HGHup♂™ TECHNICAL INFORMATION

PRODUCT DESCRIPTION:

HGHup♂ is so unique it falls into a new category altogether. HGHup♂ is the world’s first hANh™ (Hybrid Anabolic / Near Hormonal); which is defined as a product that engages a synchronization of natural and exogenous factors to produce a pronounced anabolic and hormonal response. The distinct advantage of a hANh is that the user is able to obtain maximal physiological benefits comparable to that of fully hormonal products while minimizing potential side effects and disruption of endogenous factors post-usage.

HGHup♂ promotes radical increases in serum HGH and testosterone levels without a prescription. It is the only orally viable compound that is proven to increase HGH AND testosterone in human subjects.

PRODUCT CHARACTERISTICS:

- Increases the output of growth hormone and local IGF-1 levels
- Increases the duration/viability of growth hormone pulse mass
- Increases androgen receptor structure, function, and number
- Increases natural production of testosterone

Figure 1: HUMAN GROWTH HORMONE AMINO ACID SEQUENCE
EFFECTS RELATED TO PHYSIQUE AND LIFE ENHANCEMENT:

- Greater lean muscle mass
- Lowered body fat
- Increased strength
- Faster healing of injuries and better recovery from physical stress/training
- Better skin tone
- Deeper, more restful sleep

MAIN MECHANISMS OF ACTION:

*Mucuna Pruriens, Vitamin B6 and L-Dopa: Increase Growth Hormone Output and Testosterone Production While Concurrently Decreasing Somatostatin and Prolactin.*

- **HGHup** contains highly concentrated L-Dopa derived from *Mucuna Pruriens*. *Mucuna Pruriens* is an Ayurvedic Herb that has both anti-hypoglycemic and L-Dopa-increasing qualities. (32). L-Dopa has been shown to significantly increase levels of growth hormone in human subjects when administered orally. (1, 2, 3, 33).
- Oral viability in **HGHUP** critical for product effectiveness, as growth hormone cannot be absorbed and is rendered ineffective due to the fragility of the ingredients. Several good examples are synthetic growth hormone (see Fig. 1) and growth hormone releasing hormone (GHRH, see Fig. 2). These compounds cannot be administered orally; because of their fragile amino acid sequence is destroyed by stomach acids. This
also holds true with the vast majority of the so-called “GH Boosters” and “Peptides” commonly found in sports nutrition products.

- L-Dopa and Dopamine have also been shown to inhibit prolactin, a hormone that suppresses male testosterone production. Prolactin also has a positive correlation with a second hormone called somatostatin, which decreases the both amount and effectiveness of circulating growth hormone. Therefore, by lowering prolactin (and consequently somatostatin) levels, HGHUP♂ increases both testosterone and GH production; leading to greater recovery and lean body mass (38, 39).

- Vitamin B6 is also included in the formula for HGHUP♂, as it can also help further lower prolactin levels and increase the night-time peak of GH release pulse, while at the same time increasing the rise in GH associated with exercise by as much as 23% (7).

**Huperzine-A: Increasing AChE Inhibition and Mean serum GH by Decreasing Somatostatin**

- Huperzine-A is a strong acetylcholine esterase (AChE) inhibitor. Acetylcholine esterase inhibitors have been shown in numerous scientific studies to inhibit somatostatin via a variety of synergistic biomechanisms; all of which contribute to increased levels of growth hormone (9, 10, 11, 12, 13, 14, 15, 16, 17, 18).
  - Somatostatin is a hormone that exerts effects on anterior pituitary as well as pancreatic, liver and gastrointestinal function (40, 41, 42, 43).
  - Somatostatin is of extreme importance because it directly effects growth hormone release and is the major regulating factor in slowing or even stopping growth hormone output.
  - Therefore, by inhibiting somatostatin, overall mean serum GH will increase (41, 42).
  - Somatostatin inhibits GH secretion indirectly via antagonizing GHRH secretion (41, 42, 43).

- Consequently, the Huperzine-A, in HGHUP♂ increases the length, intensity, duration of growth hormone pulses and increases mean serum GH levels, therefore allowing for more of the positive anabolic and anti-aging benefits associated with GH.(8, 10, 12-17, 19-20).

**FIGURE 3: POTENCY OF ACETYLCHOLINE ESTERASE INHIBITORS**
Green Tea Extract, and (−)-epigallocatechin-3-O-gallate (EGCG): Increasing Dopa Decarboxylase Inhibition and the AChE-inhibiting Effects of HGHUP®

- Dopamine crosses the blood/brain barrier poorly, and cannot exert optimal effects on target receptors unless enough of the compound reaches the brain. L-Dopa is freely absorbed across this barrier, and when L-dopa crosses the barrier readily, growth hormone levels increase. (1-6, 32-33)
- L-Dopa is most effective when conversion of L-Dopa to dopamine is mediated by a decarboxylase inhibitor. A decarboxylase inhibitor is a substrate that inhibits the metabolism of one biological entity into another biological entity (2, 3, 4, 5, 19, 20, 37).
- A decarboxylase inhibitor is generally administered at the same time as L-Dopa / Mucuna in order to reduce conversion of the L-dopa into dopamine in the periphery. (−)-epigallocatechin-3-O-gallate (EGCG), which is found in high amounts in the green tea extract used in HGHUP®, is a potent decarboxylase inhibitor. The decarboxylase-inhibiting qualities of EGCG have been documented in several recent studies, in that EGCG seems to prevent L-dopa from converting into dopamine; allowing more significant levels of L-dopa to reach the brain and increase growth hormone levels (1, 2, 3, 4, 5, 37).
- EGCG has also been shown to significantly increase the effects of Huperzine A on acetylcholine esterase inhibition by increasing the transport of Huperzine-A by serum albumin. This allows for greater amounts of acetylcholine to be present, therefore allowing for greater mean serum growth hormone. Increased serum GH from HGHUP® allows for increased anabolism, better recovery, and increased muscle mass (19, 20).
HGHUP♂ INCREASES ANDROGEN RECEPTOR QUANTITY AND DENSITY AND CREATES A BETTER BINDING ENVIRONMENT FOR EXISTING ANDROGENS

_L-Carnitine-L-Tartrate and Magnesium: Increasing Androgen Receptor Number and Density, and the Creation of a Better Binding Environment_

- L-Carnitine L-Tartrate is an amino acid that has been shown to increase the number of androgen receptors in skeletal muscle, creating a better binding environment for testosterone and other androgens by allowing for a greater number of intact receptors available for hormonal interactions. (21-23)
- Magnesium has been shown in more recent studies to inhibit the binding of steroid hormone binding globulin (SHBG) and free testosterone. SHBG binds free testosterone and allows it to be excreted from the body, without binding the androgen receptor. Magnesium keeps this from happening by altering the binding affinity of testosterone to SHBG; thereby allowing for increased amounts of free testosterone to remain active in the bloodstream. (24)
- Other human research has shown that supplemental magnesium, when taken along with other ingredients like DHEA and Zinc, can significantly increase free testosterone. (25-27)
- Therefore, HGHUP♂ allows for greater numbers of androgen receptors and a better binding environment for testosterone in skeletal muscle. This is a new breakthrough in sports supplementation as HGHUP♂ creates a better target for circulating free testosterone, allowing for greater binding of testosterone to the extra receptors which leads to increased protein synthesis, better recovery, and increased muscle mass.

HGHUP♂ INCREASES TESTOSTERONE

_Mucuna Pruriens, Zinc, Selenium, and Chlorophytum Borivillanum Ethanolic/Sapogenic Extract: Increasing Testosterone Levels_

- Mucuna Pruriens has been shown in several recent human studies to improve testosterone levels and spermatogenesis in animal studies and humans, via prolactin inhibition. Prolactin, as mentioned earlier, is a hormone that suppresses male testosterone production (30-31, 34-36, 38-39).
• The ethanolic and sapogenic extracts of Chlorophytum Borivaiianum have also been shown in animal studies to increase testosterone, and anecdotal data from products containing this compound also point to increased testosterone and lean body mass for users of this phyto-androgenic compound. However, the mechanism of action of Chlorophytum is poorly understood. (28-29)

**Figure 4: Chlorophytum Study Data**

![Body weight increases of animals fed Chlorophytum ethanolic extract, sapogenic extract, test propionate and control](image)

- Zinc is involved in over 200 enzymatic reactions, allowing for the action of several different hormones: GH, testosterone, and insulin all require zinc for synthesis (26-27).
- Selenium has been shown in several studies to have direct effects on the biosynthesis pathways of testosterone. Selenium is rate-limiting in testosterone production in men, and if enough selenium (selenium deficiency is very common) is not available, testosterone will not be produced in optimal levels (27).

**Administration, Timing, and Dosing**

- Normal GH pulses (see chart below) occur throughout the day. For a normal male in an average day, there are 10 pulses of GH secretion lasting on average 96.4 mins with 128 mins between each pulse. The largest GH pulse occurs during stages 3 and 4 of the sleep cycle. GH
pulses during sleep (see Fig. 5) occur at nearly triple the rate of GH pulses during the day (44-45)

- Somatostatin release is controlled in large part by the cholinergic system. The cholinergic system is responsible for regulating the amount of acetylcholine found in the body at any given time. Acetylcholine is a neurotransmitter responsible for muscular activation in the peripheral nervous system, and tends to be excitatory in the central nervous system (CNS) (10, 11, 12, 13).

- The CNS component of acetylcholine mediates the cholinergic system, and this is important because the cholinergic system is responsible for mediating growth hormone response (11, 12, 13, 14, 15).

- The mechanism through which this is accomplished is simple: by increasing acetylcholine levels, there will be an increase in mean serum GH. **HGHUP♂** increases acetylcholine via lowering levels of acetylcholine esterase or AChE (an enzyme that breaks down acetylcholine) (11, 12, 13, 14, 15).

- Taking an acetylcholine esterase inhibitor (in the case of **HGHUP♂**, Huperzine-A) before sleep will result in dramatically reduced somatostatin levels and dramatically increase serum GH levels (1-4, 5, 9-17,19, 20, 44, 45).

- Somatostatin seems to be the major inhibitory factor in sleep-related GH pulses. When AChE is inhibited by pyridostigmine (an AChE inhibitor very similar to Huperzine-A) GH pulse mass is increased, and mean serum GH almost doubled. In terms of potency, Huperzine-A has actually been shown to be more potent than pyridostigmine bromide in terms of AChE inhibition (9-17, 19-20).

- There has also been a very popular trend recently of bodybuilders taking Huperzine-A along with injectible synthetic growth hormone, because the compound is so effective at inhibiting somatostatin and increasing serum GH (46)

- Taking (−)-epigallocatechin-3-O-gallate (EGCG) along with Huperzine-A will increase Hup-A’s effectiveness in inhibiting acetylcholine esterase, and its ability to allow the cholinergic system to suppress somatostatin. This has been verified in several scientific studies (19-20).

Figure 5: The Pulsatility of GH in Humans
Taking a supplement containing L-Dopa with a decarboxylase inhibitor before sleep can allow for dramatically increased levels of GH (1-5, 32-33, 37-39).

Hypoglycemia (low blood sugar) can also increase the amount of GH released. Insulin and GH are antagonistic, and the lower the insulin level, the higher the GH level (see chart below, 44-45).

Figure 7: GH Response to Lowered Blood Sugar
Timing of the dose and manipulating insulin levels before sleep is the key getting great results with HGHUP♂ (44-45, 47)

Best results occur when a 4-6 capsule dosage is taken on an empty stomach (fasted state) 30 minutes before bedtime (44-45, 47)

Why Most OTC GH Products Are Ineffective, and How HGHUP♂ Differs

Over the last 20 years, a variety of products that claim to boost HGH orally have been promoted in the US sports supplement market. The vast majority of these products have been completely ineffective for several reasons:

- Growth hormone is a peptide (a long chain amino acid structure), that cannot be taken in an oral form, due to the destruction of the sequence by the acidic environment of the stomach. Any supplement containing “oral growth hormone” is a scam (47).
- Many products use a combination of amino acids such as arginine and lysine in “kitchen sink” formulas, and claim that their combination is “scientifically proven” to work. Many amino acids boost growth hormone levels, but most of the time, it is only when taken intravenously, or in completely unattainable dosages that would make a normal person extremely sick. And the correct dosage is in gram amounts, not in the milligram range offered in many of these products (47).
- Even if these products allow for a viable release of GH, there is nothing present to inhibit somatostatin, which has been found to be the biggest factor in controlling GH levels (47).
- Many of these products are powdered mixes that contain sugar, sweeteners, or other compounds that may increase blood sugar. As
discussed above, this will render the product virtually useless due to the inverse relationship between glucose and growth hormone (47).

- **HGHUP♂** differs from these compounds because of the nature of the formulation. Every compound in the product is designed to work in concert with the other components; no filler or ineffective components are found in this product (47).

- **HGHUP♂** utilizes the latest research on compounds which have been overlooked by other companies. The secret of the product is in the complexity, effectiveness and synergism of the blend (1-47).

- **HGHUP♂** is the first product to positively manipulate somatostatin; this alone puts it in a class by itself.

- **HGHUP♂** also utilizes components that boost androgen levels, increase the number and function of androgen receptors, and create an overall BETTER anabolic environment in which levels of testosterone and GH are optimized, leading to better recovery, increased lean body mass, and lower body fat (1-47).

### Stacks and Tips to Maximize the Product

- Take Bio-Mend Anti-Oxidant formula
  - High ORAC Value
  - Protects cellular membrane
  - Protects transcriptional factors (mRNA and DNA)

- In general, maintain a healthy diet and lifestyle:
  - Drink Plenty of water; at least 64 oz. per day
  - Ingest at least 1 gram of protein per lb. of body weight daily
  - Sleep at least 7 hours per night
  - Eat lots of fruits and vegetables
  - Eat lots of complex carbs
  - Eat 5-6 smaller protein and carb-rich meals throughout the day
  - Increase calories to at least 500 Kcal/day over your normal intake
  - BCAAs and Creatine will be helpful
  - Avoid alcohol and tobacco
  - Take **HGHUP♂** on an empty stomach before going to sleep, or take it with an all-protein meal. Remember, carbohydrates/insulin decrease the effectiveness of the product.
  - **HGHUP♂** can be stacked with synthetic growth hormone and will make it more effective

*In conclusion, **HGHUP♂** is the most effective orally administered HGH and Testosterone agonist yet to be offered in the history of sports nutrition. For more information, you can contact Applied Nutriceuticals at info@appliednutriceuticals.com.*
Studies and Clinical Info


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