

Maximizing Growth While You Sleep: The science behind GH Peak™

David M. Gundermann, M.Sc., Ph.D.

Chief Scientific Officer, Blue Star Nutraceuticals

Growth hormone (GH) is a 191 amino acid polypeptide that is secreted from the anterior pituitary gland, under the regulation of the hypothalamus. The expression of GH has profound effects of growth on many tissues, but unlike its name suggests, it actually possesses additional properties than just growth. The central focus of GH in adults is its ability to burn fat while preserving muscle. It is unusual for a single hormone to be strategically catabolic in one tissue while anabolic in another, making it so desirable for those who wish to achieve a superior physique.

As GH is released into the bloodstream it acts on several tissues by binding to GH receptors to elicit its distinct function for that tissue. For instance, in adipose tissue, GH is a potent stimulator of fat breakdown (lipolysis) via activation of the enzyme, hormone sensitive lipase (HSL). HSL is responsible for breaking down triglycerides into free fatty acids, which are then burned for energy. At the same time, GH promotes fat oxidation while reducing the storage of fat (lipogenesis) by inhibiting the enzyme acetylCoA carboxylase (ACC). By manipulating both HSL and ACC, GH is responsible for prioritizing the utilization of fat over carbohydrates or protein as a source of energy. The combination of these effects greatly influences total metabolic expenditure, and total subcutaneous fat mass contributing to the desirably lean physique.

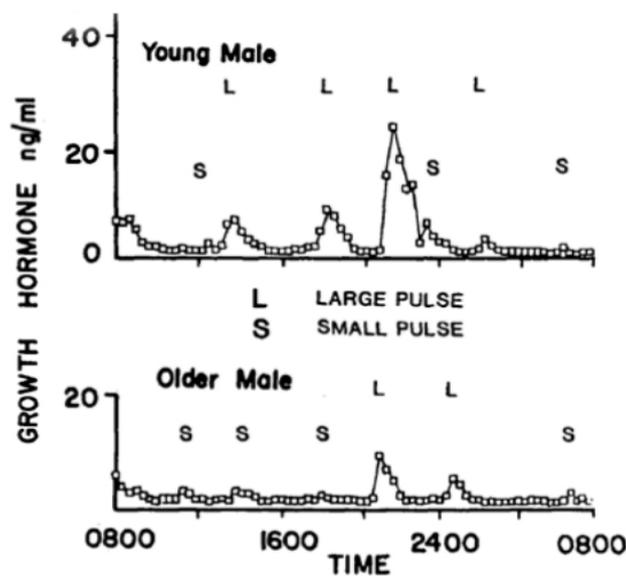
As expected, GH does more than just burn fat. GH is well documented to substantially increase lean body mass. However, the direct effect of GH on muscle is actually negligible. This is because GH uses an intermediate hormone to affect muscle anabolism and catabolism. Once GH is bound to GH receptors in the liver, the liver responds by releasing insulin-like growth factor 1 (IGF-1) into the bloodstream. IGF-1 is both the anabolic and anti-catabolic mediator that GH employs to affect muscle. IGF-1 activates several unique pathways in muscle, to enhance amino acid transport, gene transcription, protein synthesis, and reduced protein breakdown; all of which contribute to tissue building. Evidence shows that the primary anabolic effect of GH is through the synthesis of collagen in muscle as well as bone. While the increased collagen synthesis may not contribute to increased strength, it certainly contributes to increased muscle size. Altogether, the effects of GH on muscle alone results in harder, denser and more chiseled muscles.

The increase in lean body mass is still not all of what GH has to offer. For instance, GH plays a role in the hair and nail growth, preventing the process of balding; the strengthening of bones makes them more resistant to injury; and the increased

synthesis of collagen contributes to expedited effects on injury healing and recovery. In short, GH is widely considered as being a fountain of youth because its effects of rapid growth, fast metabolism, and short recovery times are the features of what life is like as an adolescent.

### “SOMATOPAUSE”

Although GH has so many desirable effects, the height of its abilities is seen during adolescence. After 20 years of age, the amount of GH secretion reaches its peak and then begins its decline. The age of 30 begins a period known as somatopause where GH levels start to become significantly lower than when at its peak. Unlike testosterone that exhibits a slow and progressive decline, GH declines at a rapid rate such that GH levels in late life are less than one quarter of the amount of youthful GH. There is still an obvious need for GH throughout the entire lifespan (otherwise it would stop production altogether), in fuel selection, growth and repair. However, over the adult lifespan the effects of GH decline become increasingly more apparent.



**Figure 1.** Pulses of growth hormone peak during sleep. The height of a growth hormone peak is dramatically reduced with age.

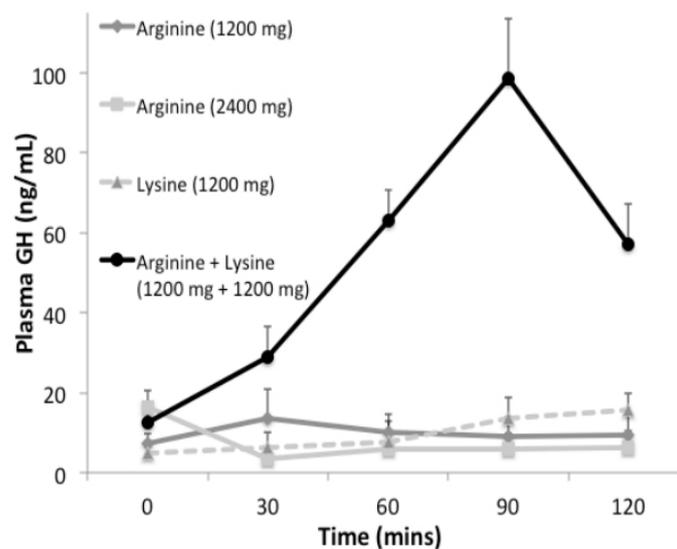
The reduction in GH is associated with the aging process along with a reduction in lean body mass (30-50%) and bone mineral density (3%), and an increase in body fat (10-50%). Moreover, as GH levels continue to decline, so do the immune

system, cardiovascular system, and sleep quality. In fact, the onset of wrinkles has been connected to the decline in GH levels.

In order to understand how to improve GH secretion, it is important to understand what triggers its secretion. GH is released in a pulsatile fashion throughout the day in response to various stimuli. By maximizing the effect of these stimuli, GH may be able to play a larger role in restoring youthful abilities.

### AMINO ACID INDUCED SECRETION OF GH

A classic study elegantly demonstrated that the oral consumption of two specific amino acids is sufficient to induce a robust and meaningful increase in GH within a short period of time in young healthy volunteers. The authors demonstrated that exactly 1200 mg of arginine pyroglutamate + 1200 mg of L-lysine brought about a marked biological response reaching a maximum peak at 90 minutes postingestion. This exact combination was imperative since the association of the two amino acids seemed to provoke a much greater GH response than either of them demonstrated alone. Individually, their influence on GH was practically non-existent, even when administered in doses equal to the total amino acid dosage of the combination.



**Figure 2.** Research data showing the exact combination arginine and lysine triggered a 695% increase in GH release.

More significantly, this effect was reproducible with repeated exposures and did not show any evidence of reduced effectiveness over time. The magnitude of the increase is the most impressive aspect of this research study. This specific combination of amino acids elicits a 695% increase in GH release.

This classic research is the reason why 1200 mg of arginine pyroglutamate + 1200 mg of L-lysine is a cardinal component to the formulation of GH Peak™.

## **SLEEP QUALITY AND GH PRODUCTION**

Pulses of GH are released throughout the day, the magnitude of which is partially dependent on activity and nutrition status. However, the opportunity for the greatest magnitude of GH release occurs during the initial phases of sleep. Therefore, to focus on maximizing GH pulses, means to focus on the events that occur during sleep. The surge of GH during sleep can be so large that it can account for over 50% of the daily GH production.

It is well established that GH is released during a deep sleep phase known as slow wave sleep (SWS). Accordingly, research shows that the duration of SWS is correlated with GH release and that sleep delay or sleep interruptions results in a net lower GH release through the night. Thus, maintaining a high quality of daily sleep is necessary to optimize GH production through the night.

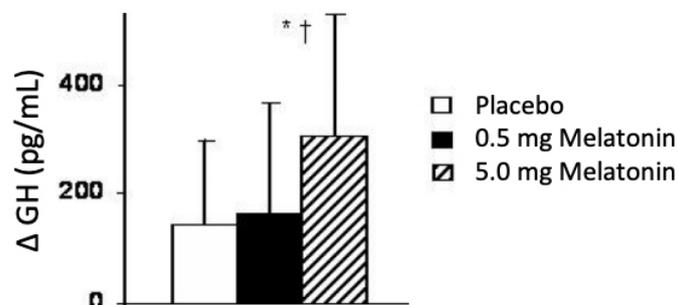
GH Peak™ takes this into account by incorporating an extract of the natural perennial flowering plant, Valerian. Commonly used in teas to relax and sedate, Valerian root extract naturally contains compounds called sesquiterpenoids such as valerenic acid that are known to interact with GABA receptors. This is important because GABA receptors are a major inhibitor of the central nervous system. The activation of GABA receptors with valerenic acid has a sedative, sleep-inducing, anxiolytic and muscle relaxant effect. Oral supplementation of valerian root has been used for thousands of years across Europe and Asia as a sedative and sleep aid. Its inclusion in GH Peak™ is introduced to be an effective method to reduce the delay onset of sleep and induce a productive night's sleep of GH production.

In addition to Valerian root, many will recognize melatonin as a sleep-inducing dietary supplement. In fact, the effects of melatonin go much deeper than that. Melatonin is a natural lipophilic hormone synthesized by the pineal gland. However, its production is inhibited by daylight, and therefore, is regulated by circadian rhythms.

As the sun goes down, the pineal gland begins the production and release of melatonin, which subsequently plays a prominent role in the regulation of tiredness and sleep. However, that's not all it accomplishes throughout the night. Melatonin is known to play a facilitatory role in the neuroregulation of GH secretion at the hypothalamic level. Research has discovered melatonin receptors in the hypothalamus, and its activation inhibits the release of a GH inhibitor called somatostatin. By reducing somatostatin, the levels of GH through the night can be greatly augmented.

As already noted, light can negatively affect the amount of melatonin naturally produced from the pineal gland. Specifically, light in 460-480 nm wavelength (blue light), inactivates an enzyme in biosynthetic pathway of melatonin. This is not an issue for the typical incandescent household light bulbs, but devices such as TVs, smart phones, and tablets emit large quantities of light at that wavelength. Thus, using these devices before bed is actually killing the ability to naturally produce melatonin. This is why melatonin supplementation is so effective with today's generation known to be dependent on such devices.

The GH effects of melatonin were demonstrated in a study where participants were given either a placebo or a dose of melatonin. This research demonstrated that a dose of 5 mg of melatonin elicited a significant 157% increase in serum GH in as little as 60 minutes post-ingestion. Melatonin is therefore effective to induce an increase in GH using two mechanisms. Firstly, it is a positive influence on sleep quality, improving total sleep time and sleep onset latency, all of which are indirectly supportive of greater GH production. Secondly, 5 mg of melatonin also directly inhibits somatostatin enhancing GH production.



**Figure 3.** Melatonin stimulates the release of GH. Data indicates that 5mg of melatonin caused a significant increase in GH release compared to placebo or 0.5 mg of melatonin. \*p<0.05 vs placebo, †p<0.05 vs 0.5 melatonin.

Melatonin being a naturally occurring hormone, it is a common assumption that it needs to be cycled on and off in order to maintain its effectiveness. Current research has addressed to this concern and has failed to demonstrate any evidence of symptoms of either dependence or tolerance after continued melatonin supplementation. One possible explanation is that the half-life of melatonin relatively short and the effects are immediate. After about 90 minutes postingestion, the majority of the oral melatonin will have disappeared, and the natural melatonin production from the pineal gland will be responsible for the continued slumber. Still, this short half-life of melatonin is like a double-edged sword. It is beneficial in that it does not evoke any dependence or tolerance, but it also means the surge of GH may only be short lived also. Yet again, GH Peak™ has the solution to this as well.

5-hydroxy-L-tryptophan (5-HTP) is the ratelimiting component in the biosynthetic pathway of melatonin. Meaning that supplemental 5-HTP is sufficient to induce an increase in melatonin production. Thus, as supplemental melatonin is eliminated after sleep has already been initiated. The production of melatonin can be further enhanced through the supplementation of 5-HTP.

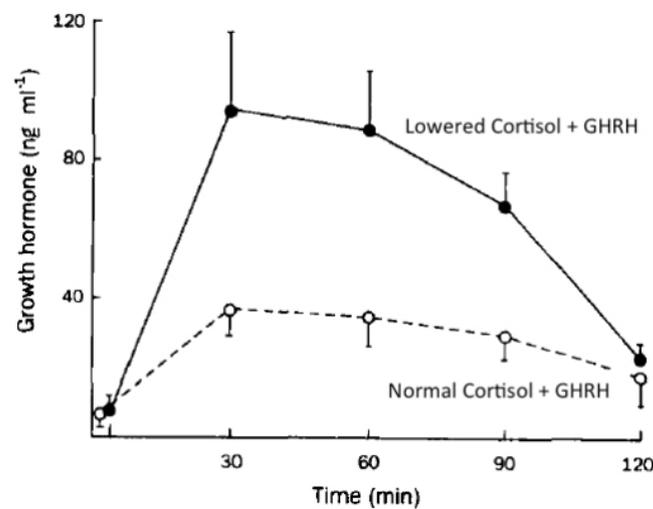
Being able to maximize GH-inducing effects of sleep is a critical strategy in overall GH production. GH Peak™ provides the most suitable combination of valerian, melatonin and 5-HTP in order accomplish the ideal environment to relax the muscles, calm the nervous system, quickly initiate sleep, and acquire maximum deep sleep, while at the same time enhancing the regulation of the synthesis and release of GH throughout the night. Using this combination is sure to provide the maximum stimulus to trigger GH to be released with the assumption that the negative influencers do not interfere.

## **CORTISOL INHIBITION**

Any GH formulation is far from complete if it does not address the most notable inhibitor of GH release. Cortisol, a hormone released from the adrenal glands in response to stress, inhibits an upstream regulator of GH called growth hormone-releasing hormone (GHRH). GHRH is a hormone released from the hypothalamus that acts on the pituitary to stimulate the release of GH. However, the typical modern lifestyle is associated with high levels of stress and associated cortisol. Chronic cortisol is a major factor that restricts the release of GH. By mitigating the effects of cortisol, GHRH can regain its ability to stimulate the release of GH. Another classic experiment

tested this theory in humans. The 1994 study was conducted on six healthy volunteers who were injected with GHRH with or without a cortisol inhibitor. Results revealed that by simply reducing the effects of cortisol, GHRH increased its potency by 163%.

The ashwagandha plant is known to be effective and safe in reducing cortisol in response to stressors likely due to the glycowithanolide content. Combining a standardized ashwagandha extract with the aforementioned ingredients substantially improve the capability of GH release.



**Figure 4.** Inhibition of cortisol relieves the inhibition on GH production.

Sensoril® is a branded ashwagandha root and leaf extract that contains a standardized minimum of glycowithanolides. Clinical studies indicate that Sensoril® ingestion is associated with the reduction of cortisol production from the adrenal glands. The use of Sensoril® in GH Peak™ ultimately alleviates the inhibition of GH release and increases the potency of GHRH. When put together in GH Peak™, the inclusion of Sensoril® allows for the perfect environment for each ingredient to function at its maximum potential.

## CONCLUSION

The effects of GH are ever fleeting, and it is only becoming worse with advancing age. With the constant decline in GH, comes hair loss, wrinkling, fat gain, loss of lean mass, and accumulating injuries with diminished capabilities for recovery. The specific combination of ingredients in GH Peak™ offer every single scientifically

backed approach to boost GH levels quickly, safely and naturally. Ingesting GH Peak™ in the hours before sleep provides the best possible advantage to get the most out of natural GH production.

**REFERENCES**

1. Auddy B, Hazra J, Mitra A, et al. A Standardized Withania Somnifera Extract Significantly Reduces Stress-Related Parameters in Chronically Stressed Humans: A Double-Blind, Randomized PlaceboControlled Study. *JANA*. 2008; 11:50- 56.
2. Barton DL, Atherton PJ, Bauer BA, et al. The Use of Valeriana Officinalis (Valerian) in Improving Sleep in Patients Who Are Undergoing Treatment for Cancer: A Phase III Randomized, PlaceboControlled, Double-Blind Study: NCCTG Trial, N01C5. *J Support Oncol*. 2012; 9:24-31.
3. Brandenberger G, Weibel L. The 24-h growth hormone rhythm in men: sleep and circadian influences questioned. *J Sleep Res*. 2004; 13:251- 255.
4. Cameron CM, Kostyo JL, Adomafio NA, et al. The acute effects of growth hormone on amino acid transport and protein synthesis are due to its insulin-like action. *Endocrinology*. 1988; 122:471- 174.
5. Dardevet D, Sornet C, Attaix D, et al. Insulin-like growth factor-1 and insulin resistance in skeletal muscles of adult and old rats. *Endocrinology*. 1994; 134:1475-1484.
6. Dietz J, Schwartz J. Growth hormone alters lipolysis and hormone-sensitive lipase activity in 3T3-F442A adipocytes. *Metabolism*. 1991; 40:800-806.
7. Dinan TG, Thakore J, O'keane V. Lowering cortisol enhances growth hormone response to growth hormone releasing hormone in healthy subjects. *Acta Phsiol Scand*. 1994; 151:431-416.
8. Goldspink G. Changes in muscle mass and phenotype and the expression of autocrine and systemic growth factors by muscle in response to stretch and overload. *J Anat*. 1999; 194:323-334.
9. Thomas GA, Kraemer W. Obesity, Growth Hormone and Exercise. *Sports Med*. 2013; 43:839-849.
10. Ho KY, Evans WS, Blizzard JD, et al. Effects of Sex and Age on the 24-Hour Profile of Growth Hormone Secretion in Man: Importance of Endogenous Estradiol Concentrations. *J Clin Endocrinol Metab*. 1987; 64:51-58.
11. Isidori A, Lo Monaco A, Cappa M. A study of growth hormone release in man after oral administration of amino acids. *Curr Med Res Opin*. 1981; 7:475-481.
12. Lemoine P, Nir T, Laudon M, et al. Prolonged-release melatonin improves sleep

- quality and morning alertness in insomnia patients aged 55 years and older and has no withdrawal effects. *J Sleep Res.* 2007; 16:372-380.
13. Lemoine P, Garfinkel D, Laudon M, et al. Prolonged release melatonin for insomnia – an open-label long-term study of efficacy, safety, and withdrawal. *Ther Clin Risk Manag.* 2011; 7:301-311.
  14. Lissett CA, Shalet SM. Effects of growth hormone on bone and muscle. *Growth Horm IGF Res.* 2000; 10:S95-S101.
  15. Liu H, Bravata DM, Olkin I, et al. Systematic Review: The Effects of Growth Hormone on Athletic Performance. *Ann Intern Med.* 2008; 148:747-758.
  16. Nassar E, Mulligan C, Taylor L, et al. Effects of a single dose of N-Acetyl-5-methoxytryptamine (Melatonin) and resistance exercise on the growth hormone/IGF-1 axis in young males and females. *J Int Soc Sport Nutr.* 2007; 4:1-13.
  17. Sartin JL, Kemppainen RJ, Coleman ES et al. Cortisol inhibition of growth hormone-releasing hormone stimulated growth hormone release from cultured sheep pituitary cells. *J Endocrinol.* 1994; 141:517- 525.
  18. Sattler FR. Growth hormone in the aging male. *Best Pract Res Clin Endocrinol Metab.* 2013; 27:541-555.
  19. Takahashi Y, Kipnis DM, Daughaday WH. Growth Hormone Secretion during sleep. *J Clin Invest.* 1968; 47:2079-2090.