Weight Loss

5-Amino 1MQ

Excess weight and obesity can be difficult to reverse or treat effectively. This can be due to changes in metabolism that reduce the ability of the body's fat stores to break down and become available as a source of energy. As a result, people affected by excess weight and obesity may find it harder to lose weight over time regardless of diets, eating styles or activity patterns.

As fat cells grow larger, they begin to overproduce an enzyme called NNMT. This enzyme acts to slow down fat cell metabolism (fat burning). This slowdown makes it harder for these cells to burn accumulating fat. As fat tissue grows and more NNMT is produced, greater amounts of hormones and pro-inflammatory signals are produced that are responsible for weight gain and other chronic diseases such as type 2 diabetes and cardiovascular disease.

Researchers at the University of Texas discovered a molecule that blocks this metabolic slowdown in white fat cells caused by excess NNMT. By blocking this metabolic slowdown, they were able to increase the metabolism within the white fat cells. Researchers add that by inhibiting the NNMT enzyme, we can increase fat cell metabolism and reduce the size of white fat deposits. We lose weight because we are treating a root cause of obesity and related metabolic disease.

What exactly is NNMT?

NNMT stands for nicotinamide N-methyltransferase. It is the culprit in this discussion. It is also a very important cytosolic enzyme which modulates cellular energy balance. To put it simply, it regulates nicotinamide and S-(5′-adenosyl)-L-methionine within a couple of intracellular pathways that deal with cellular energy regulation. How many of us have thought that as we age our metabolism just isn't the same as it used to be? Or why can't we lose the excess weight that has accumulated over time? What happens when this cellular energy balance becomes unbalanced?

It becomes what is known as the domino effect; one thing leads to the next. In this case, excess weight can lead to increased NNMT enzyme which can lead to poor fat cell metabolism which then leads to increased fat cell mass (weight gain).

Here is why we need to decrease the NNMT for weight loss. First, decreased NNMT means the fat cells won't grow. Second, decreased NNMT means fat cell metabolism can be corrected. And third, decreased NNMT means we lose weight because the fat cells shrink.

Blocking Metabolic Slowdown = Weight Loss

So how do we block the metabolic slowdown (or inhibit NNMT) so weight loss can occur? Researchers used variations of methylquinolinium (MQ) to measure the effectiveness of blocking NNMT. Out of all the variations of MQ studied, **5-amino 1MQ** came out on top as the most effective. 5-amino 1MQ is a small, selective membrane permeable molecule that blocks the NNMT enzyme. What made it even more effective is that it did not affect the activity of any other enzymes in the metabolic cycles which reduced the risks of any potential side-effects.

5-amino 1MQ has shown promise in blocking NNMT to enhance fat cell metabolism and promote weight loss. Most people don't know that NNMT has been implicated in a number of other diseases including osteoarthritis, metabolic disorders, cardiovascular disease, cancer, Parkinson's disease, kidney disease, and other neurovascular/neurological dysfunctions. 5-amino 1MQ or another variation could be promising to treat a variety of other diseases.

Benefits of 5-amino 1MQ

- Can reverse diet-induced obesity
- Can treat related metabolic conditions
- Can increase cellular energy regulators
- Can prevent lipogenesis (fat accumulation)
- Can increase $NAD^+$and SAM concentrations in fat cells
- Can regulate energy expenditure in fat cells

CJC-1295

Gland Stimulated: Pituitary *Injection*

CJC-1295 is a synthetic GHRH (growth hormone releasing hormone) analogue made up of 30 amino acids. It has been found to be highly effective with regards to the increase of growth hormone secretion and IGF-1 without negatively affecting the pulsatility of GH secretion. CJC-1295 is often combined with Ipamorelin due to its enhanced specificity as a GHRH. This peptide generates similar increases in growth hormone secretion, but without the appetite stimulation and increase in cortisol, acetylcholine, prolactin, and aldosterone seen with other peptides in its class. This peptide has been found to be very well-tolerated and perfect when combined with Ipamorelin.

Gland Stimulated: Pituitary

Benefits of CJC-1295:

- CJC-1295 increases growth hormone secretion and IGF-1 Levels with no increase in prolactin
- Increase Body Weight and Length through increased protein synthesis
- Increased Muscle Growth
- Increase Fat Loss
- Increased Cellular Repair and Regeneration
- Promotes slow wave deep sleep which is responsible for the highest level of muscle growth and memory retention and rejuvenation

Two types of CJC 1295:

GHRH (growth hormone releasing hormone) is produced in the hypothalamus. Its pulsatile release from the hypothalamus triggers a pulsatile release of GH from the pituitary gland. GHRH has a very short half-life of only a few minutes (half-life = the time required to remove half of the substance from the blood. The shorter the half-life, the more rapidly the substance is removed from the body, and the less its effect on the body).

The first 29 amino acids of GHRH is the active segment. They are available as a manufactured peptide called Sermorelin. Sermorelin was further modified to increase its half-life to 30 minutes. This is called CJC 1295. CJC-1295 was further modified by adding DAC (Drug Affinity Complex) to it. DAC binds to a blood protein called albumin, which increases it's half-life to 8 days. It is called CJC 1295 + DAC. CJC 1295 can also be compounded in a non-DAC form which mimics a more normal physiologic GH spike each night.

The longer half-life from the DAC binding to albumin means injections are only required once or twice per week. However, the long half-life and relatively constant blood level provide a constant stimulus for GH release from the pituitary through the GHRH receptor, which is not

physiological. This can decrease the GH pulse amplitude which will result in decreased GH tissue stimulation.

Safety:

It is also thought safest when using a long-acting CJC molecule, to have 'hormone holidays' of three months each three to six months, to allow the pituitary to 'recover'. During the holidays, Sermorelin is used instead of CJC 1295 + DAC. The 'hormone holidays' may also minimize the risk of GH resistance developing. This resistance, or insensitivity, may occur via antibodies forming that bind to and inactivate GH, or by a decreased number of GH receptors on tissues (down-regulation). These are theoretical concerns as no long-term studies have been undertaken to clarify the issues.

Side effects of CJC-1295 may include injection site reactions (irritation, erythema, induration, pain, itching), headache, diarrhea, vasodilation (flushing, warmth, transient hypotension), nausea, abdominal pain.

Ipamorelin

Gland Stimulated: Pituitary Gland *Injection*

Ipamorelin is one of the latest and greatest peptides in the growth factor family. Deemed one of the safest GHRP's, Ipamorelin is a selective growth hormone (GH) Secretagogue and Ghrelin receptor agonist. This peptide generates similar increases in growth hormone secretion, but without the appetite stimulation and increase in cortisol, acetylcholine, prolactin, and aldosterone seen with other peptides in its class.

Benefits of Ipamorelin:

- Decreased body fat
- Increased collagen production
- Increased lean muscle mass
- Improved sleep
- Increased cellular repair and & Regeneration
- Increased IGF-1
- Increases bone mineral content
- Counteracts glucocorticoid catabolic effects
- Less appetite stimulation than GHRP-6
- Less release of cortisol, prolactin, and aldosterone

Ipamorelin has been shown to be highly potent and has also demonstrated good safety and tolerability in human clinical studies. Research has shown that Ipamorelin is growth hormone specific, which means that the pituitary hormones (such as cortisol are unaffected).

Ipamorelin may be one of the best alternatives available to HGH therapy.

As an added perk, it does not promote increased production of the enzyme ghrelin, which stimulates hunger. This means that it will not make you hungry, due to Ipamorelin's ability to control points of gastric, appetite, and growth motility.Another very significant positive difference is that Ipamorelin does not display a capacity to significantly boost levels of cortisol, which can affect the body in unwanted ways. Patients on other types of secretagogue therapies have reported jitters, cold sweats or nervousness because therapy's overall impact on cortisol levels.

Tesamorelin

Gland Stimulated: Pituitary Gland *Injection*

Tesamorelin is a growth hormone-releasing hormone (GHRH) analog that has been shown to increase growth hormone and IGF-1 levels. **Tesamorelin is currently the most effective GH releasing hormone on the market.** It is an injectable peptide that generates greater natural production of HGH (Human Growth Hormone). It binds and stimulates human GHRH receptors with similar potency as our own natural GHRH. It has not been shown to significantly affect other pituitary hormones in the body.

Gland Stimulated: Pituitary Gland

Benefits of Tesamorelin:

- Increases natural productions of HGH (human growth hormone)
- Increases IGF-1 (Insulin Growth Factor – 1) without altering glucose parameters
- Reduced triglycerides
- Reduced Visceral Adipose Tissue (VAT)
- Reduced Carotid Intima Media Size (cIMT)
- Improved cognition in adults over the age of 60.

Tesamorelin Research:

Clinical trials have shown that tesamorelin significantly reduces abdominal fat with fewer side effects than human growth hormone itself, although abdominal fat may return after the Tesamorelin is discontinued (depending upon the individual). Tesamorelin has been shown to reduce lipodystrophy in HIV-infected individuals as well as similarly reducing abdominal fat in NON-HIV-Infected individuals.

According to one clinical study, 10.9 percent of patients who were given Tesamorelin experienced reductions in deep belly fat. These patients suffered from HIV. Reductions in trunk fat, waist size, and waist-to-hip ratios were recorded during the study. However, limbs and abdominal SC fat levels remained the same. During treatment, insulin-like growth factor 1 was boosted. However, glucose parameters were not altered. This drug didn't trigger negative side effects in most patients. However, results were temporary, as patients who were switched to a placebo lost their improvements. The study lasted six months in total. Overall, visceral fat levels decreased by eighteen percent.

Amlexanox/TTA

Amlexanox is an anti-inflammatory and anti-allergic compound which has traditionally be used to treat ulcers by reducing healing time and pain. It has multiple mechanisms of action such as inhibiting inflammation by inhibiting the release of histamine and leukotrienes. It has been shown to selectively inhibit TBK1 (TANK-binding kinase 1) and IKK-3 (Inflammatory Kinase), producing reversible weight loss and improved insulin sensitivity.

It is through this mechanism that it has produced substantial results in reducing HbA1C levels and increasing insulin sensitivity. We combine Amlexanox with Tetradecylthioacetic Acid (also known—and more easily pronounced—as TTA). It is a fatty acid that does not get used for fuel by the body, but instead helps to regulate how much fat the body stores by influencing genes that control the metabolism. TTA can help individuals feel full more quickly while the fatty acid decreases overall hunger and burns fat. In addition to regulating fat metabolism, this fatty acid has antioxidant, anti-inflammatory and immunity-enhancing properties.

Mechanism of Action:

Feedback loops of obesity

Loop 1: The first loop involves AMPK (adenosine monophosphate-activated protein kinase) and NF-KB (nuclear factor kappa B) pathways. In this loop, chronic stress triggered by obesity causes inflammation by activating the NF-KB pathway. The NF-KB pathway stimulates genes associated with inflammation and obesity including TBK1. When TBK1 is activated, it shuts down the enzyme AMPK, reducing the cell's ability to burn calories, and resulting in fat storage. **In this way, obesity reduces energy expenditure.** AMPK is one of the master regulators of energy expenditure and also senses changes in energy levels during fasting and increases expenditure by instructing cells to burn fat as an energy source. However, when fasting activates AMPK, it initiates the TBK1 enzyme, which ultimately inhibits AMPK's role in burning fat. This feedback loop blocks energy expenditure both through inflammation and fasting. Energy expenditure was restored when TBK1 was deleted from fat cells.

Loop 2: While NKFB induces TBK1, TBK1 turns around and inhibits NFKB. The activation of TBK1 normally reduces inflammation, without completely eliminating it, causing it to be low grade. Without TBK1, inflammation increases.

Benefits of Amlexanox:

- Can reduce Body Fat
- Can improve glucose control
- Can improve insulin resistance
- Can improve/normalize HbA1C

Amlexanox Research:

Growing evidence points to an inflammatory link between obesity and type 2 diabetes. Obesity produces a state of low-grade inflammation, particularly in the liver and in adipose cells. Using next generation RNA-sequencing analysis, researchers have compared gene expression in fat cells. They have found that inhibition of IKK-3 and TBK1 improves glucose control in certain patients with type 2 diabetes. The inflammatory kinases IKK-3 and TBK1 are elevated in obesity; their inhibition in obese mice reduced weight, insulin resistance, fatty liver and inflammation.

Amlexanox (an inhibitor of IKK 3and TBK1) was studied in a proof-of-concept randomized, double-blind, placebo-controlled study of 42 obese patients with type 2 diabetes and nonalcoholic fatty liver disease.

Treatment of patients with Amlexanox produced a statistically significant reduction in Hemoglobin A1c and fructosamine. Interestingly, in a group drug responders (people who reacted positively) also exhibited improvements in insulin sensitivity and hepatic steatosis (fatty liver). This subgroup was characterized by a distinct inflammatory gene expression signature from biopsied subcutaneous fat at the beginning of the study. They also exhibited a unique pattern of gene expression changes in response to Amlexanox, consistent with increased energy expenditure. Together, this data suggests that dual-specificity inhibitors of IKK-3 and TBK1 may be effective therapies for metabolic disease in certain groups of patients.

Study: TKB1 at the crossroads of inflammation and energy homeostasis in adipose tissue

Study: Inhibition of IKK3 and TBK1 improves glucose control in subset of patients with type 2 diabetes

Conclusion:

One of the reasons that diets are so ineffective in producing weight loss for some people is that their bodies adjust to the reduced calories by also reducing their metabolism, so that they are 'defending' their body weight. Amlexanox seems to tweak the metabolic response to excessive calorie storage and rev up the metabolism again to improve energy expenditure. This medication does not work for everyone, some people will respond, others will not.

AOD 9604

AOD 9604 is a modified form Growth Hormone which is a 191 amino acid peptide. The last 15 amino acids (176-191) of the Growth Hormone polypeptide have been reproduced as a specific peptide and is called GH Frag 176-191 or AOD 9604.

Benefits of AOD 9604:

- Reduces Body Fat
- Triggers fat release from obese fat cells predominantly more than lean ones
- Mimics the way natural growth hormone regulates fat metabolism
- No adverse effects on blood sugar or growth
- AOD-9604 stimulates lipolysis
- Inhibits lipogenesis that's the transformation of non-fatty foods into body fat
- AOD 9604 has been shown to have very favorable cartilage repair and regenerative properties, especially when paired with peptide BPC 157.

Mechanism of Action:

AOD-9604, also known as Tyr-hGH Frag 176-191 has been proven to have a strong fat burning capacity, without creating a desire to overeat. It doesn't affect blood sugar or tissue growth. (Heffernan 2001 Heffernan 2001, Ng 2000). AOD-9604 activates degradation and fat burning (oxidation), by a method that doesn't use hGH receptor. It has its own mechanism of action independent of hGH. Laboratory studies on rodents, pigs, dogs & humans have identified AOD-9604 mechanism where it triggers fat release from the obese fat cells predominantly and works to reduce the accumulation of new fat in fat cells as well as increasing fat burning. What is extraordinary about the AOD-9604 is its ability to reduce abdominal fat stores. **The second most potent fat loss peptide is CJC-1295**, since it leads to the increase in overall GH levels in the body (the opposite of what happens typically as individual age) This explains one of the reasons people have tended to gain fat as they get older. If your only goal is fat loss, it's usually best to avoid using products GHRP (GHRP-6, GHRP-2 or GHRH's) because they may give you the side effects of increased hunger and raised cortisol. AOD-9604 does not increase hunger & or raise cortisol.

AOD 9604 Research:

AOD-9604 (Advanced Obesity Drug) was originally developed by Professor Frank Ng at Monash University in Australia in the 1990s, with the intent of finding an anti-obesity drug that had the fat burning effects of human growth hormone (HGH) without the muscle-building effect.

Other recent findings have shown, in addition to its fat loss properties, AOD 9604 processes many other regenerative properties associated with growth hormone. Currently, trials are underway to show the application of AOD 9604 in osteoarthritis, hypercholesterolemia, bone and cartilage repair.

Results of oral glucose tolerance test demonstrated that, in contrast with hGH, AOD 9604 has no negative effect on carbohydrate metabolism. There were no anti-AOD 9604 antibodies detected in any of the patients selected for antibody assay. In none of the studies did a withdrawal or serious adverse event occur related to intake of AOD 9604.

Conclusion:

AOD 9604 displayed a very good safety and tolerability profile indistinguishable from placebo. AOD 9604 did not result in any of the adverse effects associated with full-length hGH treatment. AOD 9604 has an excellent safety profile, recently obtaining Human GRAS status in the USA.

Fat Loss Cream – Glycyrrhetinic Acid & Aminophylline Transdermal

Aminophylline and glycyrrhetinic acid transdermal cream is used for fat loss. Aminophylline and glycyrrhetinic prevent cAMP breakdown. Cyclic AMP (cAMP) functions in several biochemical processes including the regulation of glycogen, sugar, and lipid metabolism. cAMP works by activating protein kinase A (PKA) which assists in glycogen, sugar and lipid metabolism.

Aminophylline has displayed topical fat reduction from the waist. In a study examining aminophylline cream application, the reduction of waist circumference was significant for both men and women. Over a period of 12 weeks, participants in the study lost 11cm in waist circumference. In differentiated adipocytes, 18B-glycyrrhetinic acid increases the level of glycerol release and up-regulates the mRNA of hormone-sensitive lipase, adipose triglyceride lipase, and perilipin, as well as the phosphorylation of hormone-sensitive lipase.

18B-glycyrrhetinic acid alters fat mass by directly affecting adipogenisis in maturing preadipocytes and lipolysis in mature adipocytes. Therefore, aminophylline and 18B-glycyrrhetinic acid may be useful in treating obesity. Both aminophylline and glycyrrhetinic acid combined effectively combat fat loss.