifically.

TB4 eye drops have shown good results in human trials, and they've injected humans with up to 1260mg/day for 14 days with no side effects and no cancer in a 6 month follow up. There are several TB4 products in the pipeline.

Cancer cells which produce more TB4 tend to be more proliferative, and suppressing TB4 in cancer reduces proliferation. However we don't have studies on the effect of exogenous TB4 on cancer.

A variety of dosage schemes were effective in animal studies. There isn't much evidence to compare protocols. The common approach of larger, infrequent doses may have advantages for injury and tissue repair, but the anti-inflammatory and other benefits may be delivered just as well with smaller, more frequent doses. Some immune problems, such as MCAS, may react poorly to high doses.
Here are some dosing protocols:

- TB-500.com protocol . 5 weeks at 2x5mg, 2 weeks at 1x5mg.
- Tailor Made Compounding protocol. 750mcg/day for 20 days.
- Cre8 Pharmacy protocol. 450mcg/day for 30 days

What is TB-500, and how is it different from TB4?

First, let's explore Thymosin Beta 4. TB4 is a sequence of 43 amino acids with a wide range of effects. From immune modulation to actin binding and angiogenesis. Check out figure 3 for a decent summary of effects.

So TB4 does a bunch of stuff, but the individual impacts are due to certain portions of the sequence. So you don't need the full sequence for a particular effect. Here is a breakdown of active sites from Ben Greenfield's website, it appears to be written by Ryan from Tailor Made Compounding.

- 1-4 Anti-inflammatory, Anti-fibrotic, Stimulates epicardium-derived progenitor cells, Inhibits bone marrow cell differentiation, Decreases TNF-alpha release by macrophages, Suppresses Smad activation (blocks TGF-β signaling)
- 1-15 Anti-apoptotic, Protects from cytotoxicity
- 17-23 Actin binding, Promotes hair growth, Improves dermal wound healing, Stimulates angiogenesis, Induces mast cell exocytosis
- 40-43 Increases embryonic cardiac cell migration, Increases heart function post-ischemia

This information appears to be mostly pulled from figure 5 of this research summary.

Some people may want all the effects of TB4. An athlete may only want Frag 17-23, while someone with MCAS (Mast Cell Activation Syndrome) may want Frag 1-4 or everything else besides Frag 17-23, because that portion activates Mast Cells. Or they may simply want to use smaller doses of TB4 to prevent flairs.

So what is TB-500? It's a name. To most people it is synonymous with TB4. But there is evidence that it should be taken to mean Fragment 17-23 of TB4.

Doping control analysis of TB-500, a synthetic version of an active region of thymosin beta 4, in equine urine and plasma by liquid chromatography–mass spectrometry

A veterinary preparation known as TB-500 and containing a synthetic version of the naturally occurring peptide LKKTETQ has emerged.

Synthesis and characterization of the N-terminal acetylated 17-23 fragment of thymosin beta 4 identified in TB-500, a product suspected to possess doping potential

It was immediately evident that TB-500 did not contain the endogenous Tb4 (MW: 4963.4642). Therefore, elucidation of the structure of the detected species was accomplished by de novo sequencing based on HCD of the peptide precursor at 25 eV. b+ and y+ ions allowed de novo sequencing of the peptide through direct matching with theoretical data. As shown in Figure 1a and summarized in Table 1, a heptapeptide was detected, corresponding to the 17–23 fragment of human Tb4 (sequence: LKKTETQ).

Here is Jean-Francois Tremblay from CanLabs explaining the difference between TB-500 and TB4. It's worth noting that due to general perception that TB-500 was TB4, Tremblay actually sold TB4 as TB-500 for a while rather than repeatedly explain the distinction.
The counter argument is that most people believe TB-500 is full sequence TB4, and many products sold as TB-500 are in fact TB4.

TB-500.com asserts they are synonymous.

Many other sources clarify the situation by including both names. Particle Peptides Peptide Sciences

Further complicating the situation, sources may simply buy 'TB-500' from Chinese suppliers, and assume it is TB4. I have seen Chinese sources who sell both TB-500 (specified to be Frag 17-23) and TB4.

Before you assume you're being ripped off by getting Frag 17-23, consider this. You pay by the weight, and a 5mg vial of Frag 17-23 will contain more molecules. Based on the number of amino acids, perhaps around 6x. If you want the actin binding and angiogenesis effects, it's more cost effective than buying TB4.

I'm a pragmatist, so rather than correct people about what "real TB-500" is, I'm just going to say 'Frag 17-23' or 'TB4' depending on what I mean. It's no more difficult, and there's no ambiguity.
The important thing is that we communicate accurately with each other. People need to understand that TB4 has multiple active sites with various effects so they can select and purchase the products they intend.

What is the status of human testing?

The products I've found with TB4 come from RegenerX. They and their partners have patents on using TB4 in a broad range of applications including cardiac and CNS/PNS disorders, preventing or healing the damage that occurs from a heart attack, Multiple Sclerosis, diabetic-induced vascular dysfunction, and peripheral neuropathy.

RGN-259 (eye drops): Completed phase 3 trials.

RGN-352 (injections): Completed phase 1 trials.

RGN-137 (topical gel): Ongoing phase 2 trials.

I was most interested in this human injection trial

My understanding is that the study began with single IV doses of 42, 120, 420, or 1260mg. This was followed by an analysis of the safety data acquired so far. The second phase resumed with daily IV of the same dosages for 14 days. So the maximum amount injected into a single human was 18,900mg. That's right folks, nearly 19 GRAMS.

No worrisome complaints from the participants. No cancer in the follow up 6 months later.

Mean terminal half-life estimates increased with dose, from 0.95 h at 42 mg/subject, to 1.2 h at 140 mg/subject, to 1.9 h at 420 mg/subject, and to 2.1 h at 1260 mg/subject.
..mean clearance appeared to be independent of dose, ranging from 6870 to 7330 mL/h (Table 4).

..dosing for 14 days also appears to be safe and well tolerated with no reported or observed dose limiting toxicity or serious adverse events. The most frequent adverse event observed was headache, but this was seen in all doses including placebo, and there was no increase frequency or severity with increasing doses. The adverse event profile for multiple doses does not show any trend in type, severity, or frequency across increasing doses from 42 to 1260 mg. The reported potential of TB4 to influence the metastatic potential of certain malignancies through its ability to promote angiogenesis and stimulate cell migration warranted close follow-up for any potential cancers. No cancers were identified during a 6-month follow-up period.

Here is a summary of the animal studies done in preparation. No indication of cancer or other problems. I don't know how long they followed the animals' health after administering TB4.

Topical/ eye drop studies:

Recent clinical studies have shown that topical 0.1% Tβ4 (RGN-259) may be helpful in the treatment of neurotrophic keratitis. In a phase II clinical trial, topical 0.1% Tβ4 significantly improved the signs and symptoms of patients with dry eye, and no side effects were observed. (Source)

This study confirms the efficacy of 0.1% Tβ4 as a topical treatment for relief of signs and symptoms of dry eye. Significant improvements in both signs and symptoms of dry eye were observed, and the treatment exhibited a large safety window, with no adverse events reported by any subjects enrolled in the study..
..In the present Phase II clinical trial, a 28-day course of 0.1% Tβ4 ophthalmic formulation elicited significant positive effects on ocular discomfort and on corneal staining in subjects with dry eye. Results suggest that Tβ4 has a protective effect, reducing the extent of corneal staining exhibited by subjects following exposure to a controlled adverse environment. In addition, significant differences between active and placebo groups at 24 hours post-CAE are consistent with an acceleration in healing for subjects treated with Tβ4. (Source)

Results: Statistically significant differences in both symptom and sign assessments, were seen at various time points throughout the study. Of particular note at day 56, the RGN-259–treated group (12 eyes) had 35.1% reduction of ocular discomfort compared with vehicle control (6 eyes) (P = 0.0141), and 59.1% reduction of total corneal fluorescein staining compared with vehicle control (P = 0.0108). Other improvements seen in the RGN-259–treated patients included tear film breakup time and increased tear volume production.

Conclusions: In this small trial, RGN-259 eye drops were safe and well tolerated and met key efficacy objectives with statistically significant symptom and sign improvements, compared with vehicle control, at various time intervals, including 28-days posttreatment. (Source)

RGN-137 accelerated skin ulcers healing.

Two independent randomized, double-blind, placebo-controlled, dose-response phase 2 clinical trials evaluated the safety and efficacy of RGN-137 (the topical gel formulation of TB4) in the treatment of 143 total patients with chronic cutaneous (stage III/IV) pressure ulcers (full thickness) and venous stasis ulcers in which the majority of the patients had varicose veins and an open ulceration. Among those patients with wounds that healed during the 84-day treatment period, TB4 at the mid-dose increased the rate of complete wound healing in both patient populations. The rate of healing in the mid- dose TB4-treated patients was approximately one month faster than either the placebo- or other RGN- 137 dose-treated wounds.

The most interesting result was that .02% concentration accelerated healing best, and outperformed the .1% concentration.

Patients were divided into four groups and were treated with either placebo, 0.01%, 0.02%, or 0.1% TB4 gel. The percentage of patients who healed completely at day 84 was similar in the placebo and in the 0.02% TB4 treatment group at 17% while the lower and higher RGN-137 treatment doses had fewer patients who healed completely. The reason for this lower rate of healing in these two bracketing doses is unclear but was observed in the venous stasis ulcer trial as well and could be related to the bell curve of activity associated with the many receptor-mediated biological responses. An 80% wound closure from baseline healing was observed as early as two weeks in the 0.02% treatment group compared to placebo. This healing continued at a faster rate until week six at which time some wounds that had been present as long as two years, healed completely.

The healing of the placebo eventually caught up with the 0.02% RGN-137 treatment during the remainder of the 84-day treatment (Fig. 1A). Likewise, at 100% closure, the 0.02% TB4 dose showed accelerated healing over the placebo as early as three weeks (Fig. 1B). The time to healing among the wounds that did heal was much shorter in the 0.02% treatment group over the placebo group, with a median healing time of 22 days versus 57 days for the placebo (Table 2). The mean was 36 ± 25 days for the 0.02% RGN-137–treated group versus 51 ± 24 days for the placebo. The highest dose group did not have any patients who healed. The lowest dose group showed healing similar to those treated with the mid-dose, 0.02% RGN-137.

When the pressure ulcer wounds were analyzed by stage, more rapid healing was observed in the stage III group treated with 0.02% RGN-137. Heal- ing in stage IV patients occurred only in the 0.02% RGN-137 group. These data show that the mid- dose (0.02%) of RGN-137 accelerates pressure ulcer healing by more than a month.

There is a product called Oxervate, or cenegermin.

Although it doesn't seem to actually contain TB4, it contains recombinant human nerve growth factor which may increase TB4 production locally, it's not clear. Ryan from Tailor Made linked it as a TB4 product.

What does the research say about TB4 and cancer?

On the topic of cancer.. The article on Ben Greenfield's site written by Ryan from Tailor Made Compounding has this to say:

Thymosin β-4 is absolutely contraindicated for anyone with cancer. At the cellular level, it has been linked to increased risk of metastasis, but there has been no link to exogenous administration and

increased cancer risk yet due to lack of study. It may have a proliferative risk when used continuously in cancer therapy but more research needs to be done.

If you want to read about TB4 and cancer, check these out.

Tb4 overexpression was associated with increased malignant progression of various tumors as well as cell migration. According to our data, increased migration ability due to higher Rac1 activities was found in Tb4-over- expressing Tb3 and Tb4 cells. (Source)
Migration in gastric cancer cells, SNU638 and SNU668, was dependent on a relative expression level of Tb4. (Source)

Deregulated proteins of tubulin beta chain, thymosin beta-4-like protein 3, and cytochrome b–c1 complex subunit 1 may be involved in the pathogenesis of GC and serve as potential serological diagnostic biomarkers. (Source)

Thymosin beta-4 (Tβ4) is known to be involved in tumorigenesis. Overexpression of this polypeptide has been observed in a wide variety of cancers, including colorectal carcinoma (CRC).. ..Together, our results show for the first time that in vivo silencing of Tβ4 expression by its shRNA generated after adenoviral infection can suppress CRC growth. These results further demonstrate the feasibility of treating CRC by a Tβ4 knockdown gene therapeutic approach. (Source)

Tβ4 might be involved in stimulating human pancreatic cancer progression by promoting proinflammatory cytokine environment and activating JNK signaling pathway. Targeting Tβ4 and related molecules may be a novel therapeutic strategy for pancreatic cancer. (Source)

Tβ4 gene silencing in A549 and H1299 cells inhibited cell proliferation, migration, and invasion in vitro and decreased tumor growth in vivo. (Source)

Inhibition of Tβ4 expression using transcription activator-like effector nucleases (TALEN) significantly decreased lung metastasis of B16F10 cells. (Source)

TB4 also upregulates genes (PINCH, ILK, Atk) that may be undesirable in cancer (figure 1.3).

High TB4 production within cancer is fuel on the fire, but we don't know if exogenous TB4 has a similar effect.

I could explain why exogenous TB4 might be dangerous, and why it might be innocuous. But I don't want

to exaggerate the risks, or dismiss them. You'll have to decide if you're comfortable with the current level of evidence, and weigh your tolerance for perceived risk against the anticipated benefits.

Dosing, what's the deal?

Here is a popular "TB-500" dosing protocol from TB-500.com. They consider TB-500 to be the exact same thing as TB4.

Recovery Phase (week 1 - week 5)
Monday: TB-500 5mg
Thursday: TB-500 5mg

Maintenance Phase (week 6 - week 7)
Monday: TB-500 5mg

The explanation:
..the total weekly dose of 10mg TB-500 promotes a buildup of Thymosin Beta-4 in the animal for optimal healing and recovery.

There are variations, such as this one with 450mcg/day for 30 days and this one with 750mcg/day for 20 days.

I was interested in determining what the basis might be for large, infrequent doses such as 5mg 1-2x/wk. This is quite different from the popular approach to BPC-157, which is often 250mcg 2x/day.

My initial suspicion was that this was a relic of veterinary use, where small frequent doses were impractical. And also due to poor shelf life once reconstituted.

First I looked at the idea of building up TB4 in the body with a loading phase.
It seems the half-life is quite short and it's not building up in the bloodstream.

Mean terminal half-life estimates increased with dose, from 0.95 h at 42 mg/subject, to 1.2 h at 140 mg/subject, to 1.9 h at 420 mg/subject, and to 2.1 h at 1260 mg/subject. (Source)

Going from 42mg to 420mg is a 10x in dose and approximately twice the half life. With very crude math, we might expect 4.2mg (1/10th) to have a half-life of around 30min.

The researchers who conducted the human injection study had this to say:

The PK profile showed a dose proportional response, increasing half-life with increasing dose and minimal drug accumulation..

..Following 14 days of multiple intravenous administration of Tβ4 once daily, accumulation of Tβ4 was minimal. Clearance remained constant in all dose groups and was similar following single and multiple intravenous administrations, indicating the dose independency of total clearance.

The major caveat is that they tested accumulation in the blood. It's plausible that TB4 binds with g-actin on and around cells, accumulating there.

I couldn't find any animal studies suggesting accumulation. I searched for 'buildup' and variations of 'accumulation' in a lot of studies, but haven't read them all.

The other question is if more frequent dosing was effective in studies. I browsed through a bunch of studies, and TB4 has shown good results with a variety of dosing schemes, including multiple times per day.

As far as actual doses, I'm mostly seeing a range from 2mg/kg to 30mg/kg in the studies. The lowest injected dose I've seen was 2 doses of 60mcg per rat, 2 days apart. Which improved wound healing. That would likely be around 120mcg/kg. The researchers didn't seem to be looking for the lowest effective dose in animal studies, but this is substantially higher than the lowest BPC-157 doses I've seen.

Out of curiosity, I tried this species conversion which suggests it might be 20mcg/kg for a human, so 1.4mg for a 70kg adult.

Although I didn't find evidence of TB4 accumulating in the body with large infrequent doses, this video from Drew Timmermans, ND was compelling.

He does 750mcg daily non-procedure dosing, but 1.5mg/day for 7 days after surgery. His rationale is that the expression of TB4 increases substantially with an injury and then declines. So mimicking (or augmenting) that TB4 spike may be more effective than dribbling it in.

This video has the analogy of TB4 acting as a bouncer, tying up g-actin until it's time for it to join the actin filament. Exogenous TB4 effectively increases the pool of g-actin waiting to join the filament. We don't really want that actin to sit around binding with TB4 indefinitely however, we eventually want the

bouncer to let the actin join the party, preferably faster than they are being kicked out. In this analogy, larger and less frequent doses would seem to make sense.

In the end, if I were dealing with acute injury repair I think concentrating the delivery makes sense. Whether that means 5mg 1x/wk, 1.5mg/day for a week, or the TB-500.com protocol.. I don't know.

If you bought a BPC-157/TB4 blend, I think it's fine to spread TB4 injections out like you would BPC-157.

Immune, anti-inflammatory and neurological benefits may be delivered just as well with smaller, more frequent doses.

That leaves the question of stability. Information is limited, but here are instructions for storage I found.

Upon reconstitution, the preparation is stable for up to one week at 2-8ºC. For maximal stability, apportion the reconstituted preparation into working aliquots and store at -20ºC to -70ºC. Avoid repeated freeze/thaw cycles.

Upon reconstitution Thymosin B4 Human should be stored at 4°C between 2-7 days and for future use below -18°C. Please prevent freeze-thaw cycles.

Once mixed in solution, the TB 500 should be used as soon as possible. Any unused portion should be refrigerated (NOT frozen) immediately at 39F (4C). Stored this way, it will remain potent for 1-2 weeks. See below for further storage information.
This comes from RegenerX.

The development program, abbreviated herein, consisted of assessing the solubility limit of TB4 in aqueous formulations and then developing a lyophilized dosage form that, when reconstituted, is ready for use..
..Liquid formulation development, over four iterations of lyophilization development, and stability testing led to a final dosage form of 5 mL in a 10 mL vial of 100 mg TB4/mL, ***sodium citrate as buffer at a pH of 5.5, sucrose as a stabilizer and bulking agent, and glycine as the amino acid stabilizer.*** *Drug concentration and certain fill conditions were selected to improve reconstitution times, reduce viscosity, and improve syringeability. The TB4 drug product, suitable for administration as an injectable solution, is manufactured, packaged, and tested for release in accordance with cGMP.*

My interpretation is that they couldn't crack long term liquid stability, and stuck with a lyophilized powder. The section in bold might offer some strategies to improve stability.

It's worth mentioning that many peptides do surprisingly well when refrigerated. Here is some data from CanLabs on reconstituted peptides. I don't know what formulation of water they use, it's likely optimized for stability. But even MOTS-C, a notoriously unstable peptide, didn't break down substantially. This Redditer seems to have been told by TMC that their reconstituted TB4 is stable 4 months in the fridge.

I don't have firm data. It's reasonable to use your TB4 quickly. Personally, I'd be comfortable keeping TB4 in the fridge for a couple weeks, maybe a month. Which is plenty of time for most protocols.

Bonus Material

Here are some excerpts I found informative, and odds and ends I uncovered along the way.

A nearly 300 page thesis: The Role of Thymosin Beta 4 in Vascular Development. Actually a pretty easy read, considering the topic.

I came across an interesting dimeric version of TB4.
https://www.internationaljournalofcardiology.com/article/S0167-5273(17)37850-6/fulltext
http://libgen.rs/scimag/10.2147%2FDDDT.S50183
http://libgen.rs/scimag/10.1002%2Fadvs.202070045

Great summary of endogenous TB4:

TB4 is a small, naturally occurring peptide found in almost all cells with relatively higher levels in circulating cells, such as platelets and white cells. It is highly significant that TB4 is in platelets because these are the first cells to arrive at a site of injury where these cells release various factors that initiate the repair process. TB4 levels are high in wound fluid, confirming that it is naturally present at wound sites and could function to promote dermal repair (Table 1). Although many of the factors released by the platelets are important in cell growth, TB4 is not a growth factor, i.e., it does not promote cell growth. In fact, TB4 is even smaller than standard growth factors which are generally similar in size to each other (4964 Da vs. 14,000 to 16,000 Da, respectively). Also, unlike growth factors, it does not bind to heparin which is ubiquitously present in tissues; therefore, TB4 can freely diffuse deeply into tissues to promote angiogenesis, cell migration, re-epithelialization, and down-regulate inflammation, among other effects. Furthermore, TB4 is present inside all cells and is not secreted, while growth factors are secreted, stored in the extracellular matrices outside of the cells, and only produced by certain cells. (Source)

Although the action of topically administered TB4 on wound repair remains somewhat unclear, following dermal wounding, endogenous TB4 is coreleased with factor XIIIa, a tissue transglutaminase, from human blood platelets at the wound site and cross-linked selectively by factor XIIIa, to various molecules, including actin, collagen, fibrin, and fibrinogen, suggesting its role and importance in wound healing. (Source)

I found a hair growth product pdf that stated:

Thymosin-B4 is SAFE (No Cellular Toxicity) up to tested 10ppm (µg/ml) - Reported oral toxicity, Rat : LD50 > 10,000 mg/kg.

And an MSDS
https://drive.google.com/file/d/1m05e_UVQzR6bTNlWYUbubPGKtFjTyEp8/view?usp=drivesdk
https://drive.google.com/file/d/1BXkxzVApB5nH7SetIS6x0Ot6M_ziR-7t/view?usp=drivesdk

Patent information

Generally the patents related to peptides are for methods of peptide production, alterations to natural chemical structure, formulation with other ingredients, or for specific applications.

RegeneRx acquired the rights to a novel peptide from the NIH in 1999. This intellectual property for Thymosin Beta 4 (Tβ4) allowed the company to direct its focus on tissue protection and repair in multiple disease indications. (Source)
RegeneRx holds numerous issued patents and patent applications, itself or through its partners, worldwide in order to enable and protect multiple indications and applications for its product candidates.

Currently, RegeneRx has active partnerships in four major territories around the world: the U.S. and Canada, China, Pan Asia, and the EU. Our partners have been moving forward and making significant progress in each territory with RGN-259, our ophthalmic drug candidate, and have initiated Phase 2 and Phase 3 clinical trials in several ophthalmic and dermal medical indications. In each case, the cost of development is being borne by our partners with no financial obligation for RegeneRx. Patient accrual, treatment, and follow-up for the ophthalmic trials are relatively fast, as opposed to most other clinical efforts, so data is typically forthcoming in months after patients begin enrollment.

We have other significant clinical assets to develop, primarily RGN-352 (injectable formulation of Tβ4 for cardiac and CNS/PNS disorders) in the U.S., Pan Asia, and Europe, and RGN-259 in the EU. With respect

to RGN-259, our goal is to wait until Phase 3 is completed in the U.S. before moving into the EU with RGN-259 in order to maximize value for the EU market. We intend to continue to develop RGN-352, either by obtaining grants to fund a Phase 2a clinical trial in the cardiovascular or central nervous system fields or finding a suitable partner with the resources and capabilities to develop it as we have with RGN-259. (Source)

RegeneRx Biopharmaceuticals, Inc., a clinical-stage drug development company focused on tissue protection, repair and regeneration, reported today that its U.S. joint venture partner and Pan Asian licensee, GtreeBNT, has been granted a new U.S. patent for a method of preventing or treating dry eye syndrome by administering Tβ4 with non-active ingredients to provide improved pharmacodynamics. (Source)

RegeneRx Biopharmaceuticals, Inc. (NYSE Amex:RGN) ("the Company" or "RegeneRx") announced today that the Company received a patent from the Mexico Patent and Trademark Office for the use of thymosin beta 4 (Tβ4), its analogues, isoforms, and other derivatives, for preventing or healing the damage that occurs from a myocardial event, or heart attack. The patent expires in 2022. RegeneRx has similar patents pending in a number of countries, including the U.S. Based on recent clinical data, this year the Company filed additional worldwide patent applications, which, if granted, could potentially extend patent protection in this area until 2030. (Source)

RegeneRx Biopharmaceuticals, Inc. (OTCQB: RGRX) ("the Company" or "RegeneRx"), a clinical-stage drug development company focused on tissue protection, repair and regeneration, today announced that the Canadian Patent Office has issued a new patent to the Henry Ford Health System (HFHS) for treating patients with peripheral neuropathy using Thymosin beta 4 (Tβ4). Tβ4 is the active pharmaceutical ingredient in RegeneRx's proprietary drug candidate, RGN-352, a first-in-class injectable formulation designed for systemic administration. Its use for the treatment of peripheral neuropathy or diabetic-induced vascular dysfunction has previously been patented in several other countries including in the U.S., EU, Asia and Israel. (Source)

RegeneRx Biopharmaceuticals, Inc. (OTCQB: RGRX) ("the Company" or "RegeneRx"), a clinical-stage drug development company focused on tissue protection, repair and regeneration, reported today that the Korean Intellectual Property Office has issued a new patent to the Henry Ford Health System (HFHS) for a Thymosin beta 4 (Tβ4) composition for reducing diabetic-induced vascular dysfunction. Tβ4 is the active pharmaceutical ingredient in RegeneRx's proprietary drug candidate, RGN-352, a first-in-class injectable formulation designed for systemic administration for tissue regeneration and repair. (Source

RegeneRx Biopharmaceuticals, Inc. (OTCQB: RGRX) ("the Company" or "RegeneRx"), a clinical-stage drug

development company focused on tissue protection, repair and regeneration, today announced that it has received notice of Intent to Grant a patent from the European Patent Office for the treatment of patients with Multiple Sclerosis. The patent covers use of the Company's proprietary molecule Thymosin beta 4 (Tβ4) in a composition for treating or reducing deterioration of, injury or damage to tissue due to MS. The patent expiry is January 13, 2026. (Source

Peptide experiences with EDS/HSD

Note: This post doesn't translate well to Google Docs because the point was to solicit personal experiences. I'm having trouble with my Reddit posts, but you may be able to view the comments.

Hi folks,

In recent years, I've interacted with several people with EDS or HSD who have used peptides (such as BPC-157) with good results.

I'll summarize the impressions I got from others, but mostly I wanted to provide a space where people can share their experiences in their own words.

General impression:

The people with HSD or EDS I've talked to who injected BPC-157 all reported it being helpful. Specifically with injury healing and pain reduction. I think others besides myself had Dysautonomia improvements, but I'm less confident about that.
For some, the benefits were modest and transient. For others, substantial and persistent.

Those that combined BPC-157 with GH secretagogues like Ipamorelin and mod-GRF seemed to have stronger and more persistent results.

The people who used oral BPC-157 seemed to find it helpful for GI issues, but didn't report substantial help with joint pain or injury healing.

I haven't talked to as many people with HSD/EDS who tried TB4 (often called TB-500). But I've seen some positive reports. There is some question of it increasing flexibility during use. I just found it reduced muscle spasticity, but I did see someone report a problematic increase in hypermobility.

The TB4 sequence includes a section that activates Mast cells. I'm not sure how substantial it is, but it's worth keeping in mind for those with MCAS.

I don't recall anyone with HSD/EDS reporting results from GHK or GHK-Cu. But that has potential for connective tissue and neurological repair.

ARA-290 is a very interesting contender for neurological repair, and is being investigated for SFN and dysautonomia.

TA-1 has potential for improving healthy immune system response, but maybe calming excessive reactions. I'm not well versed on immune issues, so I'll leave it at that.

LL-37 has potential for clearing infections, but it's presence may set off alarm bells in the immune system. So low doses may be prudent if you pursue this.

There is a peptide called Tripepeptide-29, which is just a 3 amino acid sequence (gly-pro-hyp) that can be used as a building block for collagen. I haven't heard of anyone even considering using this. But it may be helpful for those with glycine substitutions by providing a building block with the glycine already incorporated. I think EDS Classic type has that issue. This is speculation, and I'm not aware of any injection studies in rodents, much less humans. But a person could try it topically to see if there are any benefits to skin. It's also a small enough molecule to potentially be administered transdermally.

My experience:

Diagnosed HSD, also dealt with POTS/dysautonomia. I met the POTS criteria, and doctors agreed it was dysautonomia, but was diagnosed with 'orthostatic intolerance' instead.

I started with BPC-157, 250mcg injected subQ into belly fat 2x/day. I felt drowsy, and slept more the first week. I even took some naps. It felt like my body was working through a backlog of injuries. My pain went down, and it seemed to take the edge off my dysautonomia within a month. I've lost track of the timeline.

I started Ipamorelin and mod-GRF shortly after, also around 250mcg each AM & PM. I got very lightheaded with the first injection but not subsequent. I've since come around to the idea that 100mcg of each is plenty.

Once I added the growth hormone secretagogues I started bouncing back from workouts much faster.

Small injuries that would have lingered were cleared overnight. I continued to clear injuries and my pain went down. My wrists had been a trouble area, and the tendons and ligaments seemed to become more fortified.

I ran BPC-157 and GH secretagogues pretty much daily for a solid year, then gradually tapered down. I don't know if that was necessary or cost effective. I may have seen similar results with cycles. A recent GH test showed me in a good range, whereas previous results were low.

I still had some muscle spasms, especially in my upper back/neck. And tight painful hamstrings. I used TB4, I think at 5mg 2x/wk for a couple weeks, then 5mg 1x/wk for maybe 4 more weeks. My spasticity reduced, and some lingering muscle pain cleared up. My neck pain was reduced but still present, and my hamstrings were also improved but not resolved.

I also threw in some GHK-Cu, at 1mg/day or less. I don't know what I started with, but lately I do occasional 20mg cycles. With the other peptides in the mix, I don't know how much credit to give GHK. But I kept improving.

I've also used Epithalon, and it may have helped with sleep.

All these peptides were combined with substantial changes to lifestyle, and progressive training. The one thing I'd caution people against is using them as alternatives to the fundamentals.

Update Jan 2022: I've hardly used any peptides in the past year. My recovery from minor injuries isn't quite what it was while using the peptides, but I have substantially better healing and resistance to injury than I did before starting them. Due to shifting priorities and demands on my time, I haven't been strength training as much as I'd like either. But it seems like I've built up a decent buffer, and I don't immediately backslide if I dial things back.

Conclusion

That's all folks. Best wishes.

~u/BoldMeasures