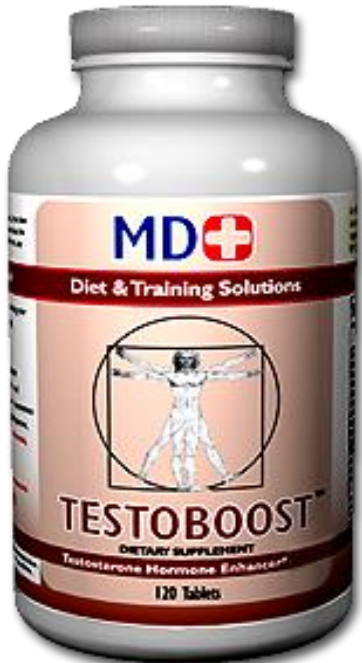


# MD+ TestoBoost version VI

## Natural Testosterone and Sex Drive Booster



TestoBoost is a safe and effective way to significantly increase your own natural testosterone production.

TestoBoost is by far the most powerful natural testosterone booster, and libido and sex drive enhancer on the market today. Version VI is the fifth reformulation of the original TestoBoost, which came out in February of 2000. Each version has been improved by considering new research, my own clinical work, and feedback from those who use it.

<https://metabolicdiet.com/product/testoboost/> – TestoBoost information updated May 11, 2019.

All my nutritional supplement products are at <https://metabolicdiet.com/shop/>

**TestoBoost is manufactured by [GMP Laboratories](#).**

**TestoBoost Version VI contains a unique formulation that will:**

- Optimize both free and total testosterone, increases androgen receptors in skeletal muscle, brain, and other organs and tissues, and stimulates more effective binding with the androgen receptor
- Provide a potent anabolic effect to improve body composition, muscle mass, strength, and physical and mental performance
- Increase libido, sex drive, performance, and fertility in both men and women
- Block excessive estrogen production
- Block excessive production of dihydrotestosterone
- Increase health, energy and well-being
- Enhance prostate health
- Increase bone density
- Improve cognitive function and decrease mental and physical decline

The information below on the new TestoBoost version VI is in near final draft form and will be expanded and revised over the next few months. For now, this latest information will give you the flavor of just what TestoBoost will do for you in helping you achieve your health, body composition and performance goals.

## The TestoBoost Controversy

Before I go into more detail about the beneficial effects of TestoBoost on optimizing testosterone levels and doing much more to improve body composition, mental and physical performance, and health, there's a matter that's been festering around TestoBoost for more than a decade.

And it's still going on as WADA tries to prove allegations about Salazar and his medal winning IOC athletes Galen Rupp and Mo Farah. You can read about it at [https://metabolicdiet.com/wp-content/uploads/2017/product\\_pdf/TestoBoost\\_Salazar.jpg](https://metabolicdiet.com/wp-content/uploads/2017/product_pdf/TestoBoost_Salazar.jpg). As an aside Salazar's athletes used my line of nutritional supplements for many years.

What I find ridiculous in this article is the statement by Dr. Rabin, referred to as the most-eminent expert in anti-doping, which he's not. I started writing and being involved on all issues concerning drug use in sports before the 1976 Olympics in Montreal, Canada and was writing articles and books and initiating drug testing programs in various sports before he was out of high school.

I was also a certified Medical Review Officer for several years (<https://www.mrocc.org/>) and even gave the presentation on ergogenic aids at my last certification.

Dr. Rabin states that my approach with TestoBoost, optimizing testosterone levels by negating any negative factors that are lowering both total and free testosterone in the body, and optimizing natural testosterone levels in both men and women is the **“wrong approach.”**

He goes on to state **“At WADA we say if you supplement these hormones, in particular testosterone, to bring it back to a level when you were 20 years old, this is cheating, because you are boosting your testosterone level and your muscles benefit from this boosting.”**

What he's saying is beyond ridiculous if we take him at his word. Just how far can you go before the banned list becomes more of a farce than it already is?

Are they now going to standardize how much protein you're allowed to use to increase performance because of the same reasoning? How about advanced training techniques under knowledgeable coaches since other athletes don't have the resources to use them because of location and/or cost?

How about banning nitrate containing foods such as beets, spinach, and celery, or even extracts of these foods as nutritional supplements as they've been shown to enhance exercise performance? And what about banning some of the many dietary and lifestyle methods that can be used by aging athletes to offset some of the adverse effects of aging and thus optimizing their performance?

The use of TestoBoost is 100% legal under WADA/IOC guidelines. TestoBoost optimizes natural endogenous testosterone correcting anything, including pollution, stress, a lifestyle that may not be optimal, and tendencies towards recovery problems and injuries. It does not contain testosterone or

any banned substance, and instead allows your body to reach its natural potential for endogenous testosterone production.

I formulate my nutritional supplements, all of which are manufactured at [\*\*GMP Laboratories\*\*](#), a pharmaceutical grade laboratory that has all the necessary quality control and certifications to produce products of the highest quality and purity.

My products are assured to produce the desired effects that allows any athlete or anyone who exercises, or even wants to optimize health, and/or body composition and/or physical and mental performance, to be the best that they can be by dealing with any personal and even genetic issues that may get in the way of their goals.

I consider my supplements as distinct and unlike the other nutritional supplements on the market today. My supplements can be considered as targeted super foods since each product in my supplement lineup contains several dozen evidence-based ingredients picked by me to work synergistically and additively, including many extracts that contain many ingredients on their own, to achieve specific results.

As far as positive doping violations, no drug tested athlete using TestoBoost, or any of my nutritional supplements, has never had a positive drug test and no athlete ever will.

There are several ways that I make sure that all my products, including TestoBoost version VI, are safe for drug tested athletes. The first is that I had TestoBoost manufactured at GMP Laboratories. Each ingredient and the final product are tested to make sure they were safe to use, have in them the intended ingredients and contain no contaminants that would result in a positive drug test for drug tested athletes.

As well, I have the final product taken at a higher dose than recommended, for example 4 tabs of TestoBoost twice a day (8 tabs in all) for several days and then have their urine and blood tested in a laboratory using WADA/IOC standards of detection to make sure that they're safe for drug tested athletes. The results for TestoBoost version VI show that it's 100% safe for drug tested athletes.

As an aside I discovered from an acquaintance at WADA that TestoBoost, along with GHboost and the rest of my MD+ nutritional supplement products, have been tested by WADA/IOC in the past few years and their testing found no banned substances thus adding to the fact that all my supplements are completely safe to use for drug tested athletes.

## **TestoBoost Imposters**

My TestoBoost has been so successful and used over the last two decades by just about anyone who is interested in its beneficial health, anabolic, body composition, and physical and mental performance that imposters by the dozens have tried to usurp its mantle of success, primarily as a testosterone booster.

These feeble and useless imposters use names that are almost identical to TestoBoost (for example making the B in lower case, putting the name all in capital letters, putting a space between Testo and Boost), or simply marketing their ineffective products as testosterone boosters.

Unlike myself they aggressively market these products in many ways including phony before and after pictures, hyped up but false information, trumped up testimonials, and other devious ways to make their product look effective. For more info on how some supplement companies try to deceive have a look at my article [Lies, Lies, and Damn Lies](#).

Research to those pushing these imposters is merely a tool to be misused by tainting the results to suit their products. For more info have a look at an article I wrote several years ago on [testosterone boosters](#).

## **Just What Does TestoBoost Do?**

TestoBoost (the new version VI just out in 2018 - see Nutritional Panel below) does just what its name suggests, it boosts testosterone levels in both men and women. But it doesn't increase testosterone levels by providing hormones or prohormones, it increases testosterone by natural mechanisms.

TestoBoost works in many ways. One is by directly stimulating testosterone production to optimal levels. It does this by stimulating the endogenous production of testosterone via optimizing the hypothalamic-pituitary-gonadal axis (the hypothalamic-pituitary-testicular axis [HPTA] in men), the natural testosterone making machinery in both men and women.

TestoBoost does this by optimizing the release of gonadotropin releasing hormone and luteinizing hormone (LH), with the latter released by the pituitary to stimulate testosterone production by the gonads, testicles in men and ovaries in women. It also manipulates the feedback mechanisms that dictates when to increase or decrease testosterone production so that the direction of the HPTA encourages the increased production (the downward arrows in the illustration below) and discourages the feedback mechanisms (the upward arrows) that would decrease testosterone production.

Indirectly TestoBoost counters the testosterone lowering effects of internal (lifestyle, diet choices, and expected and unexpected stress) and environmental stressors including endocrine disrupting chemicals and indoor and outdoor air pollution. For example, studies have shown that resveratrol, and the B vitamins in TestoBoost, can counteract some of the detrimental effects of environmental pollution especially first, second, and third hand cigarette smoke and air pollution.<sup>12</sup>

TestoBoost also increases the peripheral production of testosterone. However, this machinery is more important in women than men since ovarian production of testosterone is low and as such

peripheral testosterone production can be important, while in healthy men testicular production of testosterone can be said to account for essentially all their testosterone production.

But in many cases, it's not enough to simply optimize testosterone levels, it's also important that there is an efficient and productive binding of testosterone to the androgen receptor in order to get the maximum anabolic effect from the increased testosterone. Androgen receptor number and affinity for binding with testosterone are increased with the use of TestoBoost.

The second way that TestoBoost increases testosterone levels is by counteracting some of the negative influences in our lifestyle, diets and environment that are counter-productive for both the production of testosterone and the binding of testosterone to the androgen receptor – see below.

But TestoBoost is not a hormone and doesn't increase testosterone levels right away. Like almost all effective nutritional supplements, TestoBoost works by optimizing the internal environment so that your body ramps up testosterone more slowly. You usually won't see the full results until you've been diligently taking it for a few weeks and in some cases even more (although there are some exceptions with results felt within a few days). As well, as your body is influenced by the use of TestoBoost, you will also see beneficial effects on your health and well-being.

TestoBoost is useful for anyone who wants to naturally increase their testosterone levels in order to increase muscle mass and strength and boost sex drive. It's also useful for those who have lower than normal endogenous testosterone levels whether due to age, overtraining, stress, sickness, or even while on or after the use of anabolic steroids and prohormones.

Another plus with the use of TestoBoost rather than the use of exogenous testosterone and other exogenous hormones and drugs, is that there is no need for other medications such as finasteride, tamoxifen or various aromatase inhibitors to handle adverse effects from increased dihydrotestosterone and estrogen as safety valves for both are included in the TestoBoost formulation.

As well, the use of exogenous testosterone and other hormones and drugs causes the HPTA axis to shut down and atrophy making it difficult to reboot the axis if the exogenous substances are stopped. For example, athletes who use exogenous testosterone and/or anabolic steroids/SARMS and then want to stop using them, have a difficult time rebooting the HPTA and in some cases need testosterone replacement therapy as their endogenous testosterone production never comes back.

I wrote a book three decades ago outlining the cause and possible cures for the management of adverse effects on the HPTA, including adverse effects on endogenous testosterone production and infertility, of stopping the use of anabolic androgenic steroids.<sup>3</sup> It took a few decades before the full impact of what I wrote back then finally took hold, as seen in some recent studies and papers.<sup>456789</sup>

## Nutrition Panel for TestoBoost version VI

### Supplement Facts: Serving Size: 4 Tablets Servings Per Container: 30

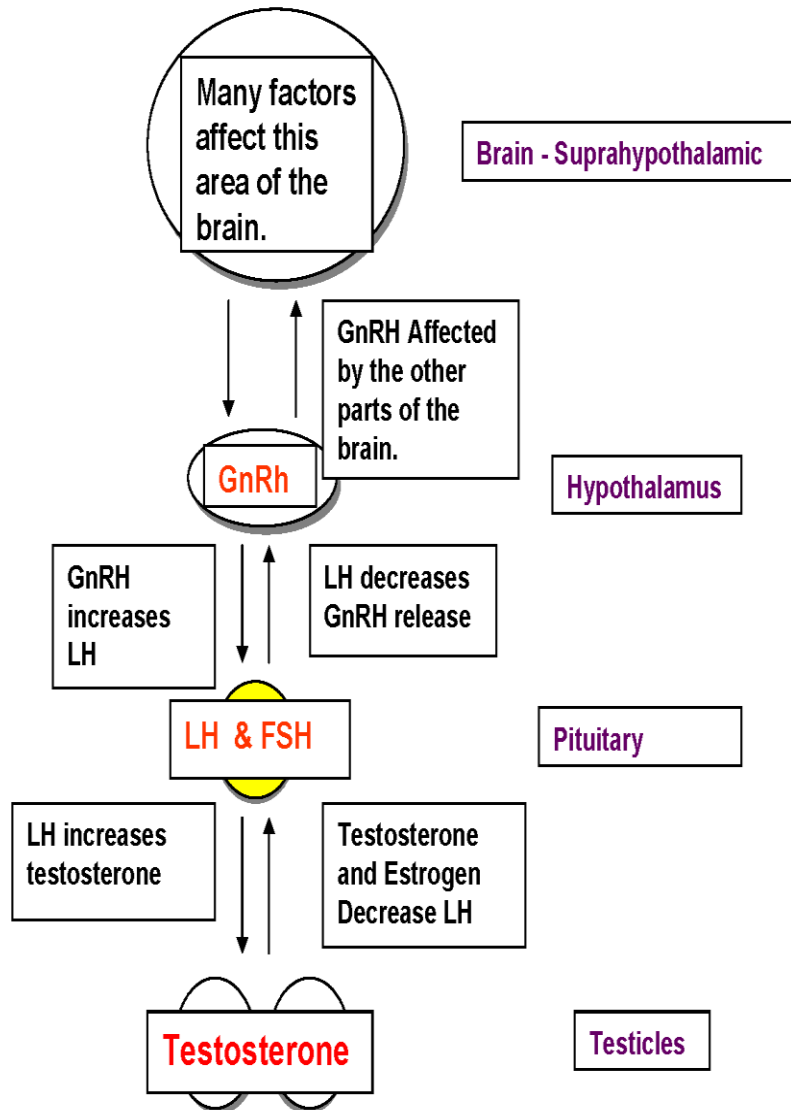
	Amount Per Serving	% Daily Value		Amount Per Serving	% Daily Value
Vitamin A (as 71% Beta Carotene and 29% Palmitate)	7000 IU	140%	Tribulus Terrestris extract (fruit) Saponins 200 mg	500 mg	*
Vitamin C (as Ascorbic Acid and Potassium Ascorbate)	200 mg	333%	Acetyl L-Carnitine HCL	300 mg	*
Vitamin D (as Cholecalciferol)	400 IU	100%	Nettle Extract (leaf)	250 mg	*
Vitamin E (as d-alpha tocopheryl succinate)	200 IU	667%	Alpha Lipoic Acid	150 mg	*
Niacin	10 mg	50%	Lycopene	10 mg	*
Vitamin B6 (as Pyridoxine HCL & Pyridoxal-5-Phosphate)	25 mg	1250%	Astaxanthin	5 mg	*
Vitamin B12 (as Methylcobalamin)	200 mcg	3333%	<b>TestoBoost Proprietary Complex: 6390 mg*</b>		
Folate	200 mcg	50%	D-Aspartate, Citrulline Malate, Catuaba (bark), Muira Puama (bark), Saw Palmetto (berry), Suma (root) Calcium D-Glucarate, Chrysin, Phosphatidylserine, Indole-3-Carbinol, Cordyceps Sinensis, Trans Resveratrol, Processed Shilajit, Epimedium Grandiflorum, Ganoderma Lucidum, Damiana (leaf), Ipriflavone, Maca (root), Eurycoma Longifolia extract (root), Prickly Pear extract (leaf), 5-Methyl Methoxy Isoflavone, Coleus Forskohlii extract (root), Schisandra (berry), Phosphorus, Quercetin Dihydrate, L-Arginine Alpha Ketoglutarate, Ginkgo Biloba extract, Grape Seed extract, Passionflower (herb), Ginger extract (root), GLA (Gamma-linolenic acid from Borage Seed Oil Powder), Chasteberry extract ( <i>Vitis agnus castus</i> ) (fruit), Oat Straw (aerial parts), Genistein.		
Calcium (as Calcium Phosphate)	400 mg	40%			
Magnesium (as Magnesium Aspartate)	300 mg	75%			
Zinc (as Zinc Monomethionine from Optizinc®)	15 mg	100%			
Manganese (as Manganese Chelate)	2 mg	100%			
Boron (as citrate)	3 mg	*			
Bioperine® ( <i>Piper nigrum</i> ) (fruit)	5 mg	*			
Coenzyme Q10	20 mg	*			

**Other Ingredients: Cellulose, Croscarmellose Sodium, Hypromellose, Hydroxypropyl Cellulose.**

**\*Daily Value not established**

# The Hypothalamic-Pituitary-Testicular Axis (HPTA)

(copyright Mauro Di Pasquale, M.D.)



The above illustration is of the HPTA in men. In women the Testicles would be substituted by the ovaries and the acronym would be the HPTO. If we generalized the axis to include both men and women, it would be the hypothalamic-pituitary-gonadal axis or the HPTG.

## The Assault on Testosterone

In the past several years there has been an exponential rise in the awareness of the importance of testosterone for men's general and sexual health and well-being. Along with this increased awareness is an increased interest in ways to restore testosterone levels either naturally or through testosterone replacement therapy. As well, although not as publicized, there has also been an increased awareness of the effects of low testosterone on women's general and sexual health and well-being.<sup>10111213</sup>

And there are good reasons for all this increased concern since low serum testosterone can result in a myriad of symptoms including low libido, erectile and orgasmic dysfunction, increases in visceral fat, decreased muscle mass and bone mineral density, fatigue, depression, irritability, cognitive decline, and sleep disturbances, all of which can dramatically reduce wellbeing and quality of life.<sup>1415161718192021222324</sup>

As we age, and in both men and women, testosterone levels decline.<sup>25262728</sup> The reason for the decline include decreasing sensitivity to pituitary luteinizing hormone, decreases in the transporters of precursors such as cholesterol, and decreases in the steroidogenic enzymes of the mitochondria and smooth endoplasmic reticulum. Most of the changes that result in decreasing production of testosterone are thought to be due to oxidative damage that accumulates with time.

However, there's more to the story. For example, marriage and fatherhood result in declining testosterone levels in men although the reasons why are obscure.<sup>2930</sup>

In middle aged men free testosterone levels drop by up to a few percentage points each year after the age of 30 to 35 and even more in elderly men. The usual 1% drop in total testosterone translates into more of a drop in the free testosterone due to an increase serum hormone binding globulin (SHBG), that basically inactivates some of the free testosterone. That drop alone is enough to negatively affect our body composition and physical performance as we age.

But there's more than age involved as far as declining testosterone levels and that's one of the reasons for the increase in concern among men. Epidemiological studies have shown that both fertility and testosterone levels have declined in men compared to what they were even 20 years ago.<sup>3132333435</sup>

The reasons for this increased decline in testosterone levels may be due to a variety of factors including:<sup>36373839404142434445464748495051525354555657585960616263646566676869707172737475767778</sup>

- Life style factors such as an increase in stress levels and sleep deprivation.
- Increase in obesity, truncal obesity, and waist circumference.
- Our changing diets that are more and more dependent on processed foods.
- Decreased levels of vitamin D (see under vitamin D below).
- An increased exposure to environmental toxins and endocrine disruptors both through direct contact, and in our food, water and air.
- An increase in the use of medications, such as statins, narcotics, tranquilizers, antidepressants, some blood pressure medications and many others.
- An increase in the use of illicit drugs including anabolic-androgenic steroids (which depress the HPTA axis and endogenous testosterone production during and after use)<sup>79</sup>, marijuana, opioid narcotics, cocaine, and methamphetamines.



- And last, but becoming more important in today's society, is the ever evolving male to female dynamics where men have to adjust to a more feminized world and partake in co-parenting, involved and attending births, sharing household chores, marriage, spending more time with female influences, loss of protective roles, making equal pay, etc.

Pollution, endocrine disruptors, and societal increased stress may be the major reasons for the drop in testosterone in all men, regardless of age and in women as well.<sup>8081</sup> At present, we're surrounded by man-made endocrine disruptors that can push testosterone levels to low normal and even below normal levels, leaving men feeling less than a man both physically and functionally and women with lowered libido and increasing sexual dysfunction.

There are many pollutants and contaminants in our environment that act as endocrine disruptors, mainly from their toxicity and/or hormonal effects. These endocrine disruptors, which affect testosterone levels, semen quality, our health and feelings of well-being, are all around us including in our homes, in items we use every day in our food, water and air. Even pollutants that aren't the norm, such as noise pollution, besides having adverse cardiovascular effects and increasing the risk of type 2 diabetes, can lead to endocrine disruption especially decreased testosterone.<sup>82</sup>

It's impossible to list them all but examples are pesticides, herbicides, synthetic fertilizers, parabens (in creams, lotions, sunscreens, shampoo, toothpaste), plastics that cover our food, and line cans used for both food and drink. They include dioxins, atrazine, phthalates, fire retardants, lead, mercury, non-stick cookware, organophosphates, glycol ethers, sprays and chemicals used to control pests, insects, and weeds, polycarbonate plastic, epoxy resins made from BPA, metals such as mercury, cadmium, and molybdenum, plant based phytoestrogens and fungi based mycoestrogens.<sup>83</sup>

The plant-based phytoestrogens include the lignans and the natural phenolic compounds with the most common being the coumestans, prenylflavonoids and isoflavones (commonly found in soy and red clover).

**For my recent article on pollution (May 7, 2019) go to [Pollution as Devolution](#).**

Many of these endocrine disruptors affect us by increasing estrogen exposure and subsequently lowering testosterone, decreasing libido, and increasing sexual performance, including erectile dysfunction. Others affect the androgen receptor and decrease the binding of testosterone to the androgen receptor thus decreasing the beneficial effects of testosterone.

These endocrine disruptors work at many levels of the testosterone making machinery of our bodies, all the way from our brains, pituitary, adrenals and gonads, and many also affect binding to the androgen receptor. In men, they can have cumulative effects on the functioning of one or more levels of the hypothalamic-pituitary-testicular axis (HPTA) and the effects of testosterone.<sup>8485</sup> The result is a decrease in testosterone levels and activity, and increasing estrogenic effects since many of the chemicals are endocrine disruptors which mimic estrogen (xenoestrogens and phytoestrogens).

It's also been shown that many medications, especially the statins used extensively to decrease cholesterol levels, that decrease testicular function and testosterone either by directly affecting Leydig cells in the testes or by inhibiting the hypothalamic-pituitary-testicular axis (HPTA).<sup>8687</sup>

TestoBoost counters these and many other disrupting influences that keep your body from having your own natural optimal level of testosterone. As well, on top of countering negative epigenetic changes induced by our exposure to stress, drugs, pollutants, and estrogenic endocrine disruptors, it

enhances positive epigenetic changes that allow our bodies to maximize our endogenous testosterone levels and effects, libido and sexual functioning at any age.

## **Who Uses TestoBoost?**

TestoBoost is used by both men and women who want to optimize their testosterone levels. Many users have lower testosterone levels and prefer boosting their own testosterone production rather than using the various forms of exogenous testosterone (injections, pellets, gels, patches, sprays, etc.), all of which can carry significant adverse effects.

TestoBoost is used by scores of drug tested athletes for two main reasons. Unlike the use of testosterone and anabolic steroids, TestoBoost doesn't shut down the Hypothalamic/Pituitary/Testicular axis (HPTA) and in fact enhances it. As such, there are no side effects involved with the use of TestoBoost and none when TestoBoost is discontinued.

TestoBoost, unlike the use of exogenous testosterone and anabolic steroids, also boosts the endogenous precursors all the way from cholesterol to testosterone, including epitestosterone – all in a natural way with no changes in the ratio of metabolites or the process, including not increasing any metabolite above the normal range. What it does is ramp up testosterone production up to optimum levels for the individual and not to pharmacological levels.

TestoBoost is also used by many middle aged and older men and women as hormonal replacement therapy since unlike the use of exogenous testosterone products, TestoBoost doesn't shut down the HPTA and in fact enhances it.

For drug tested athletes there are no banned substances in TestoBoost and because it ramps up natural testosterone production and never causes a positive drug test, unlike exogenous testosterone, anabolic steroids, prohormones, and selective androgen receptor modulators (SERMS). TestoBoost boosts the endogenous precursors in between cholesterol to testosterone, including DHEA and epitestosterone – all in a natural way with no changes in the ratio of metabolites or the process, including not increasing any metabolite ratio or level above the normal range.

What TestoBoost does is to optimize the natural endogenous production of testosterone using all the natural pathways that lead to increased testosterone production. As such, this is the reason why the use of TestoBoost by athletes 100% won't and can't cause a positive drug test.

## **History of TestoBoost**

The idea of and my original formulation for TestoBoost was decades ago. The first version of TestoBoost laid down the base for what I wanted to achieve for TestoBoost, a natural supplement that optimizes testosterone levels and sex drive in both men and women. The pathways that I targeted included stimulating all the relevant areas of the hypothalamic-pituitary-testicular axis (HPTA) through several independent mechanisms, and to decrease any potential side effects from increases in estrogen and dihydrotestosterone. Subsequent versions of TestoBoost, while keeping the base intact, added several ingredients that I felt would further increase testosterone levels and sex drive, and further decrease any potential side effects.

The basis of the formula in TestoBoost, and in all the MD+ formulations, is to involve all possible pathways that lead to the desired effects, and to use multiple ingredients that work together to produce superior results. In the case of TestoBoost the desired effect was an increase in basal and

elevated testosterone levels in the body, a decrease in counterproductive elevations in cortisol, dihydrotestosterone and estrogen, and a salutary effect on overall health, libido and sex drive.

All of this can be accomplished by using ingredients that are known or suspected to boost testicular steroidogenesis (the formation of steroids by the testes, especially testosterone), increase sexual desire, and increase physical and mental performance.

For example, using a variety of ingredients to effectively act as a testosterone sink by trapping testosterone production is the most effective way to increase endogenous androgen production.

In order to do this, you must consider all the possible pathways that are involved in maximizing testosterone production, including:

- Maximizing hypothalamic and suprahypothalamic mechanisms to increase luteinizing hormone (LH) production.
- Increasing the effect of LH on testosterone production.
- Increasing testicular steroidogenesis directly.
- Decreasing inhibitors of steroidogenesis.
- Providing vitamins and minerals that might be frankly or marginally deficient and thus not allowing the full production of testosterone - e.g. **magnesium, zinc, B6**.
- Increasing peripheral formation of testosterone.
- Decreasing peripheral formation of dihydrotestosterone and estrogens or blocking their effects.

As well, other compounds that have been shown to have effects on sexual desire and performance can be used in the mix. On top of this TestoBoost contains **biooperine**, which significantly enhances the bioavailability of the ingredients by increasing their absorption.

The list of ingredients that could prove useful for increasing testosterone levels is long and includes various vitamins such as **vitamin A, B6, and D**, minerals such as **zinc, magnesium, manganese, and other ingredients such as arginine, beta ecdysone boron, calcium-d-glucarate, catuaba bark, chasteberry (vitex agnus-castus), chrysin, citrulline malate, co-enzyme q10 (ubiquinone), forskohlin, damiana, 5-methyl methoxy isoflavone, eurycoma longifolia, cordyceps sinensis, genistein, GLA, prickly pear extract, indole-3-carbinol, ipriflavone, maca root, muira puama, phosphatidylserine, quercetin dihydrate, saw palmetto, schisandra chinensis, stinging nettle extract and tribulus terrestris**.

Other ingredients that have an indirect but still important effect on testosterone production includes various antioxidants such as vitamins C and E, alpha lipoic acid, grape seed extract (containing resveratrol), lycopene, and astaxanthin.

## **Why TestoBoost is Better than the Prohormones, Selective Androgen Modulators, Testosterone, and Anabolic Steroids**

### **Prohormones**

Over the last few decades prohormones and more so lately androgen receptor modulators have become more popular with athletes and those looking to enhance body composition and performance. At the same time the use of testosterone and anabolic steroids hasn't abated. All these substances were the fad for those who wanted anabolic steroid like effects at first legally available in some nutritional supplements and now illegally obtained through the Internet.

While their use is declining the use of androgen receptor modulators has steadily climbed. have been used extensively but since in the past fifteen years the big push for those who want “anabolic steroid-like” effects were the prohormones. And even though many have been taken off the over the counter market in the US and other countries, they are still available in one form or another either in North America through the black market, or internationally over the Internet. They range from androstenedione, to the more sophisticated ones that are supposed to be precursors to other anabolic steroids including nandrolone (Deca), boldenone, and even 1-testosterone compounds. The even include steroid like compounds that have various effects on either or both estrogen and testosterone.

The one exception is the legal availability of DHEA. However, while it may be useful for women, and for other purposes, it's useless for increasing endogenous testosterone levels in men. Most of the prohormones, including androstenedione, androstenediol, norandrostenediol, norandrostenedione, the boldenone and 1-testosterone precursors, and in fact any precursor prohormones are mostly ineffective at providing significant androgenic-anabolic effects, but can result in adverse effects, and will depress endogenous testosterone production.

The trend in these mostly useless and occasionally potent compounds, depending on what is used. For example, some of the prohormones are precursors to testosterone while others are weaker versions of the commercial anabolic steroids. The latter is the case with 1-testosterone and the 17-alpha methylated 1-testosterone, which in fact are weak anabolic steroids, with lower androgenic and anabolic effects than the more potent anabolic steroids that have been marketed over the years. Basically, the ones being produced now and passed off as over the counter prohormones/steroids by unscrupulous companies, mainly overseas but also in North America, are the cast offs of the steroid producing drug industry. Of course, actual anabolic steroids are also available over the Internet and widely use.

The problem with most of the prohormones available over the past few decades is that while they have minimal androgenic and anabolic effects, they have significant side effects, both known and unknown. The prohormones that are being developed today to be used as a substitute for commercial anabolic steroids haven't been investigated or studied for their potential short term or long-term side effects.

This is where the real problem with these compounds lies. We don't know what effects they have on various parts of the body including the liver, cardiovascular system, prostate, kidney, and especially on the hypothalamic-pituitary-testicular axis (HPTA). These products would never be allowed as prescription drugs because of the lack of proper animal and more importantly human trials. However, they're blatantly dumped on the market as nutritional supplements, when in fact they're drugs, or more correctly low level, and usually ineffective, anabolic steroids – with less efficacy than the commercial anabolic steroids, but with unknown, and potentially very harmful side effects.

While most of the prohormones and hormones that are available as nutritional supplements are of no use or marginally useful for body composition purposes, they can have significant side effects. One of the side effects that is most troubling is the effect they have on the hypothalamic-pituitary-testicular axis (HPTA), the pathway that's involved in endogenous testosterone production and control.

The worst-case scenario, and one that is common with the use of most of the prohormones, is that there is very little anabolic effect from the compounds themselves, but significant side effects, especially with a dampening effect on the HPTA, which in turn shuts off the production of endogenous testosterone. This HPTA shutdown also occurs with the use of exogenous testosterone and anabolic

steroids, and can sometimes result in permanent dysfunction of the normal HPTA, to the point where when these compounds are discontinued (as they invariably are) endogenous testosterone levels remain in the basement, and replacement therapy is sometimes the only solution to achieving normal systemic testosterone levels. In other words, they become either temporarily, or sometimes permanently eunuchoid, with a resulting need of testosterone replacement therapy.

Thus, the overall effect is a negative one in that the level of effective anabolic androgens in the body is decreased and the person thus has less anabolic hormones in their body. On top of that there are several possible side effects including a refractory HPTA, estrogen side effects, hepatotoxicity, and adverse effects on cholesterol and the cardiovascular and immune system.

And if you're a drug-tested athlete, there is the very real possibility that you will test positive for the prohormones, especially with the norsteroid and boldenone precursor prohormones. A positive test, because of the difficulty of distinguishing the metabolites of the prohormones from the metabolites of the real anabolic steroids, leads to the same severe penalties, often a two to four year ban, as a positive for anabolic steroids.

### **Replacement Therapy with Testosterone and Anabolic Steroids**

Using testosterone and/or anabolic steroids to increase your levels of androgens in your body is also the wrong way to approach the problem of low systemic testosterone levels. For example, use of exogenous testosterone shuts down the hypothalamic-pituitary-testicular axis (HPTA) that controls testosterone production on the body.

Instead of helping stimulate testosterone production, the use of testosterone and anabolic steroids decreases the natural production of testosterone and basically shuts down your internal machinery for making testosterone. Once you go off the replacement therapy, your testosterone levels often end up lower than before you started taking the exogenous androgens. In some cases, testosterone levels never even come close to recovering the pre androgen use levels, and the only alternative, if the system can't be "kick started" to produce testosterone, is to go back on replacement therapy with testosterone or anabolic steroids.

On the other hand, endogenous (developed within the body) hormone production avoids many of the problems associated with exogenous hormone use. By promoting the natural production of the hormone within the body, the regular feedback mechanisms are not by-passed and do not lead to many of the side effects associated with exogenous hormone use.

In fact the use of TestoBoost and other methods to increase endogenous testosterone production ramps up your natural testosterone producing machinery so that even if you stop taking it, your natural levels will be at least as high as before you started, and sometime higher as the body recognizes the higher level as normal and maintains that level naturally.

The bottom line is that whatever your reasons for wanting physiologically increased levels of testosterone, TestoBoost is the best way to go. Besides being more effective in increasing testosterone levels and providing an anabolic drive, the use of TestoBoost won't result in a positive drug test, as is the case with many of the prohormones, (for example the norsteroid ones), exogenous testosterone and anabolic steroids.

Even for those with below normal testosterone levels TestoBoost can be effective and is worth a try. However, in cases of HPTA dysfunction that necessitate testosterone replacement therapy there is

still some value in using TestoBoost since TestoBoost has so many other beneficial effects beyond boosting endogenous testosterone. And in some cases, TestoBoost may help keep the HPTA tuned so that the whole testosterone producing machinery doesn't totally shut down.

## The New Kids on the Block

Testosterone and anabolic steroids, while potently anabolic, have undesirable androgenic and other adverse effects. The basis for the development of selective androgen receptor modulators (SARMs) is to provide anabolic effects on bone and skeletal muscle without the androgenic and other adverse effects. The degree in which this happens depends on the chemical structure of the various SARMS.

The use of selective androgen receptor modulators (SARMs) has escalated in the past decade. One of the first SARMs is finasteride, patented in 1984 but not used to any extent until 20 years later. It's presently used mainly by men to treat an enlarged prostate or hair loss.

Finasteride may have some anabolic effects as it minimally increases testosterone. However, its true nature is that it's an anti-androgen which inhibits the formation of dihydrotestosterone. The significant adverse effects can include sexual dysfunction (which can persist after it's discontinued), gynecomastia, depression, anxiety, and suicidal ideation.<sup>888990</sup>

Lately more selective and anabolic SARMs unrelated to finasteride have been discovered that would be potentially useful for the treatment of breast cancer and cachexia but none have been approved by the FDA for any purpose.<sup>91</sup> Of course those into increasing body composition and performance have already jumped on the SARMs bandwagon and they're widely used by bodybuilders and other athletes.

So far, no SARMs has been shown to be as anabolic as the anabolic steroids but because of their decreased adverse effects their unregulated use has escalated over the past decade. They are often used in combination with anabolic steroids and other anabolic/body composition/performance enhancing hormones, peptides and drugs such as growth hormone, IGF-1, growth hormone secretagogues, clenbuterol, insulin, thyroid hormone, stimulants, opioids, and many others.

However, while potentially safer to use than anabolic steroids they also cause similar side effects including reduced activity of the hypothalamic-pituitary-testicular axis and decreased production of testosterone once they're discontinued, usually reversible over time but sometimes permanent and requiring testosterone replacement therapy.

As well, the use of the known SARMs will result in a positive drug test in drug tested athletes.<sup>929394</sup>

## Why Using TestoBoost is Beneficial Even for Those on Exogenous Hormones

For anyone using TRT or SARMs or prohormones, or in fact any exogenous therapy to increase testosterone levels it's critical to also use TestoBoost to optimize the effects but also to counter some of the adverse effects of exogenous use.

That's because the use of testosterone, anabolic steroids, SARMs and prohormones all have adverse effects to one degree or another and the use of TestoBoost minimizes these adverse effects.

TestoBoost is formulated to optimize your HPTA and as such, should you decide to go off the exogenous hormones, your system is still primed and as such the latency back to your normal testosterone production is dramatically lessened as the HPTA hasn't completely shut down.

TestoBoost also offers protection for increased levels of dihydrotestosterone (especially for those using topical testosterone in the form of patches, pumps, or gels (including AndroGel, Testogel, and Testim and Axiron). that might cause adverse effects including erythrocytosis' prostatic hypertrophy and hair loss.<sup>95 96 97</sup>

It also offers protection from increased levels of estrogen so that estrogenic effects such as gynecomastia (colloquially referred to as bitch tits) and are less likely to happen.<sup>98 99</sup>

As well, there are the various other beneficial effects that TestoBoost has on metabolism, body composition, mental and physical performance, and health.

## **New Version of TestoBoost**

Research in nutrient metabolism and its effects on the body's hormonal and other systems is accumulating daily. The advancements made in the scientific and medical fields far outstrips the advancements made in computer chip technologies. However, although Intel puts out a new improved chip on a regular basis, most nutritional supplement products are rarely updated. Rather the norm is to put out another product with similar ingredients with some added superficial changes and announce that new product as a breakthrough of one sort of another.

As well, changes made to formulations are also made to remove a substance that has been either banned by the FDA or found harmful. In this case, the new formulations and renaming of the product aren't done for the sake of improving the formula but simply to stay compliant and thus to avoid any legal problems.

Examples of this are the new formulations of weight loss products that have removed ephedra and tried to fill the gap by introducing one or two other substances to make it look like they've improved the product rather than lessened it. These reworked products are a far cry from products, such as MD+ LipoFlush that are built from the ground up without even giving a thought to the use of ephedra.

Recycling formulations for economic gain is not new in the supplement business but I want no part of it. Hence the updated versions, improving with each new version, but the same name to the product.

### **My reasons for reformulating include:**

- 1. The use of new evidence based scientific information.**
- 2. The use of information from athletes who give me feedback and comments on the products and the ingredients found in them.**
- 3. The use of information from personal use and the effects of pilot samples of updated product in a few dozen volunteers to fine tune the new formulation.**
- 4. Feedback from colleagues and others who have used the product, including their subjective results and blood work.**

## Changes in TestoBoost Version VI

Several ingredients have been added to the TestoBoost formula. TestoBoost was already a very popular and effective supplement and very few of the original ingredients have been altered except to vary the concentrations of some of them.

As well new ingredients have been added.

New ingredients include:

Trans Resveratrol  
Processed Shilajit (Mumie)  
Epimedium Grandiflorum  
Citrulline Malate  
Ginkgo Biloba  
Lycopene  
Astaxanthin

The Proprietary Complex ingredient number and amounts were increased with the major change being the addition of citrulline malate, which now is now the second most abundant ingredient in the complex. Both parts of the citrulline malate molecule are useful in TestoBoost because of beneficial effects on energy metabolism, protein synthesis and performance.

As well, the binders that are essential in having compressed tablets stay together in the bottle but make the ingredients available biologically, have been changed to reflect my focus on having my line of supplements “clean” in that there are no artificial ingredients, colors, or preservatives.

## Ingredients in TestoBoost version VI

**While I don't discuss all the ingredients in TestoBoost, their presence in the formulation add to the effectiveness of TestoBoost in boosting testosterone production either directly or by counteracting factors that tend to decrease testosterone production and/or the beneficial effects of TestoBoost.**

**But this info piece is a work in progress and various aspects of it will be covered in future articles and blogs, as well as added to this info piece as new information is published, especially for the next version formulation. Another source for updating information and reformulating is the feedback I get from athletes, exercise enthusiasts, and men and women just looking for natural ways to increase waning levels of testosterone and improving their health, vigor, and well-being.**

## Vitamin A and Beta Carotene

There are a lot of misconceptions about vitamin A's functions, metabolism and toxicity, and about the role of carotenoids.



Vitamin A has multiple important functions in the body and is important in growth and both physical and mental development, maintenance of the immune system and vision, has antioxidant and anti-inflammatory activity, and increases insulin sensitivity.

Several studies have shown that vitamin A (retinal) and retinoic acid (the active metabolite of vitamin A) are required for growth and development and have vital functions in the body on health and metabolism, including the regulation of immune, gastrointestinal, musculoskeletal, and hormonal functioning, protein metabolism, energy homeostasis, insulin responses, and adipocyte and neuron differentiation and maintenance.<sup>100, 101, 102, 103, 104, 105</sup>

Adequate levels of vitamin A are important for testicular, ovarian, pituitary, and adrenal function, and the production of testosterone and growth factors.<sup>106, 107, 108</sup> It is critical for the normal functioning of the testes, both in sperm production and the production of testosterone through effects on not only the testes but on the HPTA.<sup>109, 110, 111, 112, 113, 114</sup>

Vitamin A has significant body composition effects and is instrumental in decreasing body fat. Vitamin A reduces lipid accumulation, induces lipolysis and fatty acid oxidation, and reduces the accumulation of body fat and decreases the number and size of fat cells.<sup>115, 116, 117, 118</sup>

Vitamin A is also important for growth and development as it acts in a hormonal way to influence cellular health in all organs and tissues, including the formation of all types of blood cells, enhancing the immune system and bone metabolism, and forming healthy skin.<sup>119, 120, 121, 122, 123, 124, 125</sup>

Vitamin A has been recognized as a key regulator of adipose tissue and obesity.<sup>126, 127, 128, 129, 130</sup> As well, vitamin A alleviates some of the factors that decrease testosterone production.<sup>131</sup>

Insufficient nutritional intake of vitamin A has been reported in 20–25% of adults and many more are not in the optimal range and as such may be limiting the beneficial effects of vitamin A. As such, vitamin A is included in TestoBoost to make sure sufficient amounts are available for its many important functions, including its essential role in testosterone production and spermatogenesis.

Increased levels of vitamin A are necessary under conditions that deplete vitamin A reserves, such as high protein diets and chronic physically demanding exercise (as seen in any elite athlete), and any polymorphisms that affect the absorption, metabolism and utilization of vitamin A. There is also deficient intake in our society in those who diet to lose weight, minimize body fat, and maximize body composition.

Vitamin A toxicity is often misunderstood and while subclinical and clinical toxicities do occur, they're not common even at consistent long-term levels of 10,000 IU a day. Although vitamin A can cause liver damage, this damage typically occurs with daily doses of at least 25,000 units a day taken for several months. However, for both effectiveness and safety, MVM contains over 2,000 IU of vitamin A and a healthy dose of the pre-cursor beta-carotene.

Beta carotene has several roles in the body. It is a potent antioxidant and anti-inflammatory, has beneficial effects on the immune system., and is useful in the prevention of obesity and excess fat accumulation.<sup>132, 133, 134</sup> As well, beta-carotene has been found to have a protective effect on testicular toxicity (as has quercetin, which is also in TestoBoost).<sup>135, 136</sup> All of these properties help to enhance testosterone levels.

Beta-carotene can be converted into vitamin A, especially if there is a marginal or frank deficiency of vitamin A.<sup>137</sup> Beta-carotene's conversion to vitamin A in the body is limited by a feedback system.<sup>138</sup>

Supplementing the diet with beta-carotene does not produce any vitamin A toxicity despite its use in very high doses since it's only metabolized to vitamin A slowly and as needed. With adequate levels of vitamin A in the system the feedback mechanism markedly decreases the transformation of beta carotene into vitamin A, with the decrease being proportional to body levels of vitamin A.

### **Vitamin B6 (Pyridoxine)**

Vitamin B6 is involved in macronutrient metabolism as well as the production of neurotransmitters including dopamine, noradrenaline and serotonin. It's also an essential co-factor necessary for the metabolism of protein and a useful supplement to take with any amino acid and/or protein product.

Transamination of amino acids, important for many functions in the body including protein synthesis, anaplerosis, energy metabolism, is promoted by several enzymes among which are the aminotransferases, which are derivatives of vitamin B6. For example, in a deficiency of vitamin B6 the nonessential amino acids are synthesized only poorly and, therefore, protein synthesis cannot proceed normally.

Vitamin B6 and leucine have been shown to work together to increase fat oxidation and insulin sensitivity, improve body composition and reduce oxidative and inflammatory stress.<sup>139</sup><sup>140</sup> And the B vitamins in general, including those in TestoBoost have been shown to improve body composition and improve energy metabolism.<sup>141</sup>

TestoBoost version VI has both pyridoxine (in the form of HCL) and pyridoxal-5-phosphate (P5P) in it. P5P is the metabolically active form of vitamin B6. Pyridoxine HCL, while as easily absorbed as P5P must be converted to P5P in the body in order to be used by the enzymes involved in protein metabolism and various hormonal processes. P5P is the preferred form of vitamin B6 as it can be used directly in the body without relying on the liver's conversion of other forms of vitamin B6 into P5P. As well, less is needed to achieve the same cofactor effects. As such, half of the B6 is in P5P form, and if the body needs more, it can convert the pyridoxine HCL to P5P.

### **Vitamin B12**

Vitamin B12 is metabolically involved in almost every cell in the body, including the synthesis and regulation of DNA and neurotransmitters. It is vital for normal brain and nervous system functioning and for the formation of red blood cells.

B12 is involved in fatty acid and amino acid metabolism, helping to regulate protein synthesis and lipolysis/lipogenesis, thus helping to improve body composition. As well, it helps to decrease serum levels of homocysteine, cholesterol and C-Reactive proteins, markers of heart disease and inflammation in the body. B12 is also involved in adrenal and testicular function including normalizing testosterone and cortisol levels, and spermatogenesis.

Vitamin B12 deficiency can lead to serious problems including anemia, and damage to the brain, central nervous system, and the reproductive axis. Even marginal deficiencies can cause symptoms including cognitive decline, fatigue, depression, lower testosterone production, decreased libido, and sexual and reproductive dysfunction.<sup>142</sup><sup>143</sup><sup>144</sup><sup>145</sup><sup>146</sup><sup>147</sup><sup>148</sup><sup>149</sup><sup>150</sup><sup>151</sup>

Vitamin B12 deficiency can occur secondary to low intake relative to need, such as can happen in vegetarians and especially vegans (vitamin B12 is essentially absent from plant sources), from deficient absorption due to certain intestinal disorders and problems with intrinsic factor, and from the use of certain medications, such as metformin, a common diabetic medication.<sup>152153154155156157158159</sup>

**Vitamin B12 (as methylcobalamin)** in version VI of TestoBoost was increased from 100mcg to 200 mcg. TestoBoost contains enough B12 to make sure you receive all its benefits and none of the problems associated with low B12 levels.

Methylcobalamin is the biologically active form of B12, whereas cyanocobalamin, the form used in most supplements, is the synthetic form. As the body must change the cyanocobalamin into methylcobalamin, this process may be compromised in some people so using the metabolically active form is more efficient and improves bioavailability and function.

B12 helps to optimize macronutrient metabolism, maximize muscle mass and decrease body fat.<sup>160161</sup> As well, it helps to decrease serum levels of homocysteine, cholesterol, TNF-alpha, and C-Reactive proteins, markers of heart CNS diseases and inflammation in the body.<sup>162163</sup> Decreasing inflammation helps to decrease cortisol levels and thus increase the anabolic effects of TestoBoost.

## Antioxidants

Vitamin C is essential to proper collagen synthesis, and this is evident in the vitamin C deficiency disease scurvy, in which the collagen fibers synthesized in the body cannot form fibers properly, resulting in lesions, blood vessel fragility and poor wound healing.

Vitamin C has been shown to have some anticatabolic effects that likely involves decreasing exercise induced cortisol but may also have some effects through its antioxidant action. Conversely, some of the anticatabolic effects of antioxidants may be mediated through a decrease in cortisol.

Antioxidants may be of some use in training induced muscle ischemia and injury. Research shows that exercise can adversely affect muscle tissue by increasing the formation of free radicals. These free radicals can then lead to muscle fatigue, inflammation and muscular damage.<sup>164</sup> During normal conditions free radicals are generated at a low rate and neutralized by antioxidant enzymes in the liver and skeletal muscle and other systems. Unfortunately, the increase in free radicals caused by exercise accompanies a simultaneous decrease in the supply of antioxidants to handle them.

Oxidant stress, from whatever source, be it environmental, exercise induced, or psychological stress, affects Leydig cells and results in decreased testosterone production. Antioxidant like vitamin C, and vitamin E have been shown to protect the body against stress induced damage. Supplementation with vitamin E alone or in combination with vitamin C prevents the reduction in testosterone and rise in corticosterone levels.<sup>165</sup>

As well, antioxidants such as vitamin C, vitamin E, lycopene, astaxanthin, zinc, and coenzyme Q10 have been shown to improve male fertility.<sup>166</sup>

Antioxidants form a front-line defense against cell damage caused by free radicals, which are involved in damage to all systems in the body and in the aging process. As well, the antioxidants, immune stimulant, and other ingredients in MENS+, normalize and optimize the immune system to help deal with various problems and diseases. They are also effective in combating inflammation, free

radicals, and other destructive processes that which are known to contribute towards aging and disease.

One of the most effective means of protecting ourselves from various endogenous and exogenous insults (including stress, free radicals, poor diet, and environmental chemicals and pollutants, including mercury and other heavy metals) is by using a complimentary combination of antioxidants.

In a review on antioxidants the author found that antioxidant vitamin and trace element intakes have been shown to be particularly important in the prevention of cancer, cardiovascular diseases, age related ocular diseases and in aging. In animal models, targeted interventions have been associated with reduction of tissue destruction in brain and myocardium ischemia-reperfusion models. In the critically ill antioxidant supplements have resulted in reduction of organ failure and of infectious complications.<sup>167</sup>

Several ingredients in TestoBoost have antioxidant properties (including vitamin C, vitamin E, coenzyme Q10, alpha-lipoic acid, quercetin, lycopene, astaxanthin, and several of the herbal, amino acids, and other ingredients). These ingredients play an important role in reducing inflammation and decreasing tissue and organ damage.

There's been some adverse information published about the use of antioxidants and how they may decrease the anabolic and performance effects of exercise. These studies are misleading and done with blinders on. I'll be discussing this in detail in upcoming articles, blogs and podcasts, especially the ones I do and will be doing on SHR – [www.superhumanradio.org](http://www.superhumanradio.org).

### Vitamin D3

It's generally known that vitamin D, a fat-soluble vitamin, is essential for bone health and is important for augmenting calcium dynamics. It is needed for absorbing minerals such as calcium, iron, magnesium, and zinc, which are important for many metabolic effects, physical and mental.

Vitamin D plays key roles in cellular growth and immune function. Low levels of vitamin D are linked to lower moods and poor cognitive performance. Vitamin D has other important effects,<sup>168</sup> for example on insulin resistance,<sup>169</sup> inflammation<sup>170171</sup> and obesity<sup>172173</sup>.

But there's even more to vitamin D. Although getting adequate amounts of vitamin D is crucial to health, vitamin D deficiency is relatively common and in fact is the most widespread nutritional disorder in the world.<sup>174175176177</sup> Several studies have shown that vitamin D corrects muscle dysfunction enhances protein synthesis and has specific anabolic effects especially in athletes who may be vitamin D deficient.

Studies in athletes have found that vitamin D has multiple functions on the musculoskeletal system that enhances both body composition and performance. For example, vitamin D may reduce stress fractures, total body inflammation, common infectious illnesses, help impaired muscle function, and may also aid in recovery from exercise and injury.<sup>178179180181182183</sup>

Besides the effects of vitamin D on the musculoskeletal system, several studies have found that vitamin D has many other important functions and that vitamin D deficiency may be involved in various body dysfunctions and diseases.

It's now recognized that vitamin D receptors (VDRs) are present on various non-musculoskeletal organs and tissues, including in reproductive tissues, such as the testes, prostate, and human sperm. As such, vitamin D may be involved in regulating reproductive health, and sexual function, including testosterone levels.<sup>184185186187188</sup>

Two studies published in 2010 and 2011 found that vitamin D levels correlated with serum testosterone levels. The first study looked at the association of 25-hydroxyvitamin D [25(OH)D] levels with testosterone, free androgen index (FAI) and SHBG, as well as examining whether androgen levels show a similar seasonal variation to 25(OH)D.<sup>189</sup>

The authors found significant associations of 25(OH)D levels with testosterone, FAI and SHBG levels. As well, as would be expected by the availability of maximum sun exposure, 25(OH)D, testosterone and FAI levels followed a similar seasonal pattern with the lowest points in March and peak levels in August.

The second study looked at healthy overweight men that had low vitamin D3 levels and testosterone levels in the lower reference range. One part of the group of men were given just over 3,000 IU of vitamin D3 over a 12-month period, while the other part was given a placebo. Vitamin D supplementation resulted in increased levels of circulating 25(OH)D concentrations while the placebo group showed no increase. As well, compared to baseline values, there was a significant increase in total testosterone levels, bioactive testosterone, and free testosterone levels in the vitamin D supplemented group but no change in the placebo group.<sup>190</sup>

Other recent studies have shown a connection between vitamin D and testosterone and fertility.<sup>191</sup> One study in Korean men found that the higher level of 25(OH)D was associated with higher total and free testosterone levels and that these associations persisted after adjusting for age, season, body composition, chronic disease, alcohol use, smoking, and exercise.<sup>192</sup>

A study presented May 17, 2015 at the American Urological Association (AUA) 2015 Annual Meeting (Abstract MP51-04) found that low levels of vitamin D are significantly and independently associated with low levels of testosterone in otherwise healthy middle-aged men.

Vitamin D is also involved in aromatase activity as it has been shown to downregulate aromatase so that less testosterone is converted to estrogen and thus increasing testosterone levels.<sup>193194</sup>

It's important that the right form of vitamin D is used for supplementation. Studies have found that vitamin D3 (cholecalciferol) is more effective at raising serum levels of 25(OH) and for longer periods of time than vitamin D2 (ergocalciferol) and thus is the preferred form of vitamin D supplementation.<sup>195196197</sup> As well, **resveratrol** (found in grape seed extract which is in TestoBoost) is a potent anti-oxidant with significant anti-aromatase activity.<sup>198199200201</sup>

Vitamin D3 is seemed to decrease mortality in elderly people living independently or in institutional care while vitamin D2, alfalcidol and calcitriol had no statistically significant beneficial effects on mortality.<sup>202</sup>

Using vitamin D3 is also better for athletes as a recent study found that vitamin D2 can be counterproductive in that it amplifies muscle damage and while significantly increasing 25(OH)D2 it decreased 25(OH)D3, which is the more immediate substrate for biologically hormonally active form of vitamin D.<sup>203</sup>

The bottom line is that supplementing with vitamin D, especially in the form of vitamin D3, is important to realize all the body composition, performance, and sexual functioning benefits that it has to offer in the many who are either marginally or frankly vitamin D deficient.

## Magnesium

Magnesium, besides complementing the effects of calcium on obesity<sup>204</sup> and other functions, also has important effects on its own. Magnesium is involved in numerous processes that affect muscle function including oxygen uptake, energy production and electrolyte balance. Low levels of magnesium promote inflammation<sup>205206</sup> and impact on the body's ability to handle stress.<sup>207</sup> These functions are useful in alleviating the release of pro-inflammatory cytokines and decreasing both insulin resistance and inappropriate cortisol secretion.

There is evidence that marginal magnesium deficiency impairs exercise performance and increases oxidative stress. As well, strenuous exercise increases urinary and sweat losses that may increase magnesium requirements.<sup>208</sup>

Recent surveys have shown that a significant number of individuals are magnesium deficient based on their intake. Athletes in sports with weight classes are especially vulnerable to magnesium deficiency due to their weight loss practices. As such, in these athletes, and others who are magnesium deficient or whose levels are marginal, magnesium supplementation would have beneficial effects on exercise performance.

A recent study found that magnesium supplementation improved alactic anaerobic metabolism, even though the athletes were not magnesium-deficient.<sup>209</sup> Another study found that magnesium supplementation increased strength performance.<sup>210</sup> As well, magnesium may prove effective for muscle cramps.<sup>211</sup>

Magnesium has been shown to influence testosterone levels as well as the anabolic peptide IGF-1.<sup>212213</sup> As well, magnesium has been shown to work along with zinc and B6 (both of which are present in TestoBoost) to produce a significant anabolic effect.<sup>214</sup>

Magnesium Aspartate is used instead of the magnesium oxide as the aspartate salt has been shown influence testosterone levels and is the ingredient that is in ZMA, along with zinc monomethionine and B6, all of which are in TestoBoost).

## Zinc

Exercise can lead to an increased need for certain nutrients. Problems can arise from exercise induced mineral loss, which is further enhanced by the finding that many of us don't consume adequate amounts of many essential minerals.

Studies have shown that many athletes, and female athletes in particular, consume diets that have been found to be inadequate for certain key minerals such as zinc, magnesium, copper, and iron. The combination of strenuous exercise and compromised mineral status ultimately leads to low endurance capacity, depressed immune function, and the development of a variety of disease conditions.

One study looked at the effects of zinc deficiency on physical performance and found that low dietary zinc was associated with impaired cardiorespiratory function and impaired metabolic responses during exercise.<sup>215</sup>

Zinc deficiency in humans is widespread<sup>216</sup> and athletes may be particularly prone to lower plasma zinc levels.<sup>217</sup> Zinc is a constituent of more than a hundred fundamentally important enzymes, so zinc deficiency has many negative effects on almost every body function.<sup>218</sup> As well, zinc deficiency can adversely affect the reproductive hormones and as such impair athletic efforts.<sup>219</sup>

Zinc deficiency adversely affects protein synthesis. In one study the effects of zinc deficiency in rats, on the levels of free amino acid in urine, plasma and skin extract were investigated.<sup>220</sup> Zinc deficiency adversely affected skin protein synthesis. Especially where a deficiency may be present, supplemental zinc has resulted in an increase the secretion of growth hormone and IGF-I,<sup>221</sup> and testosterone<sup>222</sup> and to raise plasma testosterone and sperm count.<sup>223,224</sup>

A study looking at the effects of zinc supplementation on wrestlers found that the results obtained at the end of the study indicate that zinc supplementation (as well as several other ingredients in TestoBoost including NAC and ALA) prevents production of free radicals by **activating the endogenous antioxidant system**.<sup>225</sup> This activation is important as it coincides with the effects of exercise, which also activates the endogenous antioxidant system and leads to endogenous antioxidants that enhance the beneficial effects of exercise on body composition and performance. The authors concluded that “physiologic doses of zinc supplementation to athletes may beneficially contribute to their health and performance.”

It's been shown that there is an improvement in insulin resistance with **zinc** supplementation and that zinc is involved in controlling some of the aspects of obesity.<sup>226</sup> Zinc also improves calcium metabolism and thus the beneficial effects that calcium has on fat metabolism.

## Manganese

Manganese is necessary for the metabolism of proteins and fats. It's also vital for proper immune and central nervous systems functioning, increases insulin sensitivity, has antioxidant properties, and is involved in energy metabolism.<sup>227,228</sup>

Manganese is a mineral that is required in small amounts to manufacture enzymes necessary for the metabolism of proteins and fats. It also supports the immune system, regulates blood sugar levels, and is involved in the production of cellular energy, reproduction, and bone growth.

Manganese supports blood clotting, aids in digestion, and as antioxidant, is a vital component of Sodium Oxide Dismutase, a large molecule that is the body's main front-line defense against damaging free-radicals. Working with the B-complex vitamins, manganese help control the effects of stress while contributing to one's sense of wellbeing.

A deficiency in intake of manganese can retard growth, cause seizures, lead to poor bone formation, impair fertility, and cause birth defects. Researchers are also looking at new links between manganese deficiency and skin cancers.

## Coenzyme Q10 (ubiquinone-10, CoQ10)

Coenzyme Q10 (CoQ10), a coenzyme that is ubiquitous in animals, including humans, is a lipid-soluble antioxidant and acting as an electron carrier is a key component of the mitochondrial electron transport chain for adenosine triphosphate (ATP) production.<sup>229</sup> It is also one of the key antioxidant

nutrients that protect mitochondrial membrane lipids and proteins and mitochondrial DNA from free radical-induced oxidative damage.

As such it is necessary for proper energy metabolism. For example, myocardial CoQ<sub>10</sub> content is reduced by cardiac failure and aging. It is also reduced by statins, the popular cholesterol lowering drugs. Studies have suggested preventative supplementation of CoQ<sub>10</sub> for cardiac health and for those on statins.<sup>230231232233234235</sup>

CoQ<sub>10</sub> has been shown to decrease oxidative stress and mitochondrial damage leading to increases in mitochondrial mass in many tissues.<sup>236237</sup> As well, CoQ<sub>10</sub> has been shown to affect the expression of genes involved in human cell signaling, metabolism and transport. As such since many neurodegenerative disorders, diabetes, cancer, and muscular and cardiovascular diseases have been associated with low CoQ<sub>10</sub> levels, supplementation may be beneficial in many conditions and diseases<sup>238239240 241242243</sup> including alleviating intervertebral disc degeneration.<sup>244</sup>

For example, CoQ<sub>10</sub> supplementation has been shown to have anti-aging and beneficial effects on semen parameters, fertility, testicular damage, and reproductive hormones including testosterone.<sup>245246247248249250251252253</sup> In a recent study CoQ<sub>10</sub> while not found to directly increase testosterone, CoQ<sub>10</sub> supplementation **“was found to ameliorate the reduction in testosterone induced by chemical reproductive toxicants, mainly by neutralizing the damaging effect of the generated free radicals.”**<sup>254</sup>

CoQ<sub>10</sub> has also been shown to have beneficial effects on oxidative stress, inflammation, the immune system, and on exercise performance.<sup>255256257258259260261262263264265</sup>

CoQ<sub>10</sub> also regenerates and extends the action of vitamin E thus further protecting against membrane lipid peroxidation. Under the various forms of stress and inflammation, demand for coenzyme Q<sub>10</sub> increases which must be met by dietary intake in order to optimize mitochondrial function.

As well, it has been shown that the reduced form of CoQ<sub>10</sub> is an important physiological lipid-soluble antioxidant that scavenges free radicals generated chemically within liposomal membranes.<sup>266,267</sup> It has also been shown that it reduces oxidative stress associated with strenuous exercise in rats, healthy adults and young athletes.<sup>268269270271272</sup> As noted above, vitamin E and ubiquinone increase physical working capacity of experimental animals.<sup>273</sup>

Generation of free radicals and subsequent lipid peroxidation have been proposed to contribute to delayed tissue damage. One study has found that ascorbate and ubiquinol levels were decreased after trauma.<sup>274</sup> In this study, changes in tissue levels of ubiquinol, but not ascorbate reflected the degree of trauma. The authors suggest that ubiquinol levels may provide a useful marker of the oxidative component of the secondary injury response.

A recent study found that CoQ<sub>10</sub> supplementation **“significantly recovered mitochondrial function and concurrently decreased the generation of reactive oxygen species and lipid peroxides, inhibited the accumulation of lipid droplets and the formation of the NOD-like receptor family pyrin domain-containing three (NLRP3) inflammasome, and reduced interleukin-1 $\beta$  release and cell death.”** Also, the authors concluded that their results clarified **“the causal role of CoQ<sub>10</sub> in coupling the electron transport chain with  $\beta$ -oxidation”**.<sup>275</sup>



TestoBoost also contains **acetyl-L-carnitine**, the acetyl form of **L-carnitine** which are interchangeable in the body. While one forms from the other and have similar effects in the body, each also has specific effects. Studies have shown that under certain conditions CoQ10 plus L-carnitine and in some cases L-carnitine alone, significantly increases total antioxidant, LH and testosterone levels as well as improving semen parameters.<sup>276277278279280281282283284</sup>

## Astaxanthin

Astaxanthin, a powerful lipid-based antioxidant complements and adds to the many beneficial effects of TestoBoost on testosterone production, body composition, exercise performance and overall health.

Astaxanthin has been shown to have potential to improve health, enhance exercise performance, increase fat metabolism during exercise, decrease oxidative stress and muscle injury, delay exhaustion, increasing improve body composition, enhance recovery, prevents redox imbalances, and attenuates muscle damage, counterproductive inflammation and fibrosis induced by rigorous physical training as well as immobilization.<sup>285286287288289290291292293294295296297298299300301302</sup>

Some of the benefits of Astaxanthin deserve special attention. For example, astaxanthin has a protective effect on mitochondria, the cellular powerhouses that produce the energy we need to live and function optimally. Protecting the mitochondria is especially important during exercise since destructive free radical production increases almost exponentially and can damage not only the mitochondria, thus impairing energy systems, but also skeletal muscle as a whole impairing performance and recovery and increasing the chance of injury.<sup>303</sup>

But that's not all because astaxanthin, through its effects on decreasing mitochondrial damage in other parts of the body such as the testes, also increases testosterone production and thus increases the anabolic effects of exercise and has also been shown to have positive effects on sperm parameters and fertility.<sup>304</sup>

As far as testosterone production it's been found that mitochondrial function is paramount for the optimal functioning of Leydig cells, the cells in the testes that produce testosterone.<sup>305</sup> Oxidative stress, for example from exposure to hydrogen peroxide, acts directly on testicular Leydig cells impairs mitochondrial functioning and decreases steroidogenesis and thus impairs testosterone production.<sup>306</sup> Astaxanthin rescues Leydig cells from oxidative stress and thus restores normal testosterone production.<sup>307</sup>

It's also been shown that astaxanthin acts as an aromatase inhibitor, and thus decreases the effects of estrogen on the HPTA and thus acts to further increase testosterone levels. In one study a combination of astaxanthin and saw palmetto (both ingredients are in TestoBoost) increased serum testosterone, and decreased estrogen and dihydrotestosterone (DHT) production.<sup>308</sup> The end result is increased testosterone levels as there is less testosterone being metabolized to estrogen and DHT.

Unlike some other antioxidants, astaxanthin not only has intrinsic antioxidant and anti-inflammatory properties but it also increases the endogenous production of natural antioxidant defense mechanisms such as SOD and heme oxygenase-1.<sup>309</sup>

As well it works synergistically with other ingredients in TestoBoost. For example, in horses it's been shown that continuous dietary administration of astaxanthin and L-carnitine attenuates exercise-

induced muscle damage.<sup>310</sup> Also the combination of astaxanthin and saw palmetto has also been shown as an effective ancillary treatment for prostate cancer.<sup>311</sup>

For all these reasons astaxanthin plays a prominent part in the beneficial effects that TestoBoost has on all aspects of health, nutrition, exercise, and anti-aging.

## Saw Palmetto

Saw palmetto inhibits the enzyme 5-alpha-reductase, which produces dihydrotestosterone from testosterone. Because of this inhibition it increases testosterone levels by inhibiting up-conversion to dihydrotestosterone, a hormone that in adults is responsible for male pattern baldness, prostate hypertrophy, and even acne.

By means of its ability to decrease the formation of dihydrotestosterone, saw palmetto has been shown to be useful in preventing and treating prostate problems.<sup>312313314315316</sup>

As well, saw palmetto enhances erectile responses by inhibition of phosphodiesterase 5 activity and increase in inducible nitric oxide synthase messenger ribonucleic acid expression in the penile corpus cavernosum, and may also increase sexual activity.<sup>317318</sup>

## Eurycoma Longifolia (Longjack, Tongkat Ali, Pasak Bumi)

Eurycoma longifolia, also known as 'Malaysian ginseng', Longjack, Tongkat ali, and pasak bumi) is reported to have aphrodisiac and testosterone enhancing effects and has a long history of use in South-East Asia to decrease stress and improve physical strength and psychological resilience.<sup>319320</sup>

Several studies on murine models have shown that Longjack increased free serum testosterone levels and sexual drive and performance.<sup>321322</sup>

More importantly, more recent studies in humans have shown that Eurycoma longifolia increases testosterone levels and libido, shows ergogenic effects and acts as an aromatase inhibitor in both men and women, as well as increasing spermatogenesis in men.<sup>323324325326327328329</sup> The increase in free testosterone in women is thought to be due to the significant decline in sex hormone-binding globulin concentrations.

As such, it works synergistically with other ingredients in TestoBoost that work in similar ways, including **acetyl-L-carnitine**, **catuaba bark**, **maca root**, **coelus forskohlii (forskolin)**, **mura puama**, **chasteberry (vitex agnus-castus - ecdysteroids)**, **suma root (beta ecdysone – also known as beta ecdysterone and 20 beta hydroxyecdysterone)**, **schisandra chinensis**, **cordyceps sinensis**, and **avena sativa**.

For example, one study found that carnitines including **acetyl-L-carnitine (ALCAR)** worked as well as replacement testosterone therapy in improving sexual dysfunction, depressed mood, and fatigue in aging men.<sup>330</sup>

As well, ALCAR seems to have an effect on the hypothalamic-pituitary-testicular axis. Studies have shown that ALC prevented the decrease in plasma testosterone levels after chronic swimming<sup>331</sup>, and that ALC stimulates testosterone production<sup>332</sup>.

## 5-Methyl Methoxy Isoflavone

Methoxy Isoflavone has been shown to increase protein synthesis in animal models, including livestock, with no significant side effects. Anecdotal evidence over the past year has shown that it may exhibit some mild anabolic and anti-cortisol effects. Similarly, **ecdysone**, also known as **beta ecdysterone** and **20 beta hydroxyecdysterone**, has shown to have some anabolic effects.

### **Ecdysone (beta ecdysterone, ecditen, 20 beta hydroxyecdysterone)**

Ecdysone was popular with Olympic lifters and other athletes in the East and several quasi scientific studies, 2 which were never published, showed that it might have significant anabolic effects.<sup>333</sup> Real world use has not shown dramatic effects and most of the information is available through nutritional companies that vastly overstate the anabolic properties of ecdysone. Nevertheless, it makes a useful synergistic ingredient for TestoBoost even though on its own its effects are minimal.

### **Tribulus Terrestris Extract**

Tribulus terrestris (TT) saponins were used successfully by Eastern European athletes to enhance body composition, strength, and performance. Tribulus works by increasing LH and testosterone levels. It also has been shown to have some effects on sex drive and sexual function. Several recent studies have found that it does have some beneficial effects and no toxicity.

For example a study found that TT extract increased blood testosterone levels, strength and athletic performance.<sup>334</sup> Another study found that the use of TT does not result in a positive drug test.<sup>335</sup> Several studies have shown positive effects of TT extracts on rats and other animals, including increased levels of testosterone, increased libido, and positive effects on erectile dysfunction.<sup>336, 337, 338</sup>

TT has also been shown to not only elevate testosterone levels but also to increase androgen receptors and testosterone-androgen receptor binding.<sup>339</sup> The same study found that TT increased IGF-1 levels and the IGF-1 receptors. The authors of this study concluded that **“The present study provided preliminary evidence supporting the use of TT extracts as a dietary supplement for the promotion of skeletal muscle mass increase and the enhancement of athletic performance in humans performing high intensity exercise.”**

Other recent studies found that TT had positive effects on anaerobic performance in boxers and alleviated muscle damage<sup>340</sup> and that TT increased performance, body mass, and gastrocnemius mass of rats undergoing overtraining, which might be attributed to the changes in androgen-AR axis and IGF-1R signaling.<sup>341</sup>

### **Muira Puama**

There have been few clinical studies on muira puama although anecdotally this herb is best known for its aphrodisiac qualities. In 1990, at the Institute of Sexology in Paris, France, a clinical study with 262 men complaining of lack of sexual desire demonstrated muira puama extract to be effective. Those with loss of libido claimed that the treatment was helpful.<sup>342</sup>

In 2000, researchers at the Institute of Sexology published another study assessing the effectiveness of muira puama and ginkgo biloba using 202 healthy women who complained about low libido and sexual dysfunction. The study found that the combination resulted in increased libido and sexual activity, as well as increased sexual satisfaction, orgasm quantity and quality, and thoughts about sex.<sup>343</sup>

Recently, muira puama has gained more of a following and is used for several problems such as PMS and sexual dysfunction. It's also used to relieve stress and for anti-aging.

## Phosphatidylserine

phosphatidylserine (PS) has several important regulatory functions within mammalian cells,<sup>344</sup> including inhibiting the production of proinflammatory cytokines<sup>345, 346</sup> inducing anti-inflammatory responses,<sup>347, 348</sup> and inhibiting immune responses at the site of inflammation.<sup>349</sup> As well, in vitro studies have shown antioxidant effects with the ability of PS to protect cells against oxygen-derived free radicals and suppress iron-dependent lipid peroxidation.<sup>350, 351</sup>

PS administrations may be useful for treating the neurochemical and behavioral changes that occur with aging and for improving learning and memory.<sup>352, 353, 354, 355, 356, 357</sup> Studies have shown that PS is produced less with age and appears to beneficially affect brain function through interacting with brain neurotransmitters. In one study PS induced consistent improvement of depressive symptoms, memory and behavior in a group of 10 elderly women with depressive disorders.<sup>358</sup> Thus because of the potential role of PS in neuroendocrine-immune communications,<sup>359</sup> PS is one of the agents proposed for the treatment of various disorders including Alzheimer's disease.<sup>360, 361</sup>

Several research papers have indicated that PS supplementation attenuates the serum cortisol response to acute exercise stress, increases the testosterone to cortisol ratio, decreases oxidative stress, and increases exercise capacity.<sup>362, 363, 364, 365</sup>

For all these reasons PS provides significant benefits and is an important ingredient in TestoBoost.

## Genistein

Genistein (4',5,7-trihydroxyisoflavone), a major isoflavone in soybeans and a specific inhibitor of protein tyrosine kinase, acts to decrease estrogen in the body. A recent study has shown that there is a synergistic anti-estrogenic effect of **indole-3-carbinol** and genistein.<sup>366</sup> As well as these two ingredients, TestoBoost also contains other anti-estrogenic compounds including **calcium-d-glucarate**,<sup>367</sup> **chrysin**,<sup>368</sup> **ginkgo biloba extract**,<sup>369</sup> and **ipriflavone**.<sup>370, 371</sup> The addition of piperine as **Bioperine** increases the absorption of these and other ingredients increasing the biological synergistic effects of the combination of ingredients on lowering estrogen effects.

## Prickly Pear Extract \*

This extract is felt to have neuroprotective and antioxidant effects. Also has insulin like effects and has been shown to have a favorable effect on cholesterol in the body. There is some anecdotal evidence that the use of prickly pear acts as an adaptogen, boosting recovery via an anti-cortisol action. As such it works with other ingredients in TestoBoost to boost recovery and decrease counterproductive cortisol levels.

## Schisandra Chinensis

Schizandra is a woody vine with clusters of red berries that is found in northern and northeastern China and adjacent regions in Russia and Korea. It is used to treat a variety of medical conditions and is widely known as a longevity herb and aphrodisiac. Athletes have used schisandra in the belief

that it will increase endurance and combat fatigue under physical stress.<sup>372</sup> It is also felt to have liver protective effects.

## Chrysin

Chrysin has been shown to increase testosterone directly and indirectly as an aromatase inhibitor.<sup>373374375</sup>

## Cordyceps Sinensis

*Cordyceps sinensis*, a fungus grown in the high mountain ranges of the Himalayas and Tibetan plateau, is parasitic on caterpillars, using the caterpillar's body as a host. It has been used for centuries in the Orient as a medicine for numerous ailments and an aphrodisiac. It is particularly valued for its beneficial effects on libido and sexual performance. Although research in humans is lacking, cordyceps has been shown to raise testosterone levels in rats and mice.<sup>376377378379380381</sup>

Cordyceps is also used by athletes for performance enhancement. It became popular when it was reported that it was used by the female Chinese runners when they won several track events in 1993. Although the coach said that their performance was due to a tonic from caterpillar fungus, it was later shown that it was due to the use of anabolic steroids (between 1990 and 1998 28 Chinese swimmers tested positive for anabolic steroids, amounting to half of all the positive drug tests worldwide in that period of time) and other performance enhancing drugs.

While not an anabolic steroid, cordyceps does have some anti-inflammatory, metabolic, and antioxidant effects that could make it useful for enhancing exercise performance and health.  
382383384385386387

## Avena Sativa (Oat Wheat Straw)

*Avena sativa* has been shown to have many effects on health and sexual functioning. Because of anti-inflammatory, antioxidant, immunological, cardioprotective, cognitive enhancing, and other properties, it's felt to be a therapeutic agent in the prevention and treatment of various conditions and diseases.<sup>388389390391392393</sup>

*Avena sativa* is also considered to be an aphrodisiac and able to enhance sexual functioning.<sup>394</sup>

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Crit Rev Food Sci Nutr. 2013;53(2):126-44. doi: 10.1080/10408398.2010.526725.

*Avena sativa* (Oat), a potential nutraceutical and therapeutic agent: an overview.

Singh R, De S, Belkheir A.

### Abstract

The aim of the present review article is to summarize the available information related to the availability, production, chemical composition, pharmacological activity, and traditional uses of *Avena sativa* to highlight its potential to contribute to human health. Oats are now cultivated worldwide and form an important dietary staple for the people in number of countries. Several varieties of oats are

available. It is a rich source of protein, contains a number of important minerals, lipids,  $\beta$ -glucan, a mixed-linkage polysaccharide, which forms an important part of oat dietary fiber, and also contains various other phytoconstituents like avenanthramides, an indole alkaloid-gramine, flavonoids, flavonolignans, triterpenoid saponins, sterols, and tocopherols. Traditionally oats have been in use since long and are considered as stimulant, antispasmodic, antitumor, diuretic, and neurotonic. Oat possesses different pharmacological activities like antioxidant, anti-inflammatory, wound healing, immunomodulatory, antidiabetic, anticholesterolaemic, etc. A wide spectrum of biological activities indicates that oat is a potential therapeutic agent.

## Curcumin

The active constituent in turmeric, known as curcumin, is a potent antioxidant with anti-inflammatory properties and has a wide range of therapeutic effects.<sup>395</sup> Turmeric exhibits marked anti-inflammatory action and has been shown to be as effective as some anti-inflammatory drugs. For example, in a double-blinded trial, post-surgical patients receiving curcumin experienced reductions in stiffness and joint swelling comparable to the effects of phenylbutazone, a potent anti-inflammatory drug.<sup>396</sup>

Of all the spices and herbal preparations, it seems that only the spice turmeric has any anti-inflammatory effects. This was the conclusion of a study of a variety of Ayurvedic and herbal preparations, which was presented at the 9th Asia Pacific League of Associations for Rheumatology Congress. In this study, a variety of herbal and Ayurvedic preparations were tested in rats. The rats were fed oral doses of the varied herbal and Ayurvedic recipes. Only turmeric showed anti-inflammatory effects when tested on irritated paws of the rats.

It works by inhibiting cyclooxygenase and lipoxygenase enzymes that catalyze the formation of inflammatory prostaglandins.

Several studies have shown the effectiveness of curcumin, especially when coupled with piperine which increases absorption of curcumin (both are in GHboost) on exercise induced muscle damage and soreness, and recovery as well as on improving body composition and exercise performance.<sup>397398399400401402403</sup> In one study the combination of curcumin and piperine resulted in an improvement of in sprint mean power output 24 hours post-exercise.<sup>404</sup>

As well, other studies have shown the value of curcumin in the prevention and treatment of neurological dysfunction such as Alzheimer's disease and other neurological diseases.<sup>405406</sup>

Since testosterone levels are compromised by acute and chronic inflammation, the anti-inflammatory effects of turmeric, along with the other potent antioxidants in TestoBoost, such as **vitamin C and E, resveratrol (in grape seed extract), alpha lipoic acid, lycopene, astaxanthin, and other ingredients in TestoBoost**, relieves the effects of inflammation on testosterone secretion and thus results in increased Testosterone levels in the body.

## Alpha Lipoic Acid

Besides having potent antioxidant properties, likely secondary to increasing levels of intra-cellular glutathione, ALA also increases insulin sensitivity. Alpha lipoic acid (ALA), a potent antioxidant<sup>407408409</sup> that can recycle other antioxidants such as vitamin C, vitamin E and glutathione.<sup>410411</sup> ALA can be used to increase testosterone secretion and insulin functioning and sensitivity<sup>412413</sup> by its actions on the pro-inflammatory cytokines<sup>414415</sup> and because of its effects on decreasing secondary cortisol elevations.

## Bioperine

TestoBoost contains piperine marketed as Bioperine,<sup>416</sup> which significantly enhances the bioavailability of supplemented nutrients through increased absorption and decreased metabolic inactivation.<sup>417418419420</sup>

### The Advantages of Bioperine®

Bioperine® is the only product sourced out of piperine to obtain a patented status for its ability to increase the bioavailability of nutritional compounds. Secondly, it is the only source from piperine to have undergone clinical studies in the U.S. to substantiate its safety and efficacy for nutritional use.

The subtle, yet potent properties of Bioperine® have been measured in several clinical studies with healthy volunteers in the U.S. These studies measured the absorption of three distinct categories of products. The categories evaluated with and without Bioperine® were fat-soluble (beta-carotene), water-soluble (vitamin B 6 ) and a mineral (selenium, in the form of selenomethionine). Gastrointestinal absorption of all the studied nutrients, as measured by amounts present in the blood, increased dramatically when administered with Bioperine® as compared to the control group receiving the nutrient alone. Selenium levels increased by 30%, beta-carotene increased by 60%, and the vitamin B 6 increase was slightly higher than beta-carotene.

### Truth in ancient wisdom

A recognized feature of the 6000-year-old practice of Ayurveda is its preoccupation with the proper functioning of the digestive tract, specifically the digestion and absorption of nutrients. Nearly two-thirds of all traditional Ayurvedic formulas contain a special blend of ingredients, which includes black pepper, for this purpose.

There are various reasons discussed in scientific literature for the unfavorable nutritional status of a given population, but the focus essentially comes down to one single problem-nutrient bioavailability. By far, the greatest factors that reduce the bioavailability of nutrients are those that diminish the intestine's absorption capacity. Even today, there is a growing consensus among nutritionists that the obstacle to better nutrition clearly lies in the efficient delivery of nutrients to the body. It is not what you eat that counts, it is what you absorb.

Bioperine improves bioavailability of ingredients in TestoBoost but it also has several other beneficial properties, including thermogenic effects, reducing cholesterol and protecting against neurodegeneration and cognitive impairment. As well, it has been shown that it may have immunomodulatory, anti-oxidant, anti-asthmatic, anti-carcinogenic, anti-inflammatory, anti-ulcer, and anti-amoebic properties.<sup>421422423424425426427</sup>

For current information on the beneficial effects of piperine as the trademark Bioperine go to <https://www.bioperine.com/index.php/aboutbioperine>.

## Arginine and Citrulline

Arginine, citrulline (alone and converted to arginine), and the BCAAs and other ingredients in TestoBoost, increase GH, IGF-I and insulin secretion and response, thus providing a synergistic

anabolic effect on muscle and canceling out insulin's lipogenic and anti-lipolytic effects. In other words, you get all the good anabolic and fat burning effects from the synergism and none of the bad.

Arginine and citrulline also increase nitric oxide formation, which is felt to have a beneficial effect on blood flow in muscle and thus enhance nutrient and oxygen delivery, buffering and the clearing of metabolic by products, and increasing protein synthesis.

Arginine has beneficial effects on exercise performance, protein synthesis, the immune system, increasing growth hormone levels, increasing insulin sensitivity, and serving as substrates for other amino acids, creatine, and polyamines.<sup>428</sup> As well, arginine (and thus citrulline) has been shown to work in concert with the BCAAs to improve performance.<sup>429</sup>

On a whole-body basis, synthesis of arginine occurs principally via the intestinal–renal axis, wherein epithelial cells of the small intestine, which produce citrulline primarily from glutamine and glutamate, collaborate with the proximal tubule cells of the kidney, which extract citrulline from the circulation and convert it to arginine, which is returned to the circulation. As a consequence, impairment of small bowel or renal function can reduce endogenous arginine synthesis, thereby increasing the dietary requirement.

Citrulline is made from ornithine and carbamoyl phosphate in one of the central reactions in the urea cycle. It is also produced from arginine as a byproduct of the enzymatic production of nitric oxide from the amino acid arginine, catalyzed by nitric oxide synthase.

Citrulline has several effects, including increasing ammonia clearance, increasing bicarbonate, ornithine, and arginine levels. However, it may have benefits that the other amino acids do not have and that are independent of its conversion to arginine.

Citrulline does have some advantages over arginine in that citrulline possesses a highly specific metabolism that bypasses splanchnic extraction because it is not used by the intestine or taken up by the liver. As such the absorption of citrulline from diet or supplementation, as well as the citrulline synthesized de novo in the kidneys and endothelial and immune cells, reaches higher levels in the

body than if arginine is used. It's estimated that less than 40% of dietary arginine reaches the systemic circulation compared to over 60 percent of citrulline.

As such oral citrulline can be used to deliver arginine to the systemic circulation and thus may provide all the benefits of oral arginine. As well, it's recently been shown that citrulline, while not used in the formation of proteins, stimulates protein synthesis in skeletal muscle through the mammalian target of rapamycin signaling pathway.<sup>430</sup>

Overall, studies suggest that citrulline supplementation (along with asparagine, which is in TestoBoost and is metabolized to malate thus giving the advantages of citrulline malate, which is also in TestoBoost) can boost athletic performance and enhance recovery in a number of ways. First and foremost is its ability to raise extracellular and intracellular levels of arginine. By eliminating the amino acid breakdown products of protein metabolism and augmenting the detoxifying capacity of liver cells in removal of ammonium and lactate from the blood citrulline decreases fatigue, enhances recovery and facilitates the shift from the catabolic training state to the post exercise anabolic state.<sup>431432433434435436437</sup>

However, even though citrulline has been praised in internet articles as superior to the use of arginine, that is not necessarily the case.



- One of the problems with using citrulline as against arginine is that energy is needed to synthesize arginine. Arginine is synthesized from citrulline in arginine and proline metabolism by the sequential action of the cytosolic enzymes argininosuccinate synthetase (ASS) and argininosuccinate lyase (ASL). In terms of energy, this is costly, as the synthesis of each molecule of argininosuccinate requires hydrolysis of adenosine triphosphate (ATP) to adenosine monophosphate (AMP), i.e., two ATP equivalents. In essence, taking an excess of arginine gives more energy by saving ATPs that can be used elsewhere, including fueling exercise.
- Citrulline on its own is unable to affect plasma insulin or growth hormone levels, a different story to that of increased arginine or ornithine.
- The use of arginine results in higher spikes of arginine in the body, giving increased biological effects, while citrulline results in more constant but lower levels of arginine in the body.

So, what's the answer? It seems that using both citrulline and arginine in the TestoBoost formulations allows the best of both worlds as far as the beneficial effects of arginine and citrulline, within certain limits.

## L-Citrulline Malate

**Citrulline Malate (CM)**, a mixture of citrulline and malate, was added for several reasons. Citrulline has several effects, including increasing ammonia clearance, increasing bicarbonate, ornithine, arginine, and citrulline levels. Malate, a tricarboxylic acid cycle (TCA) intermediate, has beneficial effects on energy metabolism mainly by facilitating aerobic ATP production through anaplerotic reactions.

Overall, studies suggest that citrulline malate supplementation can boost power and endurance athletic performance, enhance recovery by various pathways including direct effects on skeletal muscle function and contractile force, decreasing post-exercise muscle soreness, eliminating the amino acid breakdown products of protein metabolism and augmenting the detoxifying capacity of liver cells in removal of ammonium and lactate from the blood.<sup>438439440441442443444445446447448449450451452453454455</sup> These actions decrease fatigue, enhance recovery and facilitate the shift from the catabolic training state to the post exercise anabolic state.

Adding to the effect on energy metabolism is the presence of **arginine**, **glycine** and **methionine** in Amino. That's because creatine can be produced endogenously via a two-step process involving these three amino acids.

As well, the combination of arginine and glycine, along with the ketoisocaproic acid (GAKIC) that is formed from leucine, make up a trio that has been found to be a useful combination if used after exercise, and before doing any further exercise.<sup>456</sup>

## L-Arginine Alpha-Ketoglutarate

There's 250 mg of L-Arginine alpha-ketoglutarate in TestoBoost. While this compound has both its pluses and its minuses it has several important effects. There is evidence that alpha-ketoglutarate preserves muscle mass and acts as an efficient anticatabolic compound.<sup>457,458</sup> Addition of alpha-ketoglutarate to postoperative total parenteral nutrition prevented the decrease in muscle protein synthesis and free glutamine that usually occurs after surgery.<sup>459</sup> One study has found that an alpha-

ketoglutarate-pyridoxine complex may have some beneficial effects on human maximal aerobic and anaerobic performance.<sup>460</sup>

Thus, by ingesting AKG in sufficient quantities, the demand for muscle glutamine might ultimately be spared to some degree, thereby allowing muscle protein synthesis to proceed unhindered (e.g. such as during the muscle hypertrophic response which follows a resistance training workout) and reducing the catabolism of muscle tissue.

Studies have shown that:

1. AKG reduces the decline in muscle free glutamine that is associated with reductions in protein synthesis.<sup>461</sup>
2. The use of AKG, instead of glutamine, prevents the decline in protein anabolism observed following surgery.<sup>462</sup>

AKG seems to exert anti-catabolic effects by preserving muscle glutamine.<sup>463</sup> These results are not surprising in that the carbon skeleton of BCAAs can be used to synthesize glutamine after the transamination reaction of BCAAs, and ketoglutarate is the immediate carbon donor for glutamine synthesis. The utilization of arginine and ornithine as a carbon source for glutamine synthesis is also a possibility.

A study looked at the effects of L-arginine alpha-ketoglutarate (AAKG) on measures of body composition and performance.<sup>464</sup> Two separate studies were conducted to assess the pharmacokinetic profile of ingesting two forms of AAKG, timed released and non-timed release, in the blood (study 1) and the effects of dietary supplementation of AAKG on training adaptations in resistance-trained men (study 2).

The study found that the 2 formulations have different pharmacokinetic patterns that may affect arginine release, uptake, and/or physiologic effect over time. As well, the L-arginine alpha-ketoglutarate (AAKG) in both formulations positively influenced strength (as measured by one rep maximum bench press) and Wingate peak power performance.

Another study found that AAKG plus creatine supplementation are effective in improving upper body muscle endurance and improving peak power output on repeated Wingate tests.<sup>465</sup>

**Arginine** also has several beneficial health effects. If used in lower doses studies have shown that it does not increase nitric oxide (NO) but still has beneficial effects on protein synthesis, the immune system, increasing growth hormone levels, increasing insulin sensitivity, and serving as substrates for other amino acids, creatine, and polyamines.

## **Too Much Nitric Oxide Production Can Be Counter Productive**

**Recent research has shown the ergogenic effects of Increasing nitric oxide in the body. As used by bodybuilders and other athletes the use of nitric oxide inducing supplements and ingredients has some benefits in improving exercise tolerance and performance, as well as providing more of a pump when training. The overall impression given by the studies and articles is that increasing nitric oxide production over both the short and long term provides significant ergogenic effects.**

**its detrimental effects on testosterone makes the use of nitric oxide supplements containing one or more of large amounts of L-arginine, L-arginine precursors such as citrulline, nitrates and nitrites counterproductive for muscle hypertrophy, body composition and athletic performance.**

The amount of arginine and citrulline taken by supplementation is critical for its beneficial effects. Too much of arginine/citrulline/nitrites/nitrates can be counterproductive as long-term use of supplements that have excessive amounts of these nitric oxide producing ingredients leads to larger increases in nitric oxide in the testes, which results in decreased testosterone levels.

In higher doses, and especially if combined with nitrate/nitrite, arginine and citrulline increase NO formation and facilitates vasodilation, improves sexual functioning, and helps keep you cool during exercise.<sup>466, 467</sup>

But there is an important caveat. The ability of arginine/citrulline in higher doses, and especially if coupled with nitrates/nitrites, to increase nitric oxide is one of the reasons that T contains only 200 mg of arginine and 500 mg of L-citrulline in the form of citrulline malate. That's because excessive production of nitric oxide, whether through the exogenous use of significant amounts of one or more of arginine, citrulline, and nitrates/nitrites can result in both a decrease in muscle contraction and myotoxicity (negative effect on skeletal muscle),<sup>468, 469</sup> and more importantly a lowering of endogenous testosterone production since nitric oxide inhibits testicular Leydig cell steroidogenesis.<sup>470, 471</sup>

Since there is a hierarchy of effects depending on the substrate availability for NO production and the amount of NO produced, excessive amounts of substrates go beyond the beneficial endothelial

effects (increasing blood flow, oxygen, and nutrients to muscles thus increasing clearance of waste products and increasing protein synthesis) and result in long term counterproductive effects.

The nitric oxide (NO) signaling pathway has also been identified in testicular Leydig cells (the cells that produce testosterone) and is coupled to cGMP production.<sup>472, 473, 474</sup> This signaling system appears to act in opposition to modulate testicular steroidogenesis, providing stimulation at lower concentrations of nitric oxide and inhibition at higher concentrations mediated by the direct effect of

nitric oxide on the activities of steroidogenic enzymes.<sup>475, 476, 477</sup> Thus, lower levels of testicular nitric oxide can be beneficial for testosterone production, but higher levels are detrimental.

The reasons behind nitric oxides effects on testicular steroidogenesis are complex and this is not the place to go into all the details. However, we'll be devoting an entire article on this subject in the near future.

There's no doubt that increasing nitric oxide can lead to short term improvements in exercise tolerance and performance, as well as producing more of a pump when training. These effects that users feel when using the high dose NO products make for good marketing but bad science.

The overall impression given by supplement companies with NO products, and articles on the Internet, including some studies, is that significantly increasing nitric oxide production over both the short and long term provides anabolic and performance enhancing effects.

The bottom line, however, is that the detrimental effects of long term excessive nitric oxide on skeletal muscle and especially on testosterone makes the use of nitric oxide supplements containing one or more of large amounts of L-arginine, L-arginine precursors such as citrulline, nitrates and nitrites counterproductive for muscle hypertrophy, body composition and athletic performance.

It's also been shown that nitric oxide and D-aspartate are factors in the control of testosterone production in the testes, with D-aspartate increasing and nitric oxide decreasing testosterone production.<sup>478479</sup>

Normally I simply cite the references as endnotes but in the case of nitric oxide and D-aspartate I thought it would be useful for you to actually see not only the citations but the abstracts as well. As such I've included several from PubMed about both ingredients so you can see why I limit arginine/citrulline and increase the amount of d-aspartate in TestoBoost version VI.

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[Mol Cell Endocrinol](#). 2002 Aug 30;194(1-2):39-50.

## **Nitric oxide potently inhibits the rate-limiting enzymatic step in steroidogenesis.**

[Drewett JG](#), [Adams-Hays RL](#), [Ho BY](#), [Hegge DJ](#).

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### **Abstract**

This study tested the hypothesis that nitric oxide (NO) inhibits the rate-limiting catalytic step in steroidogenesis, cytochrome P450 cholesterol side-chain cleaving enzyme (CYP11A1), independent of soluble guanylyl cyclase (GC-S) stimulation. To assess CYP11A1 activity, pregnenolone levels were quantified in murine adrenocortical Y1 cells in the presence of the 3beta-hydroxy-Delta(5)-steroid dehydrogenase inhibitor, 2alpha-cyano-17beta-hydroxy-4,4',17alpha-trimethylandrosta-5-ene-3-one. The NO donor, (Z)-1-[2-(2-aminoethyl-N-(2-ammonioethyl)amino]diazene-1-ium-1,2-diolate(deta nonoate), inhibited vasoactive intestinal peptide-, forskolin- and 22alpha-hydroxycholesterol (22HC)-facilitated pregnenolonogenesis in the absence of GC-S activation and in the presence of a GC-S inhibitor, 1H-[1,2,4]oxadiazolo[4,3-a]quinoxalin-1-one (ODQ). CYP11A1 was also heterologously expressed in monkey COS7 cells. Deta nonoate inhibited 22HC-facilitated activity of the over-expressed enzyme in the absence of GC-S activation and in the presence of ODQ. The NO-independent, GC-S agonist, 1-benzyl-3-(5'-hydroxymethyl-2'-furyl)indazole did not inhibit steroidogenesis. The IC(50) for effects of free NO on CYP11A1 was potent and in the 0.4-2 microM range. **These results support the hypothesis that NO inhibits the rate-limiting enzyme in steroidogenesis independent of GC-S activation.**

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[Biol Reprod](#). 2010 Sep;83(3):434-42. Epub 2010 May 12.

## Testosterone-induced modulation of nitric oxide-cGMP signaling pathway and androgenesis in the rat Leydig cells.

[Andric SA](#), [Janjic MM](#), [Stojkov NJ](#), [Kostic TS](#).

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### Abstract

Testosterone, acting as a systemic and local factor, is one of the major regulatory molecules that initiate and maintain testicular function. In the present study, different experimental approaches were used to evaluate the role of testosterone in regulation of the nitric oxide (NO)-cGMP pathway in Leydig cells derived from normal and hypogonadotropic male rats treated with testosterone for 24 h and 2 wk. Real-time quantitative PCR and Western blot analysis revealed increased inducible NO synthase (NOS2) expression followed by increased NO secretion from Leydig cells ex vivo after continuous treatment with testosterone for 2 wk in vivo. The cGMP-specific phosphodiesterases Pde5, Pde6, and Pde9 were up-regulated, whereas PRKG1 protein was decreased after a 2-wk testosterone treatment. Induction of Nos2 and Pde5 in Leydig cells was blocked by androgen receptor antagonist. In experimental hypogonadotropic hypogonadism, expression of NOS2 was significantly reduced, and treatment with testosterone increased NOS2 expression above control levels. PDE5 protein level was unchanged in hypogonadal rats, whereas treatment of hypogonadal rats with testosterone significantly increased it. In contrast, hypogonadism and testosterone replacement reduced PRKG1 protein in Leydig cells. In vitro treatment with testosterone caused gradually increased Nos2 gene expression followed by increased nitrite and cGMP production by purified Leydig cells. **In summary, testosterone up-regulated NO signaling via increased NOS2 expression and contributed to down-regulation of cGMP signaling in Leydig cells. Thus, testosterone-induced modulation of NO-cGMP signaling may serve as a potent autocrine regulator of testicular steroidogenesis.**

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[Med Hypotheses](#). 2000 Oct;55(4):310-3.

## Is steroid deficiency the cause of tolerance in nitrate therapy?

[Panesar NS](#).

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### Abstract

The award of the Nobel Prize in Physiology and Medicine for 1998 bears witness to the 'explosive' field of nitric oxide (NO), and who would have thought the explosive nitroglycerin owed its therapeutic effectiveness to this little molecule? NO is also involved in causing penile erection, which has brought sildenafil to the aid of patients with erectile dysfunction. However, emerging evidence in animals and in vitro studies indicates that NO also inhibits steroidogenesis, which may have repercussions in humans. The decrease in androgen secretion may impact on secondary sexual characteristics, including penile size. The tolerance to the nitrate therapy in

angina, characterized by volume expansion and not due to sodium retention, may also be related to steroid hormone deficiency. Decreased cortisol secretion may impair water excretion, resulting in volume expansion. Impaired aldosterone secretion would cause hyponatraemia with resultant raised renin. **I hypothesize that continuous therapy with nitrates and sildenafil will result in diminished levels of steroid hormones with predicted sequelae.**

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[Toxicol Appl Pharmacol.](#) 2000 Dec 15;169(3):222-30.

## Decreased steroid hormone synthesis from inorganic nitrite and nitrate: studies in vitro and in vivo.

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### Abstract

Nitrites and nitrates are consumed nonchalantly in diet. Organic nitrates are also used as vasodilators in angina pectoris, but the therapy is associated with tolerance whose mechanism remains elusive. Previously, we found inorganic nitrate inhibited steroidogenesis in vitro. Because adrenocorticoids regulate water and electrolyte metabolism, tolerance may ensue from steroid deficiency. We have studied the effects of nitrite and nitrate on in vitro synthesis and in vivo blood levels of steroid hormones. In vitro, nitrite was more potent than nitrate in inhibiting human chorionic gonadotropin (hCG)-stimulated androgen synthesis by Mouse Leydig Tumor cells. At concentrations above 42 mM, nitrite completely inhibited androgen synthesis, and, unlike nitrate, the inhibition was irreversible by increasing hCG concentration. The cAMP production remained intact but reduced with both ions. The nitric oxide (NO) scavenger, 2-(4-carboxyphenyl)-4,4,5,5-tetramethylimidazoline-1-oxy-3-oxide (c-PTIO) significantly increased hCG- or cAMP-stimulated androgen synthesis in all buffers, suggesting that NO is a chemical species directly involved in the nitrite/nitrate-induced inhibition. This is further supported by c-PTIO countering the inhibitory action of methylene blue on androgen synthesis. Rats given distilled water containing 50 mg/L NaNO(2) or NaNO(3) for 4 weeks drank significantly less daily. At the end, their blood corticosterone and testosterone levels were significantly decreased. The adrenocortical histology showed bigger lipid droplets, which are pathognomonic of impaired steroidogenesis. **Nitrite and nitrate are metabolized to NO, which binds heme in cytochrome P450 enzymes, thereby inhibiting steroidogenesis. Therapeutic nitrates likewise may decrease adrenal (and gonadal) steroidogenesis.** Cortisol deficiency would impair water excretion causing volume expansion, and aldosterone deficiency would cause sodium loss and raised renin. Paradoxically, volume expansion without sodium retention and raised renin has all been reported in tolerance.

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[Theriogenology.](#) 2007 Jan 15;67(2):249-54. Epub 2006 Sep 22.

## D-Aspartic acid and nitric oxide as regulators of androgen production in boar testis.

[Lamanna C](#), [Assisi L](#), [Vittoria A](#), [Botte V](#), [Di Fiore MM](#).

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### Abstract

D-Aspartic acid (D-Asp) and nitric oxide (NO) are two biologically active molecules playing important functions as neurotransmitters and neuromodulators of nerve impulse and as regulators of hormone production by endocrine organs. We studied the occurrence of D-Asp and NO as well as their effects on testosterone synthesis in the testis of boar. This model was chosen for our investigations because it contains more Leydig cells than other mammals. Indirect immunofluorescence applied to cryostat sections was used to evaluate the co-localization of D-Asp and of the enzyme nitric oxide synthase (NOS) in the same Leydig cells. D-Asp and NOS often co-existed in the same Leydig cells and were found, separately, in many other testicular cytotypes. D-Asp level was dosed by an enzymatic method performed on boar testis extracts and was  $40 \pm 3.6$  nmol/g of fresh tissue. NO measurement was carried out using a biochemical method by NOS activity determination and expressed as quantity of nitrites produced: it was  $155.25 \pm 21.9$  nmol/mg of tissue. The effects of the two molecules on steroid hormone production were evaluated by incubating testis homogenates, respectively with or without D-Asp and/or the NO-donor L-arginine (L-Arg). After incubation, the testosterone presence was measured by immunoenzymatic assay (EIA). **These in vitro experiments showed that the addition of D-Asp to incubated testicular homogenates significantly increased testosterone concentration, whereas the addition of L-Arg decreased the hormone production.** Moreover, the inclusion of L-Arg to an incubation medium of testicular homogenates with added D-Asp, completely inhibited the stimulating effects of this enantiomer. Our results suggest an autocrine action of both D-Asp and NO on the steroidogenic activity of the Leydig cell.

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### D-Aspartate

D-aspartate (D-Asp) was increased to 1.2 grams per dose for two reasons. First of all, aspartate has been shown to increase reproductive function and testosterone production in murine and human models.<sup>480481482483484485</sup> A study set up to see if a relationship exists between the presence of D-Asp and the hormonal activity<sup>486</sup> had the following results:

- 1) Both D-Asp and testosterone are synthesized in rat testes in two periods of the animal's life: before birth, about the 17th day after fertilization and, after birth, at sexual maturity.
- 2) Immunocytochemical studies have demonstrated that this enantiomer is localized in Leydig and Sertoli cells.
- 3) In vivo experiments, consisting of i.p. injection of D-Asp to adult male rats, demonstrated that this amino acid accumulates in pituitary and testis (after 5 h, the accumulation was of 12 and 4-fold over basal values, respectively); simultaneously, luteinizing hormone, testosterone and progesterone significantly increased in the blood.

4) Finally, in vitro experiments, consisting of the incubation of D-Asp with isolated testes also demonstrated that this amino acid induces the synthesis of testosterone.

**Recent studies have shown that D-Asp has similar effects in man in that it has a role in the regulation and physiological levels of luteinizing hormone and testosterone.**<sup>487</sup>

For the full PDF version of the latter study go to

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2774316/pdf/1477-7827-7-120.pdf>.

**D-aspartate also increases growth hormone levels and has significant metabolic effects, including AMP production, improving the salvage of ATP from in muscle cells, and acts as an anaplerotic precursor and thus increases TCA flux and ATP formation. This aids in the synthesis of hormones, including testosterone and growth hormone.**<sup>488</sup>

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[J Endocrinol Invest.](#) 2016 Feb;39(2):207-13. doi: 10.1007/s40618-015-0333-4. Epub 2015 Jun 28.

## **D-Aspartic acid stimulates steroidogenesis through the delay of LH receptor internalization in a mammalian Leydig cell line.**

[Di Nisio A<sup>1</sup>](#), [De Toni L<sup>1</sup>](#), [Ferigo M<sup>2</sup>](#), [Rocca MS<sup>1</sup>](#), [Speltra E<sup>1</sup>](#), [Ferlin A<sup>1</sup>](#), [Foresta C<sup>3</sup>](#).

[Author information](#)

### **Abstract**

#### **PURPOSE:**

Recent experimental evidence on non-mammalian animal models showed that D-Aspartic acid (d-Asp) administration increases testosterone levels through upregulation of StAR in Leydig cells. In this study, we aimed to investigate in vitro the signaling pathway associated with d-Asp stimulation in MA-10 murine Leydig cells.

#### **METHODS:**

MA-10 cells were stimulated with different concentrations of d-Asp, in presence or absence of hCG. Then total testosterone (T) levels in the culture medium were evaluated by electrochemiluminescence immunoassay, and StAR and LHR protein expressions were quantified by the means of Western blotting. LHR cellular localization after hormonal stimulation was assessed by immunofluorescence.

#### **RESULTS:**

Stimulation with the sole d-Asp did not induce any relevant increase of T release from cultured cells. On the other hand, stimulation with hCG induced significant increase of T ( $P = 0.045$ ). Concomitant stimulation with hCG and d-Asp, at the concentration of 0.1 and 1 nM, induced additional and significant increase of released T ( $P = 0.03$  and  $P = 0.04$ , respectively). StAR protein levels increased after concomitant stimulation with hCG and d-Asp 0.1 nM, compared with stimulation with the sole hCG ( $P = 0.02$ ), whereas no variation in LHR protein expression was observed. Finally, d-Asp attenuated displacement of LHR staining, from cell membrane to cytoplasm, subsequent to hCG stimulation.



**CONCLUSIONS:**

In this study, we confirmed a steroidogenic role for d-Asp, in concert with hCG, on murine Leydig cells, which is mediated by an increase in StAR protein levels. In addition, we showed that the possible mechanism subtending the effect of d-Asp could rely on the modulation of LHR exposure on the cell membrane.

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[Reprod Biol Endocrinol.](#) 2009 Oct 27;7:120.

## **The role and molecular mechanism of D-aspartic acid in the release and synthesis of LH and testosterone in humans and rats.**

[Topo E](#), [Soricelli A](#), [D'Aniello A](#), [Ronsini S](#), [D'Aniello G](#).

**Source**

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**Abstract****BACKGROUND:**

D-aspartic acid is an amino acid present in neuroendocrine tissues of invertebrates and vertebrates, including rats and humans. Here we investigated the effect of this amino acid on the release of LH and testosterone in the serum of humans and rats. Furthermore, we investigated the role of D-aspartate in the synthesis of LH and testosterone in the pituitary and testes of rats, and the molecular mechanisms by which this amino acid triggers its action.

**METHODS:**

For humans: A group of 23 men were given a daily dose of D-aspartate (DADAVIT) for 12 days, whereas another group of 20 men were given a placebo. For rats: A group of 10 rats drank a solution of either 20 mM D-aspartate or a placebo for 12 days. Then LH and testosterone accumulation was determined in the serum and D-aspartate accumulation in tissues. The effects of D-aspartate on the synthesis of LH and testosterone were gauged on isolated rat pituitary and Leydig cells. Tissues were incubated with D-aspartate, and then the concentration (synthesis) of LH and cGMP in the pituitary and of testosterone and cAMP in the Leydig cells was determined.

**RESULTS:**

In humans and rats, sodium D-aspartate induces an enhancement of LH and testosterone release. In the rat pituitary, sodium D-aspartate increases the release and synthesis of LH through the involvement of cGMP as a second messenger, whereas in rat testis Leydig cells, it increases the synthesis and release of testosterone and cAMP is implicated as second messenger. In the pituitary and in testes D-Asp is synthesized by a D-aspartate racemase which convert L-Asp into D-Asp. The pituitary and testes possesses a high capacity to trapping circulating D-Asp from hexogen or endogen sources.

**CONCLUSION:**

**D-aspartic acid is a physiological amino acid occurring principally in the pituitary gland and testes and has a role in the regulation of the release and synthesis of LH and testosterone in humans and rats.**

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[Brain Res Rev.](#) 2007 Feb;53(2):215-34. Epub 2006 Nov 21.

## **D-Aspartic acid: an endogenous amino acid with an important neuroendocrine role.**

[D'Aniello A](#).

**Source**

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**Abstract**

D-Aspartic acid (d-Asp), an endogenous amino acid present in vertebrates and invertebrates, plays an important role in the neuroendocrine system, as well as in the development of the nervous system. During the embryonic stage of birds and the early postnatal life of mammals, a transient high concentration of d-Asp takes place in the brain and in the retina. d-Asp also acts as a neurotransmitter/neuromodulator. Indeed, this amino acid has been detected in synaptosomes and in synaptic vesicles, where it is released after chemical (K<sup>+</sup>) ion, ionomycin) or electric stimuli. Furthermore, d-Asp increases cAMP in neuronal cells and is transported from the synaptic clefts to presynaptic nerve cells through a specific transporter. In the endocrine system, instead, d-Asp is involved in the regulation of hormone synthesis and release. For example, in the rat hypothalamus, it enhances gonadotropin-releasing hormone (GnRH) release and induces oxytocin and vasopressin mRNA synthesis. In the pituitary gland, **it stimulates the secretion of the following hormones: prolactin (PRL), luteinizing hormone (LH), and growth hormone (GH)** In the testes, it is present in Leydig cells and is **involved in testosterone and progesterone release.** Thus, a hypothalamus-pituitary-gonads pathway,

in which d-Asp is involved, has been formulated. In conclusion, the present work is a summary of previous and current research done on the role of d-Asp in the nervous and endocrine systems of invertebrates and vertebrates, including mammals.

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[Life Sci.](#) 1996;59(2):97-104.

### **Involvement of D-aspartic acid in the synthesis of testosterone in rat testes.**

[D'Aniello A](#), [Di Cosmo A](#), [Di Cristo C](#), [Annunziato L](#), [Petrucci L](#), [Fisher G](#).

#### **Source**

Department of Biochemistry, Zoological Station of Naples, Italy.

#### **Abstract**

D-Aspartic acid (D-Asp) is an endogenous amino acid which occurs in many marine and terrestrial animals. In fetal and young rats, this amino acid occurs prevalently in nervous tissue, whereas at sexual maturity it occurs in endocrine glands and above all in pituitary and testes. Here, we have studied if a relationship exists between the presence of D-Asp and the hormonal activity. The following results were obtained: 1) Both D-Asp and testosterone are synthesized in rat testes in two periods of the animal's life: before birth, about the 17th day after fertilization and, after birth, at sexual maturity. 2) Immunocytochemical studies have demonstrated that this enantiomer is localized in Leydig and Sertoli cells. 3) In vivo experiments, consisting of i.p. injection of D-Asp to adult male rats, demonstrated that this amino acid accumulates in pituitary and testis (after 5 h, the accumulation was of 12 and 4-fold over basal values, respectively); simultaneously, luteinizing hormone, testosterone and progesterone significantly increased in the blood (1.6-fold,  $p < 0.05$ ; 3.0-fold,  $p < 0.01$  and 2.9-fold,  $p < 0.01$ , respectively). 4) Finally, in vitro experiments, consisting of the **incubation of D-Asp with isolated testes also demonstrated that this amino acid induces the synthesis of testosterone. These results suggest that free D-Asp is involved in the steroidogenesis.**

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## **What Can You Expect from TestoBoost version VI?**

First, let me be clear about **what you can't expect** from using TestoBoost version VI and that's the same effect as using moderate to high doses of anabolic steroids, including exogenous testosterone. The use of these hormones will raise the level of androgenic-anabolic hormones significantly above physiological levels, while at the same time shutting down the production of endogenous testosterone. TestoBoost won't do that.

What TestoBoost will do is ramp up your testosterone production from the ground up so that all normal pathways are accentuated and none are shut down. We've already covered the ways that TestoBoost will do this. What we haven't discussed is what you can expect from its use.

The new TestoBoost version VI can double levels of free testosterone in those who have levels that are in the low normal range. Those who have testosterone levels in the high normal range generally get less of an effect, in many cases only increasing free testosterone levels by 15% or less. There are exceptions and I've seen TestoBoost increase testosterone levels to 10-20% above the upper limit of the normal range, but suprphysiological levels, while they occur are not the norm.

TestoBoost is especially effective in those who have depressed testosterone levels for a variety of reasons, including stress, training intensity and duration (see two abstracts below), and illness.

Considering all the testing I've done/supervised in the past 2 decades on people using TestoBoost this is what can be expected from its use.

- **Men with low or below normal levels can expect an increase in free testosterone that can put them up as far as the mid normal range – the increase can be anywhere from 15% to 200% depending on the initial levels.**
- **Men with mid-range testosterone levels can usually expect a 15 to 50% increase in free testosterone levels.**
- **Men in the high normal range can expect up to a 15% increase in free testosterone levels.**
- **In men with testosterone levels below the normal range the results are extremely variable, from no effect at all to raising free testosterone levels up to the mid normal range. The variability results from the many reasons that testosterone levels can plummet below normal levels.**
- **In women, the results are also extremely variable and can result in minimal effects (5-10% increase) up to a doubling of free testosterone levels.**

## Health Benefits and Protective Effects of TestoBoost

Although TestoBoost is formulated to increase testosterone levels and enhance anabolism, it's also formulated to provide substantial health benefits. For example, it has several ingredients, including **saw palmetto (serenoa repens)**, **zinc**, **quercetin**, **GLA** (in **borage oil**) and **stinging nettle** that enhance prostate health in males, and provide anti-inflammatory effects in both males and females.

Some of these ingredients also decrease the formation of dihydrotestosterone from testosterone,<sup>489</sup> thus maximizing testosterone levels while at the same time decreasing the adverse effects of higher systemic and tissue levels of dihydrotestosterone, which includes adverse effects on the prostate and hair loss.<sup>490</sup>

TestoBoost also contains several potent antioxidants, such as **alpha lipoic acid**, **beta carotene**, **vitamin C**, **vitamin E**, **Coenzyme Q10**, **turmeric**, **lycopene**, and **astaxanthin**, which act to improve pituitary and testicular/ovarian function, and decrease the adverse effects of free radicals on the hypothalamic-pituitary-testicular/ovarian axis, and the associated pathways that are responsible for maximizing endogenous testosterone production.

For example, one study has found that vitamin E and vitamin C protect the testes from damage secondary to oxidant damage.<sup>491</sup> Alpha lipoic acid (ALA), because it is a Sulphur compound, can bind and help eliminate heavy metals such as copper, iron, mercury and cadmium, all of which can cause oxidant damage to the gonads (testes and ovaries).

Alpha lipoic acid (ALA) has a double antioxidant effect as it has significant antioxidant properties on its own, but also regenerates glutathione, the most important endogenous antioxidant. ALA and glutathione have been shown to have significant effects in decreasing mercury toxicity in the body.<sup>492</sup>

Forskolin alone and the combination of forskolin and antioxidants in TestoBoost impact on Leydig cell function (these are the testicular cells that make testosterone) and result in combating the normal decrease in testosterone seen with various toxins, aging and stress.<sup>493494</sup> Forskolin, along with increasing serum testosterone has also been shown to help lose body fat and improve body composition.<sup>495</sup>

TestoBoost also contains several other vitamins, minerals and nutrients that are important for optimizing testosterone levels. These include **vitamin A, vitamin B6, vitamin B12, niacin, calcium, magnesium, manganese, boron, zinc, ginger and Coenzyme Q10.**

**The bottom line** is that TestoBoost version VI is the most effective testosterone booster on the market today. And although it doesn't contain any prohormones, which can have significant side effects, it surpasses any prohormone formulation in increasing testosterone levels and in providing several benefits including potent anabolic, anticatabolic and fat burning effects.

## NitAbol

If increasing your anabolic drive and maximizing muscle mass while minimizing body fat is important to you, check out [NitAbol](#), the nighttime anabolic, fat burning combo that combines [TestoBoost](#) with [GHboost](#) and [Myosin Protein](#).

NitAbol is also perfect for those who want to lose weight but would prefer to maintain the muscle they have and strictly lose body fat. In this case, I'd also recommend that you use [LipoFlush](#) as the ultimate fat loss supplement. Information on all these supplements can be found on my website at <https://metabolicdiet.com/shop/>.

TestoBoost also works synergistically with GHboost and Metabolic to provide the full spectrum of metabolic and hormonal optimization. The combo of all three is available at a discount as the [Hormonal Enhancement Combo](#).

And TestoBoost also works additively and synergistically with [GHboost](#) and [LipoFlush Extreme](#) or [LipoFlush Competition](#) for the optimization of body composition and mental and physical performance.

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