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Increasing Circulating Testosterone: Impact of Herbal Dietary Supplements

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Abstract

Low circulating testosterone levels can present numerous problems related to the overall health and well-being of individuals, men in particular. This finding is well-documented in the literature and low testosterone appears more prevalent in older men, in particular those who are physically inactive and who present with elevated levels of body fat. Multiple botanical (herbal) products have been claimed to elevate circulating testosterone in men; however, data pertaining to the use of such herbal preparations obtained from human clinical trials are limited. This review examines the research to date pertaining to the use of herbal ingredients with regards to their ability to elevate blood testosterone levels. A collective summary of the findings indicate that certain herbal supplements may actually yield an increase in testosterone (e.g., *Longjack* root), while most others have little to no evidence in support of their use in human subjects. Additional, well-controlled clinical trials are needed to generate data relative to the use of herbal dietary supplements to increase circulating testosterone.

Overview of Herbal Dietary Supplements

Plants having medicinal or therapeutic properties which are marketed and used to maintain or improve health are frequently referred to as herbal products, botanical products, or phytomedicines. The practice of utilizing plant-based products to aid in the overall health status of an individual has been commonplace for thousands of year [1-4]. Specifically, herbal supplementation is thought to potentially remedy a large range of ailments and/or diseases such as diabetes [5], cardiovascular disease [6,7], chronic liver disease [8,9], eye diseases [10], and prostate disease [11,12]. The use of herbal products worldwide has experienced exponential growth since the 1970's. Recent estimates indicate that approximately half (49%) of all US adults partake in some form of dietary supplementation [13], often involving herbal products. Investigations have been conducted on the effectiveness of herbal supplementation over a wide range of applications including: pregnancy [14], obesity [15], depression [16], and physical performance [17], as well as involving herbal supplementation to treat various diseases [8,10,11,18].

In recent years, a wealth of research has surfaced focused primarily on the effects of herbal supplementation in relation to altering specific hormone concentrations [17,19,20-22]. More precisely, this area of research aims to delineate whether certain herbal ingredients have properties that may enhance the body's ability to produce these hormones naturally. The potential benefits of utilizing botanical supplements as a means to increase specific hormone concentrations in individuals who are deficient are numerous, and may be considered a highly desirable form of treatment as compared to pharmaceuticals. In theory, the natural make-up of herbal ingredients may potentially lessen certain side effects many people face when taking synthetic medications, while achieving favorable results. In addition, instead of receiving exogenous sources of specific hormones when levels are low, these herbal supplements may naturally improve the body's ability to synthesize the hormone being targeted.

Specifically, testosterone and growth hormone (GH) have been highlighted as two of the primary focal points in this area of research [23-27]. Both testosterone and GH levels are known to decline in humans with aging, leading to a host of undesirable effects such as a decrease in metabolism, sex drive, bone density, muscle mass, and appetite, as well as outlook on life-all factors that may greatly impact the quality of life and in some cases be life-threatening [27-31].

A multitude of herbal ingredients have been claimed to increase, or potentially increase, levels of these hormones in the body. These include but are not limited to: astragalus root (***Astragalus membranaceus***) [32-34], Chinese yam[35], Greek hay (***fenugreek seed extract***) [36], ***barrenwort (herba epimedium)*** [37], ***Longjack*** root (***eurycoma longifolia***) [38,39], passionflower extract (***passiflora incarnate***) [22,40], velvet bean extract (mucuna pruriens) [41-43], ginkgo biloba [44,45], ginseng [46,47], and tribulus terrestris [17,24,48]. Several of these ingredients have been studied in great detail with regards to impacting testosterone and GH concentrations, while others have only scant research investigating their efficacy.

Following a brief overview of testosterone, the present review is focused on the influence of botanical agents in relation to testosterone concentrations. While the bulk of the discussion is centered on herbal ingredients, some recently studied dietary ingredients which are not considered botanicals (e.g., D-aspartic acid [DAA] [26,49], are included for discussion.

Testosterone Overview

Testosterone, a steroid hormone from the androgen group, is naturally produced in the body and is secreted primarily from the Leydig cells of the testes in men (> 95%) [50,51] and to a lesser extent in the theca cells of the ovaries in women, the zona reticularis of the adrenal cortex, and the skin [52]. In men, testosterone is the principle sex hormone and plays a critical role in the development of reproductive tissues and promotion of secondary sex characteristics such as muscle growth and strength, bone mass, and growth of body hair [51]. While testosterone production is significantly higher in men than in women, the hormone is important in the health and well-being [29-31] of both men and women and plays a vital role in preventing osteoporosis [53,54].

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Testosterone is generally measured as either "free" (unbound) or "total" (unbound and chemically bound). Men who have a morning serum testosterone level < 300 ng/dL are considered to be "low" and may be a candidate for testosterone replacement therapy—which has become more common in recent years due to the increased diagnosis of andropause [55]. Insufficient levels of testosterone due to either impaired production or uptake can present serious health consequences due to the wide array of applications of testosterone within the human body. Areas including skeletal muscle health, muscular strength, and overall well-being/vitality seem to be significantly affected by testosterone status.

The role of testosterone in muscle growth has been investigated extensively in both humans and animals [56-62]. One study in men concluded that the testosterone-induced increase in muscle volume is due to muscle fiber hypertrophy [63]. A follow-up study conducted a year later noted muscle hypertrophy in men over a period of 20 weeks of treatment with a gonadotropin-releasing hormone agonist and a 125-, 300-, or 600-mg weekly dose of testosterone enanthate. The main findings from this study indicated that testosterone administration was associated with a significant increase in myonuclear number in men receiving the 300- and 600-mg doses.

Muscular strength is another important factor that has been shown to be affected by testosterone levels in the body [56,61,62,64- 66]. A recent investigation utilized 267 men with stages 2-4 of Chronic Kidney Disease to assess the impact of testosterone level on a variety of variables [64]. This study found that testosterone was significantly and independently associated with handgrip strength, muscle mass, and nutritional status as the disease progressed. Another study explored short-term testosterone administration via intramuscular injections in elderly men and found that testosterone increased skeletal muscle strength and protein synthesis [62]. This suggests that synthesis of new structural proteins and/or preferential breakdown of older, less functional proteins can enhance muscle strength. Additional studies have administered testosterone supplementation in the form of gel and/ or a patch and noted similar findings in increased muscular strength [65,66].

Testosterone also seems to have a direct effect on overall well-being and vitality. A recent study of 274 men randomized to either T/gel® or placebo gel noted that those in the T/gel® group had improved body composition, quality of life, and physical function [65]. Another study randomized 227 men to either a 50 mg/day of T/gel®, 100 mg/day of T/gel® or a T patch and found that increases in sexual function, mood, muscle strength, and body composition were positively correlated with an increase in testosterone levels [66].

Methods of Increasing Testosterone

Acute Exercise

There are several methods currently known to stimulate an increase of testosterone *in vivo*. The effects of acute exercise on testosterone stimulation have produced mixed results over the past few decades [67-70]. For example, a study investigating acute hormonal responses in elite junior Weightlifters found that the exercise protocol utilized caused a significant increase in serum testosterone, cortisol, GH, and whole blood lactate as compared to pre-exercise measures [68]. Interestingly, upon subsequent analysis, it was found that while not significantly older, subjects with >2 years training experience exhibited significant exercise-induced increases in serum testosterone from pre exercise to 5 minutes post-exercise. Subjects with ≤2 years of training, on the other hand, showed no significant exercise-induced testosterone

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differences during this time period, suggesting that training experience and/or level of physical fitness may play a significant role in increasing testosterone levels in response to acute exercise. A recent study found that testosterone levels increased in both young (n=10) and middle-aged (n=8) men in response to acute, moderate intensity resistance exercise [67]. The results of another study indicated that serum testosterone levels were unchanged in men aged 55-70 years after a single bout of acute resistance exercise, despite an 18-fold increase in GH [70]. Linnamo *et al.*, investigated the effects of maximal heavy resistance exercise on testosterone and GH levels in both men and women and found that GH increased in both genders while testosterone levels increased only in men following exercise [69]. Due to differing subject criteria and variations in research design in these studies, it is difficult to pinpoint the exact reason for which mixed results were obtained. It is clear that additional research in this area is needed, as there is very likely a specific mechanism responsible for the increased levels of testosterone noted in response to acute exercise.

Pharmaceuticals

Aside from exercise, a wide array of pharmaceuticals are also currently available that claim to dramatically increase circulating testosterone levels. Examples of common testosterone treatments include gels (Androgel ®, Testim®) [71,72], skin patches (Androderm) [73], mouth patches (Striant) [74], injections [75] and implants (Testopel) [76]. Men who present with low testosterone and also display specific symptoms such as chronic fatigue, depression, and irritability may wish to partake in one of these treatments. However, as with all drugs, testosterone therapy may carry with it unwanted side-effects and because long-term risks have not been extensively studied for all current treatments within human subjects, caution should be taken prior to beginning a program of testosterone replacement. This may be particularly true for injectable and oral forms of testosterone which have been used for decades [77-79]. Generally, these products are attractive to bodybuilders and other athletes, but may be less widely used by the average man who may be deficient in testosterone.

Nutrient Intake

Nutritional interventions have been suggested as a natural

method to favorably increase low testosterone levels. However, few studies have analyzed the effects of varying the dietary ***macro***nutrient content in an attempt to raise testosterone levels. One recent study in our lab investigated alterations in macronutrient content and meal size in relation to the hormonal response during the acute postprandial period [80]. Results from this study indicated that regardless of meal size or macronutrient content, testosterone levels decreased immediately following the meal. Similar and mixed results have been reported for testosterone in other studies examining chronic dietary interventions that manipulate macronutrient content [81-83]. From a collective review of literature pertaining to the influence of macronutrient mix on circulating testosterone, it appears that increased carbohydrate intake [84] and increased saturated fat intake [85] yield increases in testosterone. Of course, individuals need to consider the overall importance of these findings in the context of their collective dietary goals. That is, some individuals may opt to reduce the overall carbohydrate and saturated fat load in an attempt to improve metabolic health. If so, altering this plan in the hopes of increasing circulating testosterone may not be acceptable. Each individual will need to determine what is best for them. Clearly, additional research is needed to determine the optimal dietary pattern with regards to overall health, including hormonal health.

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The manipulation of dietary ***micro***nutrient content has also been investigated in relation to circulating testosterone. A deficiency in zinc, which is prevalent throughout the world, has been associated with hypogonadism in men. One study found that zinc supplementation for 6 months in marginally zinc-deficient elderly men resulted in an almost two-fold increase in serum testosterone levels [86]. The same study also found that young men who underwent dietary zinc restriction for a period of 20 weeks had a significant reduction in serum testosterone levels. The study concluded that zinc may play an important role in modulating serum testosterone levels in normal men. Recent studies have affirmed what seems to be a distinct relationship between zinc and selenium in regard to testosterone, in which the direct mechanism is still unknown [87,88]. In addition, the effects of vitamin D on testosterone level have been investigated in both animal [89] and human models [90,91]. Findings from these studies confirm that vitamin D seems to have a direct positive relationship with total testosterone levels and further research is warranted to elucidate the mechanisms of action related to this finding. Vitamin C [92], boron [93], conjugated linoleic acid [84,95], and magnesium [96] are other micronutrients of interest as pertaining to testosterone. Preliminary studies have indicated that these micronutrients may play a role in mediating testosterone levels. However, research in this area is relatively scarce and additional studies need to be conducted to further contribute to our present knowledge base.

Non-Herbal Dietary Supplements

Currently, there are a variety of dietary supplements on the market reported to increase testosterone levels. In particular, these supplements involve either pure single-ingredients or multi-ingredient formulas. With regards to single ingredient supplements, D-aspartic acid (DAA) is likely the most widely discussed and utilized. This amino acid has been studied extensively in animals for its ability to increase testosterone and improve associated outcomes. However, only two published studies to our knowledge have investigated the lone use of DAA in human subjects, with mixed results [49,97].

Derived from arginine, DAA was first discovered in 1827 by Plissan in asparagus juice. Two forms of aspartic acid exist in “L-aspartic acid” and “D-aspartic acid” and appear to have different functions. L-aspartic acid is directly incorporated into proteins and used as a building block while its enantiomer, DAA, is more limited and is currently being marketed and investigated for its potential ability to increase testosterone levels. D-aspartic acid occurs naturally within all animals, but in much lower amounts than L-aspartic acid [98]. DAA appears to have an important neuroendocrine role that may impact testosterone levels due to its ability to stimulate the release of sex hormones from the pituitary gland and testes in animals. An **in vitro** experiment from over a decade ago, involving the incubation of DAA with isolated rat testes, demonstrated that DAA induces the synthesis of testosterone [99]. **In vivo** experiments in this study, consisting of an intraperitonial injection of DAA in adult male rats, demonstrated that this amino acid accumulates in both the pituitary gland and testis (after 5 h, the accumulation was of 12- and 4-fold over basal values, respectively). The study concluded that DAA is involved in steroidogenesis. Additional studies using rodents have found similar results [100,49].

Studies of DAA involving human subjects are scarce. In the first published study, Topo and colleagues found that testosterone levels were significantly elevated in response to DAA supplementation [49]. Forty-three healthy male volunteers were divided into two groups and the subjects of the experimental group (n=23) were given a 10 ml 2.0 M solution of sodium D-aspartate solution in the morning with breakfast

for 12 days. As indicated via blood samples, testosterone levels in the experimental group were significantly elevated following 6 days and 12 days of DAA treatment. In this same study, the perceived mechanism of action was evaluated using the rat model and it was noted that DAA regulates the synthesis of testosterone in the pituitary and the testis. It is believed that this action is mediated within the pituitary by cGMP and within the testis by cAMP, which act as second messengers in the signal transduction pathway in these tissues.

In contrast to the above findings, Willoughby ***et al.*** found that both free and total testosterone levels were unchanged in 20 healthy men over a four-week period [97]. Subjects in this study ingested 3 grams of DAA daily while also partaking in a resistance training protocol. One important note from this study was the average age of the subjects (22.8 ± 4.67), which may have had an influence on the overall change in testosterone levels. That is, younger men in this study presented with moderate levels of testosterone and this may have dampened the ability of DAA to yield an increase, in particular as compared to those subjects tested in the study of Topo and colleagues [49]. It is possible that a higher dosage of DAA may be necessary to bring about an increase in testosterone. Indeed, studies concerning DAA in humans are scarce and dosages may vary in future studies in an attempt to determine what might be optimal for both efficacy and safety. Pertaining to the latter, we are unaware of reports of adverse outcomes in

humans ingesting up to 3 grams of DAA per day.

Willoughby *et al.* also studied DAA within a mixed dietary supplement referred to as N-methy-D-Aspartate (NMDA). NMDA is an alleged testosterone-boosting supplement that contains a blend of DAA, *Longjack* root, and velvet bean extract; all of which have been shown to increase testosterone levels in rats. The investigators found that both free and total serum testosterone levels were unaffected by 28 days of NMDA supplementation [26]. We are presently completing a study in our lab involving DAA supplementation, which should provide additional evidence for or against the use of this amino acid for purposes of testosterone elevation.

Herbal Agents and Testosterone

Supplements containing astragalus root (*Astragalus membranaceus*) [32-34], Chinese yam [35], Greek hay (*fenugreek seed extract*) [36], *barrenwort (herba epimedium)* [37], velvet bean extract (*mucuna pruriens)* [41-43], *ginkgo biloba* [44,45], *ginseng* [46,47], passionflower extract (*passiflora incarnate*) [22,40,101], *Longjack* root (*eurycoma longifolia*) [38,39,102], and *tribulus terrestris* [17,24,48] are all touted to have health benefits and to increase testosterone levels. Of these, *Longjack* root and tribulus terrestris are of particular interest in the research community and will be explored in greater detail throughout the remainder of this review.

Astralagus root is a traditional Chinese herb used primarily for overall healing and, in particular, the treatment of diabetes. The root is the medicinal component of the plant and is harvested specifically from 4-year-old plants. Although historically claimed to boost testosterone, there are currently no studies to our knowledge that specifically examine the effect of *astragulus root* on testosterone levels.

The Chinese yam has also been touted to increase testosterone levels. Studies have utilized the Chinese yam in unison with a mixture of other ingredients and found testosterone levels to be increased in animals [103]. However, like *astragalus root*, studies utilizing human subjects are nonexistent at this point, at least to our knowledge.

Fenugreek is found primarily in Middle Eastern countries

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Afghanistan and Iran and has been used for centuries as a food source and also for its nutritional profile. A recent study utilizing fenugreek in resistance trained males (n = 45) found that it did not affect hormonal status and showed no anabolic potential [36]. Because the subject population of this study consisted of young college-aged males (21.4 ± 2.95) it may be beneficial to conduct a follow-up study utilizing older men. Another study found that a fenugreek formulation improved certain aspects of libido and quality of life in a sample of healthy men [104]. Potential mechanisms explaining an increase in testosterone due to fenugreek supplementation are currently unknown and may be explained to a greater extent providing future research is conducted in this area. Based on the limited data, it appears that fenugreek may offer some benefits but additional work is needed to extend the current findings.

Barrenwort is another herbal agent that warrants further investigation in human studies. A recent animal study noted increased testosterone levels in rats treated with epimedium herb extract for a period of eight weeks, as compared to a control group consisting of a high-fat dietary intervention [37]. These findings were similar to a separate group of rats who received testosterone undecanoate for the same eight week period.

The velvet bean is native to Africa and Asia and is utilized for a range of medicinal properties including the treatment of snakebites [105] and Parkinson's disease [106]. Recently, a study was conducted to investigate the effects of *Mucuna pruriens* on raising testosterone levels in Wister male albino rats (n = 18), noting positive results [41]. Specifically, the study concluded that after a 30-day treatment of velvet bean seed extract, both serum and testicular testosterone levels were significantly elevated-a finding that should be explored further by investigating velvet bean within human subjects.

In the United States, *ginkgo biloba* is a very popular supplement derived from dried leaves of the ginkgo tree. A study in 2005 conducted in a clinical laboratory by Markowitz *et al.*, found that in both men (n = 6) and women (n = 5) who supplemented with 240 mg of ginkgo biloba extract (GBE) for 14 days noted no significant increase in any measured endogenous steroids, including both free and total testosterone [107]. Interestingly, a year prior to the previously mentioned study, an animal study was conducted analyzing the effects of GBE supplementation in 5-week old male Wistar rats [108]. The authors noted favorable effects with a 70 mg daily dose of GBE with regards to raising testosterone 6-β-hydroxylase activity. The increase after one week of supplementation was 5.4 times higher than the control level. Following cessation of supplementation, each week for three weeks, testosterone 6-β-hydroxylase activity dropped linearly back to baseline levels.

Ginkgo biloba has proven to be effective for antidepressant-induced sexual dysfunction, possibly achieved via improved circulation and prostaglandin agonist effects, neurotransmitter and nitric oxide second messenger modulation, or a combination of both [109]. Despite minimal human research, GBE continues to be a popular supplement world-wide, based primarily on claims alone, as research has not yet proven its effectiveness in human subjects for purposes of elevating testosterone.

Dietary supplementation with ginseng has been investigated in relation to testosterone levels. Rats treated with 5% Panax Ginseng in their diet for 60 days experienced a significant increase in blood testosterone level [46]. Research has also shown that Panax ginseng enhances the libido possibly through its effects on the CNS and gonadal tissues, as well as by increasing stamina during intercourse [110].

However, it would be of interest for future studies to focus specifically on potential changes in the testosterone level following ***Panax ginseng*** treatment and the molecular mechanisms responsible for such changes. To our knowledge there have been no additional follow-up studies concerning testosterone in humans since this animal study was concluded in the early 1980's.

The genus ***Passiflora*** consists of an estimated 500 species that are found in warm and tropical regions. Traditionally, this plant was used widely throughout West India, Mexico, South America, Italy and the Netherlands for its medicinal properties. ***Passiflora*** incarnate has been mentioned in ancient Ayurvedic medical writings as a promising cure for male-impotence, post-menopausal decline in libido in women, menstrual irregularity, ***morphinism***, alcoholism, and tobacco addiction [101]. Chrysin, a bioflavonoid from Passiflora, inhibits aromatase activity in men as it does in women. Bodybuilders began using ***chrysin*** as a testosterone "booster" in response to the claims that it inhibits the conversion of testosterone to estrogen, which leaves more testosterone to power muscle building [111]. Several studies have found that bioavailability of chrysin could be boosted by the addition of an extract from black pepper, called piperine, which acts to increase flavanoid absorption in the intestines [112,113].

Current research is relatively scarce concerning passionflower extract on raising testosterone levels. Dhawan ***et al.***, found that in albino Wistar rats, testosterone levels were increased when supplemented with ***passiflora*** extracts suspended in simple syrup [40]. The proposed mechanism of action was the inhibition of aromatase activity, a member of cytochrome P-450 enzyme family, which prevented the metabolic conversion of testosterone to its metabolites, thereby, maintaining testosterone levels in the gonadal tissue. This would explain the results of increased free testosterone and decreased free estrogen found in the previously mentioned study [114]. We are currently conducting a trial investigating the potential impact this herbal supplement with regards to increasing testosterone levels in middle-aged men.

Longjack root

Longjack root is used traditionally in Malaysia, Indonesia, and Vietnam, where the root of the plant is boiled and consumed as a tonic for increased sexual potency, malaria, high blood pressure, fatigue, migraine, fever, arthritis, and increased sports performance. Known popularly as "***Tongkat*** Ali", the tree from which ***Longjack*** root is harvested reaches a height of around 10 meters, is slender and often unbranched, and contains reddish brown petioles. Currently, ***Longjack*** products are available as a raw crude powder of the root, a capsule, mixed in proprietary blends, and as an additive mixed with coffee.

Studies have provided evidence in support of the claim that a particular compound called eurycomanone, extracted from ***Longjack*** root, can increase testosterone levels in rats [102,115-117]. A recent study in humans involved supplementation of 76 of 320 patients suffering from late-onset hypogonadism with a 200 mg serving of a standardized water-soluble extract of ***Tongkat*** ali for 1 month [39]. Data from this study indicate that treatment of late-onset hypogonadism patients with ***Tongkat*** ali extract significantly elevated serum testosterone concentrations. Following treatment, 90.8% of the subjects exhibited normal testosterone values.

Another study found that in 14 men who participated in an intensive 8-week weight training program, the seven men who were supplemented with 100 mg/day of aqueous ***Longjack*** root extract experienced a 5 % increase in lean mass, a decrease in fat mass, and

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an average of 1.8 cm increase in arm circumference while those in the placebo group did not [118]. This study did not find that ***Longjack*** root supplementation increases testosterone concentration; however, the positive findings indicate the need for future research in this area as many of the results are consistent with an increase in testosterone.

A later study on 31 middle-aged women between the ages of 45-59 years, found very similar results. This study used the same daily 100 mg supplement of ***Longjack*** root as the previous 2003 study in men. The findings indicated increased muscle strength and larger quadriceps muscles [119]. Another recent pilot study utilizing both men (n = 13) and women (n = 12) cyclists aged between 57 and 72 years, found that a dose of 400 mg/day aqueous extract of ***Longjack*** root (Physta®) led to significant increases in both muscle strength and testosterone level [120].

Multiple mechanisms of action have been proposed concerning the increase in testosterone levels with ***Longjack*** root supplementation. The earliest possible mode of action was described by Pihie, whereby ***Longjack*** root was found to increase cAMP levels [12]. This increase in cAMP enhances glucose utilization and may have a significant attribution to the energy increasing effects. In a more recent study, ***Longjack*** root extract induced testosterone synthesis and elevated LH and FSH but reduced oestrogen levels in the plasma [116]. This finding provides evidence that treatment with ***Longjack*** root extract may potentially down-regulate the oestrogen-mediated feedback effect on LH and LSH secretion in the hypothalamic-pituitary-gonadal axis [122]. The same study suggested that the enhanced production of testosterone by Leydig cell explants is the mechanism of action, owing to the inhibition of phosphodiesterase and aromatase by eurycomanone [116]. Eurycomanone is the derivative (a major quassinoid compound) mentioned earlier in this review that is present in ***Longjack*** root extract. Additional research is needed to more fully elucidate our understanding of the mechanisms underlying an increase in testosterone as a result of ***Longjack*** root supplementation.

Tribulus Terrestris

Tribulus Terrestris (TT) is an herb that has been used for centuries to promote urinary health, increased sexual desire, and as a general tonic. This botanical agent has gained renewed interest due to claims that it can enhance testosterone. A limited number of animal studies have found that TT significantly increases testosterone levels. For example,

two of three recent studies utilizing Wistar rats found serum testosterone levels to be significantly increased following varying dosages of TT taken once daily [42,123,124]. Martino-Andrale ***et al.*** found no significant increase in serum testosterone levels but supplemented the wistar rats with the lowest level of TT between the three studies [124], suggesting that dosing is a factor in achieving desired outcomes. An additional study investigated the effects of TT supplementation in primates (n = 5), white rabbits (n = 24), and Sprague-Dawley rats (n = 40) both before and after treatment [125], noting a significant increase in testosterone in primates but not in white rabbits or rats.

Studies involving TT supplementation in humans have failed to yield positive outcomes with regard to elevating testosterone [23,24,126,127]. One of the previously referenced investigations found a 38% increase in free testosterone yet failed to find a significant increase in total testosterone [23]. Many of these studies, however, had relatively low sample sizes, utilized women only [127], and enrolled subjects who were relatively young-between the ages of 19 and 29 [24,126]. A recent study by Rogerson ***et al.,*** inclusive of 22 men aged 19 to 22 years who ingested one capsule (450 mg) of TT daily over a 5 week period, found no significant increase in testosterone [126]. Another study found that men (n = 21) aged 20 to 36 years who ingested three daily capsules of either 10 mg/kg or 20 mg/kg of Bulgarian TT for a period of 4 weeks experienced no significant increase in total testosterone [24]. In addition to these findings, a study by ***Brown et al.*** utilized men of ages 19 to 29 years over an 8-week period [128]. The daily supplement consisted of 750 mg TT, 300 mg Androstenedione, 150 mg DHEA, 625 mg Chrysin, 300 mg Indole-3-carbinol, and 540 mg Saw Palmetto One all taken three times daily. This investigators measured both free and total testosterone and noted no significant increase in either measure.

Supplement	Reference	Subjects	Intervention	Outcome Measures	Results on T level
Fenugreek	Bushey *et al.*, [36]	45 men; 19-23 years	500 mg/day fenugreek extract; 8 wks	Free T	—
	Steels *et al.*, [104]	60 men; 25-52 years	600 mg Testofen daily; 6 wks	Serum T	—
Ginkgo biloba	Markowitz *et al.*, [107]	11 (6 men; 5 women)	240 mg/day GBE; 14 days	Total T/Free T	—
Longjack root	Tambi *et al.*, [39]	76 men	200 mg/day Tongkat ali; 1 month	Serum T	+
	Hamzah, *et al.,* [118]	14 men	100 mg/day; 8 wks	T related measures	N/A
	Sarina *et al.*, [119]	31 women; 45-59 years	100 mg/day; 12 weeks	T related measures	N/A
	Henkel *et al.*, [120]	25 (13 men; 12 women); 57-72 years	400 mg/day Physta®	Total T	+
Tribulus terrestris (TT)	Brown *et al.*, [128] Brown *et al.*, [23] Neychev *et al.*, [24] Rogerson *et al.*, [126] Saudan *et al.*, [127]	20 young men 58 men; 30-59 years 21 men; 20-36 years 22 men; 19-23 years 2 women; 26 & 40 years	ANDRO-6 (includes 750 mg TT); 8 wks DION (includes 750 mg TT); 4 wks TT 10 or 20 mg/kg/bw – 3xdaily; 4 wks 450 mg/day TT; 5 weeks 500 mg/day Tribestan® 3xdaily; 2 days	Free T/Total T Free T/Total T Serum T Urinary T/E ratio Urinary T/E ratio	—/— +/— — — —

Table 1: Herbal dietary supplements and the effects on circulating testosterone in human subjects.

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The proposed mechanism by which TT can theoretically raise serum testosterone levels is by stimulating androgen receptors in the brain, which causes the posterior pituitary gland to secrete additional luteinizing hormone, thus stimulating the testes to secrete more testosterone [129]. Evidence to date suggests that TT supplementation is ineffective in increasing testosterone levels in humans and further research inclusive of a larger sample size and participation by individuals of greater age may be needed.

Conclusions and Future Research

The potential benefits of maintaining adequate testosterone levels are numerous and highly sought out among men wishing

to improve their overall health and outlook on life, their physical and mental performance, and their overall physique. When considering treatment to increase or maintain testosterone levels-as well as the associated health-related parameters impacted by testosterone-specific herbal supplements may prove an effective alternative to pharmaceuticals. However, it appears that most herbal ingredients either lack effect when studied in human subjects or quite simply, have not been studied in a clinical trial. Hence, there exists no concrete evidence to support their use. That said, there does appear to be at least some evidence for the use of **Longjack** root to elevate circulating testosterone.

Indeed, additional research is needed in the area of herbal supplementation to determine exactly which herbal agents may prove efficacious, as well as what specific dosage of each agent will be needed to yield the most beneficial results. Most importantly, relevant studies need to be conducted within human subjects, as few well-controlled trials currently exist. These studies may include both men and women, as very few, if any, studies have included within the research designs. Such studies should not only focus on the potential efficacy of these agents, but also on the safety of their intake over time. When collectively considering the herbal agents currently available for use (Table 1), it appears that **Longjack** root extract may be the most promising in regards to raising testosterone levels based on the current literature.

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