

Testosterone Boosting: The Science Behind Blue Star Nutraceuticals Status™

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Testosterone is an anabolic and androgenic hormone that regulates muscle protein metabolism, bone metabolism and plasma lipids in addition to other physiological processes such as sexual and cognitive functions. The anabolic aspect of testosterone stimulates protein synthesis and consists of tissue building and generating a high muscle–mass to fat-mass ratio. The androgenic aspect of testosterone, on the other hand, is responsible for producing masculine characteristics.

On a daily basis, the average healthy young male naturally produces 7mg of testosterone from the testes in order to maintain normal testosterone levels above 300ng/dL. Testosterone is released from the testes, into the blood stream and circulates for 30 minutes to two hours. In that time, testosterone is either transferred to the target tissues, or is inactivated and excreted by the kidneys. Testosterone exerts its effects by travelling to the desired tissue, passing through the cell membrane and activating an androgen receptor (AR) in the cytosol. Together, the testosterone-AR complex then travels inside the cell's nucleus and binds to a nuclear receptor to stimulate RNA transcription, leading to increased cellular protein synthesis.

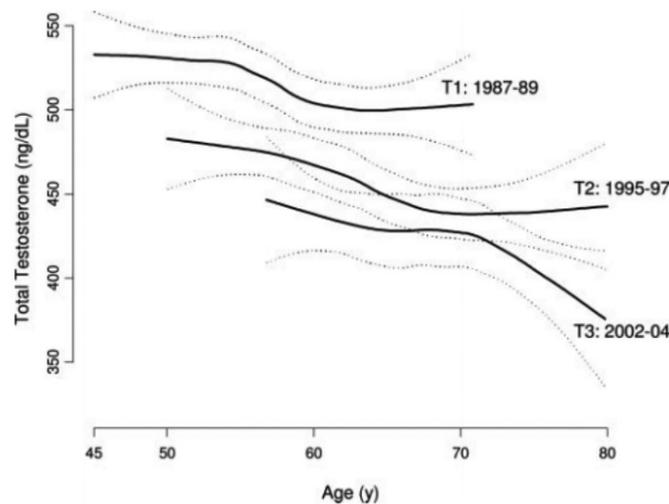


Figure 1. The decline of testosterone production by generation independent of age.

In men, testosterone levels peak in the 3rd decade of life then gradually and progressively decline at a rate of approximately 1% per year after the age of 30. Even worse, recent research data from the Massachusetts Male Aging Study involving 1709 participants, indicated that male serum testosterone levels appear to vary by generation, even after age is taken into account. Their data showed that in 1988, men had higher

serum testosterone concentrations than men of the same age in 1996, which was also higher than comparable men in 2003. This suggests that age is not the only factor contributing to testosterone loss, but our lifestyle changes over the decades are likely involved as well and today's generation is not looking good.

A decline in testosterone is linked to insulin desensitization, fat gain, obesity and an increased risk of cardiovascular disease. It also affects energy production and utilization, resulting in storage of lipids, the formation of new fat cells (a process called adipogenesis), and altering mitochondrial function. Clinical research shows that restoring healthy testosterone levels improves insulin sensitivity, lipid oxidation and reduction in fat mass with concomitant gain in fat-free mass. One of the major hallmarks of testosterone is inhibiting adipogenesis, and increasing lipid oxidation. Thus, with low levels of testosterone, being able to keep off unwanted body fat is very difficult, if not impossible.

WHY YOU SHOULDN'T TAKE PRO-HORMONES TO BOOST TESTOSTERONE:

Testosterone pro-hormones (or precursors) are peptides that are required for testosterone biosynthesis. It is a very easy assumption that supplementing with pro-hormones would improve testosterone levels and many supplements are marketed specifically to convey this message. However, an increase in pro-hormone concentration does not actually promote the conversion to testosterone nor affect testosterone concentration in any male who is not hypogonadal. The enzymes involved in this conversion are controlled by plasma testosterone concentrations, therefore, unless you have been clinically diagnosed with excessively low testosterone, these products may not have any beneficial effect at all. In fact, the excess pro-hormone may actually skip being converted to testosterone and instead be converted, through a process termed aromatization, to an estrogen called estradiol, thus having the opposing effects than desired.

STATUS™ MANIPULATES YOUR OWN NATURAL TESTOSTERONE PRODUCTION

Status™ is not a steroid and does not contain any actual testosterone. Therefore, there is no reason to worry about drug testing. Using Status™ simply takes advantage of

your own physiology to manipulate your natural testosterone production, accumulation and disposal in order to maximize the therapeutic benefits. The new and improved Status™ formula uses a unique FIVE-pronged approach to make sure you get the maximal benefit of your testosterone.

1. Micronutrient Support

Virtually all cells require zinc, but muscle and bone require the highest concentrations to optimize function and won't give it up if your diet lacks zinc. Zinc deficiency has been shown to reduce circulating luteinizing hormone (LH) and testosterone concentrations.

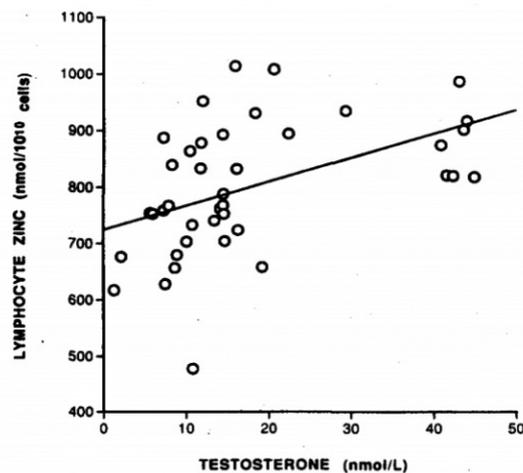


Figure 2. The direct correlation between zinc levels and testosterone production.

Zinc affects testosterone levels in many ways, as deficiency is associated with elevated estrogen receptors, a reduction in androgen receptors and higher aromatization of testosterone.

Independent evidence indicates that magnesium can up-regulate testosterone secretion through an unknown mechanism. It has been argued that magnesium, by decreasing oxidative stress may possibly be a contributing factor that up-regulates testosterone secretion.

68% of diets have less than two-thirds of the recommended daily allowance (RDA) for zinc and 39% contain less than two-thirds of the RDA for magnesium. Furthermore, zinc losses may be exacerbated through exercise, both long duration and high intensity, and sweating. Supplementing with these minerals will effectively reverse

these effects. Vitamin B6 has been shown to increase the bioavailability of zinc and magnesium making the trio an ultimate combination.

The tried and true combination of zinc, magnesium and vitamin B6 at the specific doses of 30, 450, and 10.5mg respectively has been shown to improve micronutrient status and result in a 32% increase in total testosterone, a 33% increase in free testosterone, a 3.6% increase in IGF-1 and a reduction in cortisol. It is for this reason, the formulation of Status™ starts with this well-established combination of micronutrients.

2. Hypothalamic Hormonal Control

Testosterone biosynthesis is a long elaborate process that is tightly regulated by the Hypothalamus-Pituitary-testicular (HPT) axis. The hypothalamus is the master regulator of hormonal production and controls the amount of testosterone your body produces.

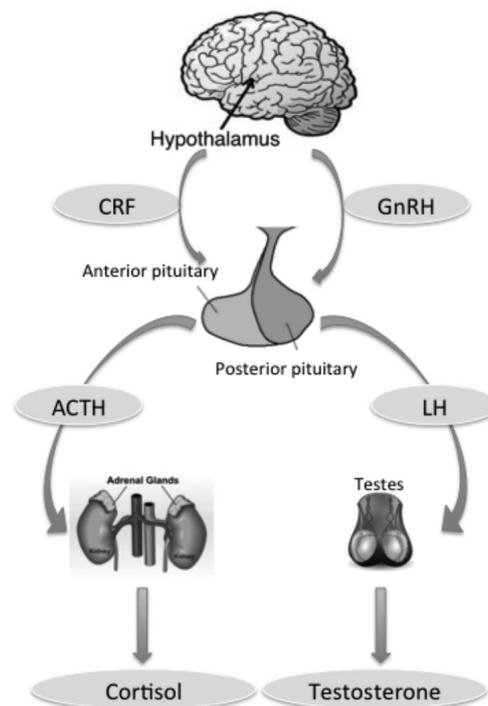


Figure 3. The production of cortisol and testosterone are both regulated initially by the hypothalamus. CRF: corticotropin releasing factor, ACTH: adrenocorticotropic hormone, GnRH: gonadotropin releasing hormone, LH: luteinizing hormone.

Cortisol production is also controlled by the hypothalamus and indeed plays

a role in inhibiting testosterone production at multiple sites of the HPT axis. In fact, the biology behind those with low testosterone occurs from a recognizable dysfunction of the HPT axis. Thus, the primary mechanism in Status™ to boost testosterone production is by affecting the influence cortisol has on testosterone production.

KSM-66® is a root extract of a natural Indian herb called Ashwagandha that has been long touted to treat low testosterone levels by directly affecting the hypothalamus, pituitary and testes. Cortisol is known to negatively affect the production of testosterone directly at the testes and via inhibiting the production of gonadotropin releasing hormone (GnRH) and LH. By relieving this inhibitory influence on testosterone synthesis, KSM-66® has been well documented to improve the overall concentration of testosterone.

To take it one step further, KSM-66® was tested against the greatest known endogenous testosterone booster: heavy resistance exercise. Weight training is well-known to significantly increase testosterone levels. Recent data published in the Journal of the International Society of Sports Nutrition showed definitive evidence that Ashwagandha root extract (KSM-66®) when combined with weight training in young healthy men can induce a 434% greater increase in testosterone levels compared to weight training alone. Furthermore, this boost in testosterone was accompanied by a 74% greater increase in bench press strength, a 67% greater increase in arm muscle size, and 127% greater decrease in body fat percentage after 8 weeks of resistance training. This substantial data is how KSM66® earned its place in the Status™ formulation.

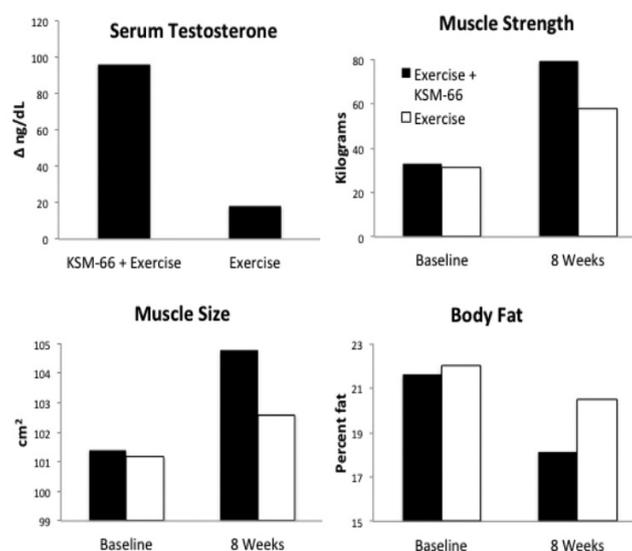


Figure 4. KSM Clinical data: Daily ingestion of 600mg of KSM-66® coupled with 8 weeks of resistance exercise training.

3. Reductase and Aromatase Inhibition

As mentioned earlier, testosterone does more than just build muscle and burn fat. In addition to the testosterone's direct effects, it is also a precursor for two other less desirable molecules namely dihydrotestosterone (DHT) and estradiol. The conversion of testosterone to either DHT or estradiol is undesirable and should be considered in the formulation of a testosterone booster. DHT is the product of testosterone undergoing a process called 5 α -reduction via the enzyme 5 α -reductase. DHT can activate the AR, although its effects are less anabolic and more androgenic once activated. Estradiol, on the other hand, is a type of estrogen that is produced from the aromatization of testosterone, via the aromatase enzyme. Estrogens are steroids that have feminizing effects upon binding of the estrogen receptor, along with being an inhibitor of GnRH to lower testosterone production.

The formulation of Status™ takes this into consideration with the inclusion of Testosurge®. As an extract of fenugreek, it has been clinically tested to be both a 5 α -reductase and aromatase inhibitor. This has two distinct functions. By slowing these two reactions, your natural production of testosterone is allowed to accumulate in your system to increased levels compared to the average man. Secondly, the reduced estradiol concentration actually relieves its inhibition of GnRH production, resulting in more testosterone production in the process. Supplementation with Testosurge® has demonstrated reductions in body fat without a reduction in muscle strength.

4. Estrogen Blocking

Just because we can reduce the aromatization of testosterone to estrogen doesn't mean you should ignore your estrogen levels. Even if you slow down the testosterone conversion, estrogen will still be present to exert some negative effects. You may have heard that cruciferous vegetables such as broccoli and cabbages are effective at reducing the effects of estrogen. Cruciferous vegetables contain a glucosinolate called Glucobrassicin. Once broken down it releases a compound called indole-3-carbinol. The digestion of indole-3-carbinol yields a compound called 3,3'-diindolylmethane, otherwise known simply as DIM.

DIM is the key constituent that can reduce the effect of estrogens with a two-in-one mechanism. DIM has been shown in human clinical trials to enhance the conversion of the estrogen subtype, estrone, into 2-hydroxyestrone. This serves a

dual purpose because estrone activates the estrogen receptor and 2-hydroxyestrone antagonizes the estrogen receptor. Therefore, DIM effectively reduces the total estrogen content while at the same time blocks estrogen receptors from responding to other estrogens. Status™ harnesses this estrogen blocking effect by skipping the vegetables and directly incorporating DIM into its formula.

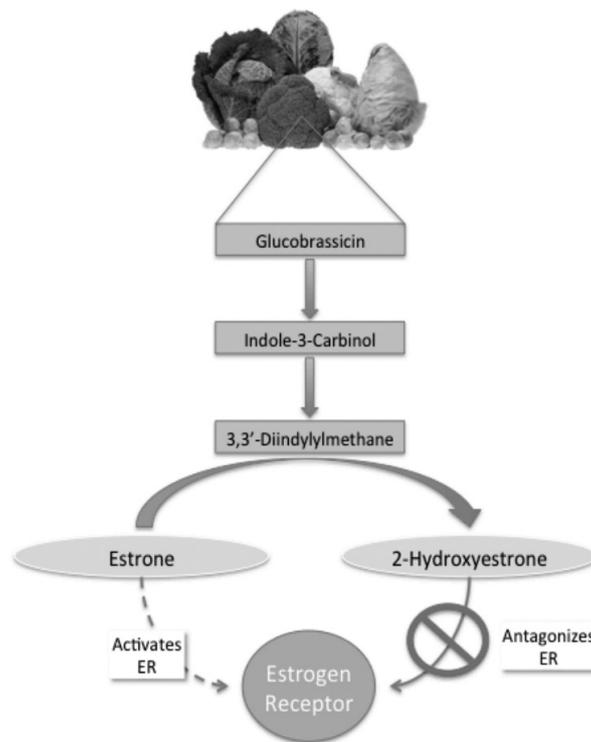


Figure 5. 3,3'-Diindolylmethane (DIM) is derived from cruciferous vegetables and enhance the conversion of active estrone to inactive 2-hydroxyestrone to decrease estrogen receptor activation and also block further estrogen receptor agonists.

5. SHBG Inhibition

98% of testosterone is protein-bound to either albumin or sex hormone-binding globulin (SHBG). This large portion of bound testosterone is biologically inactive and unable to have any desired effects. While only 2% of your testosterone is biologically active at any point of time, this is an important advantage your body uses to quickly manipulate testosterone activity via changing SHBG concentrations instead of using the cumbersome biosynthesis pathway. Theoretically speaking, this means your body naturally produces, and has access to 50X the amount of testosterone that your

body ever uses as any given time. Unlocking even a small fraction of this potential can make dramatic improvements in the bioactivity of your natural testosterone. *Eurycoma longifolia* has been shown to significantly increase the concentration of free testosterone due to its tendency to reduce SHBG. Status™ incorporates *Eurycoma longifolia* in order to complete the full gamut in augmenting the effects of testosterone.

THE BLUE STAR PROPRIETARY DELIVERY SYSTEM

There is a growing consensus among nutritionists that the obstacle to better nutrition clearly lays in the efficient delivery of nutrients to the body. The core ingredients in Blue Star Nutraceuticals XD Delivery Technology Complex™ are proven to increase the bioavailability of nutritional compounds through increased gastric and intestinal transit time and increased absorption.

CONCLUSION

Through harnessing the maximal potential in promoting testosterone production, freeing up bound testosterone, optimizing testosterone accumulation through diminishing its elimination, and reducing any estrogenic properties, Status™ truly possesses the ultimate combination of ingredients to maximize natural testosterone production.

REFERENCES

1. Ananda, S., et al. Zinc Status and Serum Testosterone Levels of healthy Adults. *Applied Nutritional Investigation* 12(5): 344-348, 1996.
2. Brilla, L.R., et al. Effects of a Novel Zinc-Magnesium Formulation on Hormones and Strength. *Journal of Exercise Physiology* 3(4): 26- 36, 2000.
3. Chandrasekhar, K., et al. A Prospective, Randomized Double-Blind, Placebo-Controlled Study of Safety and Efficacy of a High Concentration Full-Spectrum Extract of Ashwagandha Root in Reducing Stress and Anxiety and Adults. *Indian Journal of Psychological Medicine* 34(3): 255-262, 2012.
4. Henkel, R.R., et al. Tongkat Ali as a Potential Herbal Supplement for Physically Active Male and Female Seniors – A Pilot Study. *Phytotherapy Research* 28: 544-550, 2014.
5. Mokashi, M., et al. Effects of glycosides based fenugreek seed extract on serum testosterone levels of healthy sedentary male subjects: An exploratory double blind placebo controlled, crossover study. *Asian Journal of Pharmaceutical and Clinical Research* 7(2): 177-181, 2014.
6. Poole, C., et al. The effects of a commercially available botanical supplement on strength, body composition, power output, and hormonal profiles in resistance-trained males. *Journal of the International Society of Sports Nutrition* 7(34): 1-9, 2010.
7. Traish, A.M. Testosterone and weight loss: the evidence. *Obesity and Nutrition* 21(5): 313-322, 2014.
8. Travison, T.G., et al. A population-level decline in serum testosterone levels in American men. *The Journal of Clinical Endocrinology & Metabolism* 92(1): 196-202, 2007.
9. Travison, T.G., et al. The Relative Contributions of Aging, Health and Lifestyle Factors to Serum Testosterone Decline in Men. *The Journal of Clinical Endocrinology & Metabolism* 92(2): 549-555, 2007.
10. Wankhede, S., et al. Examining the effect of *Withania somnifera* supplementation on muscle strength and recovery: a randomized controlled trial. *Journal of the International Society of Sports Nutrition* 12(43): 1-11, 2015
11. Wankhede, S., et al. Beneficial effects of fenugreek glycoside supplementation in

male subjects during resistance training: A randomized controlled pilot study.
Journal of Sport and Health Science 5(2): 1240-1243, 2016.

12. Wilborn, C., et al. Effects of a Purported Aromatase and 5 α Reductase Inhibitor on Hormone Profiles in College-Age Men. International Journal of Sport Nutrition and Exercise Metabolism 20(6): 457-465, 2010.