

# *Withania somnifera* and *Trigonella foenum-graecum* as ingredients of testosterone-boosting supplements: Possible clinical implications

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## Abstract

This narrative review provides an overview of scientific studies on dietary supplements that may affect circulating testosterone (T) levels to explore which substances are scientifically proven to increase T concentration. We also review the scientific literature for their potential mechanisms and laboratory test changes triggered by their use. Based on the analysis of existing data on substances used to increase endogenous T levels, especially double-blind placebo-controlled randomized clinical trials, we selected 2 herbal extracts with the best documented positive effects on T levels, *Withania somnifera* root and root extracts/leaves and seed extracts of *Trigonella foenum-graecum*. Although these substances have different postulated mechanisms of action, both significantly increase T levels in men. *Withania somnifera* may inhibit the effects of cortisol and prolactin on the hypothalamic–pituitary–gonadal axis and directly affect the hypothalamus. *Trigonella foenum-graecum* seeds contain the active substance diosgenin, which is a precursor for sex hormone synthesis in gonads.

**Key words:** *Trigonella foenum-graecum*, *Withania somnifera*, testosterone, testosterone boosters

## Cite as

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## Introduction

Dietary supplement use has increased in recent years and is currently a growing global trend. According to Bailey et al., dietary supplements used in the USA between 2003 and 2006 were used by 49% of the population (44% of men and 53% of women) and as many as 70% of adults over 70.<sup>1</sup> The most frequently used dietary supplements (33%) were multivitamin and multi-mineral preparations, with plant supplements used by approx. 20% of adults, mainly older people.<sup>1</sup>

A survey conducted by the dietary supplement industry trade association, i.e., the Council for Responsible Nutrition (CRN), in a group of 2,000 people per year in 2007–2011 found that the prevalence of supplement use ranged from 64% to 69% in 2007–2011. The percentage of people regularly using dietary supplements increased from 28% to 36%, with a statistically significant increase in 2010–2011. Furthermore, supplement consumption increased with age in 2011 and was higher in women than men, with multivitamins being the most commonly used supplements.<sup>2</sup>

According to data from The National Health and Nutrition Survey, in 2017–2018, 57.6% of people over 20 declared dietary supplement use in the last month, which was more common in women than in men, amounting to 63.8% and 50.8%, respectively, and increased with age, with the highest percentage of people using dietary supplements in women over 60. An increase in supplement consumption was also observed compared to data from 2007–2008, as age-adjusted consumption increased by 7.7% during this period.<sup>3</sup>

The European Prospective Cancer and Nutrition Study on dietary supplements conducted from 1995 to 2000 on 36,034 men and women aged 35–74 found that, as in the USA, dietary supplement use was highest in the oldest age groups in most European countries.<sup>4</sup> According to more recent data, 18.8% of 2,359 adult respondents from European countries used at least 1 plant-based dietary supplement. Characteristics of those using dietary supplements included older age, better education, non-smoking, and self-assessment of health as “good or very good.”<sup>5</sup>

A recent survey of 13,200 adults across 14 European Union countries found that 88% of respondents had used supplements at some point in their lives, and 93% of this group had used them in the last 12 months.<sup>6</sup> An online survey conducted in Poland between November 26, 2019, and March 11, 2020, on 1,560 people aged 18–90 showed that the average use of dietary supplements within the past 30 days in people surveyed before the coronavirus disease 19 (COVID-19) pandemic was 80%, and 78% during the pandemic.<sup>7</sup>

Research conducted on 10,520 women and men in Iran by Mahdavi-Roshan et al. indicated that 25% of people used dietary supplements, and the factors associated with their use were female gender, older age, better education, and the presence of chronic diseases, such as cardiovascular

diseases, hypertension and diabetes.<sup>8</sup> More recent data from a cross-sectional survey of 501 individuals aged over 45 residing in Saudi Arabia in 2021 showed that the prevalence of dietary supplement use was 50.7% and was lower in those under 60 (54.9%) compared to older people (59.9%).<sup>9</sup>

Statistical data on the consumption of dietary supplements indicate a growing interest in products that improve health and slow the aging process, which is promoted by media marketing.<sup>10</sup> Some plant-based anti-aging dietary supplements may protect against age-associated health problems, such as sarcopenia and metabolic syndrome, perhaps by affecting hormone concentrations.<sup>11</sup> One of the potential targets of anti-aging dietary supplements may be testosterone (T) due to its complex anabolic and anti-catabolic effects and its ability to improve metabolism, vital strength and sexual function. Testosterone is responsible for the development of primary and secondary sex characteristics in men, including sexual organs, changes in voice depth and facial and body hair growth.<sup>12</sup> Furthermore, it is a basic anabolic steroid that influences the production of proteins in skeletal muscles, increases muscle strength, power and endurance,<sup>13</sup> improves bone density, mass and strength, and is active in the male sexual response.<sup>14</sup>

Recent research emphasized the critical role that T plays in several metabolic functions in men, with T deficiency associated with metabolic disorders such as type 2 diabetes, impaired glucose tolerance, insulin resistance, obesity, increased triglycerides, total cholesterol, and decreased high-density lipoprotein (HDL) cholesterol, contributing to cardiovascular risk. Additionally, clinical studies indicate that T replacement therapy improves insulin resistance and glucose metabolism and reduces fat mass, cholesterol and triglycerides. The mechanisms by which T influences metabolism are not fully understood, but it is suggested that it is involved in controlling the expression of proteins involved in lipid and cholesterol metabolism regulation and the glycol axis and glycogen synthesis.<sup>15,16</sup>

Leydig cells of the interstitium of the testes produce approx. 95% of T, which is secreted into the bloodstream and transported bound to proteins (98%), mainly sex hormone binding globulin (SHBG) and albumin. Testosterone bound to SHBG is inactive, while T unbound and bound to albumin is active. Testosterone can exert its biological effects directly by interacting with its receptor or indirectly through being metabolized to dihydrotestosterone (DHT) by the cytoplasmic enzyme 5-reductase, which is highly expressed in the skin, male reproductive organs and brain.<sup>16</sup> Testosterone synthesis is regulated by the hypothalamic–anterior pituitary–gonadal axis, with gonadotropin-releasing hormone (GnRH) secreted by the hypothalamus. Under its influence, luteinizing hormone (LH) is released into the circulation from the anterior pituitary gland to stimulate Leydig cells in the testes to synthesize T. Testosterone directly and indirectly inhibits GnRH and LH release in a negative feedback loop, with GnRH release

regulated by, among others, several hypothalamic neuro-peptides, including kisspeptin.<sup>17</sup> Testosterone exerts its direct biological effects by binding to the androgen receptor (AR), though DHT binds to the same AR with approx. 5 times greater affinity.<sup>18</sup> The T-AR complex binds directly to specific DNA nucleotide sequences in the cell nucleus to regulate gene transcription and act as a transcription factor.<sup>19</sup> In adipose tissue, T is converted to estradiol (E2) with the participation of aromatase.<sup>18,19</sup> There are many dietary supplements available for sale that claim to increase T concentrations.

## Objectives

There is a need to identify dietary supplements that have a proven effect on T concentrations. Our study aimed to compile a scientific review of literature published between 2013 and 2023 on supplements that impact T concentrations, identify substances with the best evidence of increasing T concentration, explore the potential mechanisms of their action and highlight changes in laboratory tests caused by their use. We also aimed to determine their effectiveness, whether they have additional properties, which patients can use them (why and under what conditions), their effects on diagnostics, and if they have legal consequences for athletes.

## Methods

This review aimed to assess T-booster effectiveness, summarize the evidence on this topic, and explain how they work and in which patients (why and under what conditions). Therefore, we used realist synthesis as the most appropriate method. The study followed the RAMES (Realist and Meta-narrative Evidence Syntheses: Evolving Standards) guidelines, based on which the intervention was explained as supplementation with T-boosters to increase T concentrations in men, with the intervention considered under conditions of low T concentrations. The results focused

on which T-boosters had the best-documented effectiveness, how much they increased T concentrations, and what mechanism and factors influenced their effectiveness.

Publications for this review were obtained by searching Google and Medline/PubMed. Search terms included testosterone boosters, testosterone boosting supplements, *Withania somnifera*, ashwagandha, *Trigonella foenum-graecum*, and fenugreek, covering 2013 to 2023. The last search date was September 15, 2023. Only substances with the best-documented ability to increase T levels were selected for systematic review and analysis of the magnitude of effect and contributing factors in randomized controlled trials and crossover studies. Systematic reviews and animal studies were reviewed to discuss potential T mechanisms of action.

## Results

The final analysis included 4 systematic reviews, with Table 1 summarizing the key findings on the effects of various ingredients found in dietary supplements on T concentrations.<sup>20–34</sup> *Withania somnifera* (ashwagandha) and *Trigonella foenum-graecum* (fenugreek) extracts played the most significant role in this mechanism.

Two crossover studies and 4 randomized controlled trials of ashwagandha and 5 randomized controlled trials of fenugreek were included in the analysis of the extent of their effectiveness on T levels and contributing factors, with the results presented in Table 2.

## Discussion

### Which ingredients of dietary supplements have scientifically proven effectiveness in increasing testosterone concentration in men?

Clemesha et al. attempted to identify dietary supplement ingredients affecting T concentration. Based on scientific research,<sup>31</sup> the authors selected the 50 most popular

**Table 1.** Key findings on the effects of various ingredients present in dietary supplements on testosterone concentrations presented in selected scientific reviews

Scientific review			
Clemesha et al., <sup>31</sup> (2020)	Balasubramanian et al., <sup>32</sup> (2019)	Lazarev et al., <sup>33</sup> (2021)	Smith et al., <sup>34</sup> (2021)
Key findings			
A significant increase in T concentration was found for the following 12 substances: <i>Anacyclus pyrethrum</i> ; <i>Bulbine natalensis</i> ; <i>Eurycoma longifolia</i> (Tongkat ali); <i>Trigonella foenum-graecum</i> (fenugreek); Epimedium (horny goat weed); L-arginine; L-carnitine; magnesium; <i>Mucuna pruriens</i> ; pantothenic acid; selenium; and shilajit	Five out of 10 substances had scientific evidence to increase T concentration: <i>Eurycoma longifolia</i> (Tongkat Ali), <i>Serenoa repens</i> , boron, <i>Withania somnifera</i> (ashwagandha root), and <i>Trigonella foenum-graecum</i> (fenugreek)	Components with the strongest evidence of their positive effect on T concentration: <i>Eurycoma longifolia</i> (Tongkat Ali), <i>Withania somnifera</i> (ashwagandha) and <i>Trigonella foenum-graecum</i> (fenugreek)	Two herbal extracts with the best documented positive effects on T concentrations in men: <i>Trigonella foenum-graecum</i> (fenugreek) seed extracts and <i>Withania somnifera</i> (ashwagandha)

**Table 2.** Key findings on the efficacy of *Withania somnifera* and *Trigonella foenum-graecum* on testosterone levels from controlled trials

Study, year	Design	Subjects	Intervention	Outcome
Mahdi et al., <sup>20</sup> 2009	prospective	normozoospermic heavy smokers (n = 20), normozoospermics under psychological stress (n = 20) and normozoospermics with infertility of unknown etiology (n = 20); the control group comprised of 60 age-matched healthy men who had previously initiated at least 1 pregnancy and exhibited a normal semen profile	<i>Withania somnifera</i> root powder, orally, in a single dose (5 g/day) for 3 months.	The ability of <i>Withania somnifera</i> to treat stress-related infertility; T level improved in normozoospermics by 13%, normozoospermic cigarette smokers by 10%, and infertile normozoospermics under psychological stress by 22%.
Ahmad et al., <sup>21</sup> 2010	prospective	75 normal healthy fertile men (control subjects) and 75 men undergoing infertility screening	Infertile men were prescribed <i>Withania somnifera</i> root powder (5 g/day) orally for 3 months.	Treatment recovered the levels of T in normozoospermic, oligozoospermic and asthenozoospermic men significantly ( $p < 0.01$ ).
Chauhan et al., <sup>22</sup> 2022	randomized, double blind, placebo-controlled	50 participants with lower sexual desire	300 mg of ashwagandha root extract or placebo capsules twice daily.	Compared to placebo, ashwagandha root extract supplementation was associated with a statistically significant increase in serum T levels
Ambiye et al., <sup>23</sup> 2013	randomized, double blind, placebo-controlled	the placebo-treated group (n = 25) and the ashwagandha-treated group (n = 21)	Study participants in the ashwagandha-treated group were administered 1 capsule (containing 225 mg of a high-concentration full-spectrum root extract of the ashwagandha plant) orally, thrice daily for a period of 12 weeks.	Serum T increased significantly by 17% following treatment with ashwagandha root extract.
Lopresti et al., <sup>24</sup> 2019	randomized, double blind, placebo-controlled	50 overweight men	A placebo or an ashwagandha extract (Shoden beads, delivering 21 mg of withanolide glycosides a day) for 8 weeks.	Ashwagandha intake was associated with an 14.7% greater increase in T ( $p = 0.01$ ).
Lopresti et al., <sup>25</sup> 2019	randomized, double blind, placebo-controlled	60 healthy adults	A placebo or 240 mg of a standardized ashwagandha extract (Shoden) once daily for 60 days.	T levels increased in men ( $p = 0.038$ ) but not in women ( $p = 0.989$ ) over time, although this change was not statistically significant compared to the placebo ( $p = 0.158$ )
Wankhede et al., <sup>26</sup> 2018	prospective, double-blind, randomized, placebo-controlled	60 male healthy volunteers (30 in Fenu-FG group and 30 in placebo group)	Study participants were randomized to receive 1 of the 2 treatments, namely Fenu-FG (1 capsule, 300 mg, twice a day) or matching placebo in 1:1 ratio.	On 8 weeks of treatment, the levels of free T was found to have steep (98.7%) increase from baseline ( $p < 0.001$ ) in Fenu-FG group, whereas placebo group showed moderate (48.8%) increase from ( $p < 0.01$ ); the increase in free testosterone from baseline was found significantly between the groups ( $p < 0.05$ ); subjects from Fenu-FG and placebo groups showed mild but non-significant increased levels of total T as compared with corresponding baseline values; the increase in total T from baseline was also not significant between the treatment groups (Fenu-FG vs placebo).
Mokashi et al., <sup>27</sup> 2014	randomized, double blind, placebo-controlled	16 healthy and non-exercising men, 2 groups (controlled and placebo; of 8 each)	Single dose of 600 mg (2 capsules of 300 mg) of glycosides based standardized fenugreek seed extract (IND9).	Significant increase in T levels (free-, total- and bioavailable-T) on acute administration of IND9 supplementation as compared with placebo group.
Rao and Grant, <sup>28</sup> 2020	randomized, double blind, placebo-controlled	100 healthy men with symptoms of benign prostate hyperplasia	Oral dose of either 600 mg <i>Trigonella foenum-graecum</i> per day or placebo for 12 weeks.	There were no differences in the total T or free T levels in either group after treatment as measured as change from baseline ( $p = 0.36$ and $0.44$ , respectively)
Rao et al., <sup>29</sup> 2016	single-site, randomized, double-blind, placebo-controlled	120 healthy men randomly allocated either the placebo comparator group or the active intervention group; 111 completing the study (56 vs 55, respectively)	The active treatment was standardized <i>Trigonella foenum-graecum</i> seed extract at a dose of 600 mg/day for 12 weeks.	Total T levels were similar between both groups at baseline. There was a small but significant difference in the change from baseline ( $\Delta$ ) values between the active treatment and placebo groups for T and calculated free T at week 12
Guo et al., <sup>30</sup> 2018	randomized, double-blind, placebo-controlled	40 healthy male athletes	Placebo or Furosap capsules (250 mg/day) for 12 weeks.	A significant change in serum total T level was observed in the Furosap-treated subjects compared to the group receiving placebo.

T-boosters from available databases and analyzed the effectiveness of 109 ingredients contained in them. No scientific studies were found on the effects of 67, while 11 had evidence that they decreased T concentrations, and 27 demonstrated an increase in T concentrations. For most of these ingredients, single clinical studies confirmed their effectiveness. For 4 ingredients, 4 publications indicated that they increase T concentration. Only 1 substance had a beneficial effect on T concentration in 5 studies, as did another in 6 studies. Regarding 6 (of 27) substances for which an increase in T concentration was documented, conflicting data indicated a T concentration decrease. Clemesha et al.<sup>31</sup> found that 12 substances – fenugreek, *Anacyclus pyrethrum*, *Bulbina natalensis*, *Eurycoma longifolia* (tongkat ali), epimedium (horny goat weed), *Mucuna pruriens*, shilajit, L-arginine, L-carnitine, magnesium, pantothenic acid, and selenium – had the best data supporting increased T concentrations. Unfortunately, the authors did not provide data on which of the ingredients had the most convincing evidence of their T-boosting potency. Data for 9 supplements indicated that their use led to an increase in T concentrations or did not cause changes in T concentrations, including ashwagandha root, panax ginseng, *Lepidium meyenii* (maca), vitamin D, caffeine, resveratrol, boron, calcium, and zinc.

Another attempt to identify substances with a scientifically proven effect on T concentrations was made by Balasubramanian et al.<sup>32</sup> The authors analyzed 10 most popular T-boosters sold online at amazon.com, with 5 showing that they could increase T levels, including tongkat ali, ashwagandha root, fenugreek, *Serenoa repens*, and boron.

The latest systematic review of T-boosters increasing T concentration by Lazarev and Bezuglov analyzed Medline/PubMed and the Cochrane Library for scientific studies on 15 ingredients identified in the 2 reviews mentioned above.<sup>33</sup> The authors found studies on 10 ingredients, including fenugreek (7), L-arginine, boron (3 studies each), tongkat ali, ashwagandha root, L-carnitine, selenium (2 studies each), magnesium, shilajit, and *Serenoa repens* (1 study each). According to the authors, tongkat ali, ashwagandha root, and fenugreek had the strongest evidence of a positive effect on T concentration, while only single studies showed a positive effect of magnesium and shilajit. Meanwhile, L-arginine, L-carnitine, *Serenoa repens*, selenium, and boron data were conflicting. There were very limited data on their safety profiles.

Methodological caveats of the reviews mentioned above included the use of only 1 search term, using only the Google search engine, and testing only selected ingredients of T-boosters. Moreover, the studies only aimed to identify substances with scientifically proven effectiveness in increasing T concentrations, regardless of the methodology used. No such limitations were found in the systematic review by Smith et al.<sup>34</sup> Their comprehensive review only considered controlled studies conducted on the effectiveness of single herbal ingredients on T concentrations in men,

apart from its fractions or binding proteins ( $\geq 18$  years). The study followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines and extracted English-language publications from PubMed, Scopus, the Cochrane Library, and the Cumulative Index to Nursing and Allied Health Literature (CINAHL), and only included randomized controlled trials (including a cross-over study) in adult men ( $\geq 18$  years) (or a subset of adult men). Other inclusion criteria were the effect of monotherapy with a single herb, spice, plant, or extract on T concentrations in serum, plasma or saliva, compared to a placebo or control group. After applying these criteria, only 32 of 4,384 studies published between 2001 and 2019 were included in the analysis, with 9 showing statistically significant increases in T levels. Most studies were conducted in young populations, with 16 including men  $< 40$ . Based on the analyzed data, they identified fenugreek seed extracts and ashwagandha root and root/leaf extracts as 2 herbal extracts with the best documented positive effect on T concentration.

## What are the characteristics of T-booster ingredients with a positive effect on testosterone concentration?

### Ashwagandha

Ashwagandha, also called winter cherry or Indian ginseng, was used in Ayurveda, the traditional Indian system of medicine. The plant belongs to the *Solanaceae* family and grows in subtropical India, Egypt, Morocco, Congo, South Africa, and Jordan. Several alkaloids and steroid lactones have been isolated from its roots, aerial parts and berries.<sup>35</sup> Withanine is the primary alkaloid, though pseudo-withanins, somniferins, somnins, withanins, tropines, pseudo-tropines, choline, anaferins, cuscohygrins, and isopelleterins should also be mentioned. Steroid lactones include ergostane-type steroid lactones, withaferin A, withasomniferin-A, withanolides A-Y, withasomniferols A-C, withanone, and withasomidienone.<sup>36,37</sup>

Plant phytochemical composition can vary by location. The roots are used most often for medicinal purposes, but whole plants, leaves, stems, green berries, fruits, seeds, and bark are also applied in medicine. Ashwagandha is available as an extract, loose powder and tincture. Due to the lack of withanolide standardization in some preparations, there may be significant inconsistency in their volume between preparations. The use of ashwagandha usually does not lead to serious interactions or side effects.<sup>38</sup>

Sengupta et al. proposed a mechanism for the effects of ashwagandha on T concentrations and male fertility using detailed analysis of human and animal studies. According to them, ashwagandha prevents the reduction of T levels induced by stress under the influence of cortisol (C) and prolactin (PRL), leading directly to increased GnRH and

LH concentrations. In addition to normalizing T concentrations, ashwagandha improves the antioxidant potential of seminal plasma by reducing oxidative stress.<sup>39</sup> A research paper also showed that ashwagandha reduced nandrolone decanoate-induced hepato-renal toxicity in Wistar rats.<sup>40</sup>

As mentioned earlier, GnRH stimulates the anterior pituitary to release follicle-stimulating hormone (FSH) and LH to act on the gonads to regulate T production and spermatogenesis. Therefore, when hormones such as PRL and C disrupt the hypothalamic–pituitary–thalamic axis, it reduces T production and spermatogenesis. Ashwagandha root extract is believed to normalize C concentrations by lowering the stress response. Observations by Sengupta et al.<sup>39</sup> confirmed the results of research by Mahdi et al.,<sup>20</sup> who analyzed the effect of ashwagandha on infertile men with normozoospermia exposed to mental or environmental stress (challenging smokers), or whose infertility was idiopathic. The study used ashwagandha root powder at a dose of 5 g daily with skimmed milk for 3 months and found a reduction in morning and afternoon C levels and an increase in T levels by 13–22% and LH concentrations by 11–21%, depending on the experimental group. At the same time, the concentrations of FSH and PRL decreased.<sup>20</sup> Similarly, Ahmad et al. examined the effect of ashwagandha on T concentration in infertile men and showed that after using its powdered form (5 g daily with skimmed milk for 3 months), there was an increase in the mean T concentration by 0.85–1.43 ng/mL, which was accompanied by an increase in LH and a decrease in FSH and PRL.<sup>21</sup>

Chauhan et al. showed that using ashwagandha root extract at a dose of 300 mg in an aqueous solution (standardized using high-performance liquid chromatography to contain more than 5% withanolides) for 2 months in a double-blind, randomized study of adult men aged 21–45 without significant medical history caused a 17% increase in T concentration without reducing PRL.<sup>22</sup> Another double-blind, randomized trial using 225 mg of aqueous root extract (standardized to more than 5% of total withanolides) for 3 months in infertile men between the age of 22 and 40 demonstrated an increase in T concentration by 17% and LH by 34%.<sup>23</sup> Two additional double-blind, randomized studies on the effect of ashwagandha on hormone concentrations, including T, were conducted using 300 mg of ashwagandha root and leaf extract (standardized to contain 35% withanolide glycosides). Lopresti et al. showed that men aged 40–70 with clinical symptoms of mild-to-moderate fatigue and reduced vitality had significant increases in T ( $\geq 45.58$  pmol/L) and dehydroepiandrosterone sulfate (DHEA-S) ( $\geq 1.49$  nmol/L) without a substantial reduction in C concentrations after 4 months of treatment.<sup>24</sup> Lopresti et al. examined the effect of the same preparation at a dose of 240 mg for 2 months on T and DHEA-S concentrations in adult men and women aged 18–65, demonstrating a reduction in C concentration by 23% and DHEA-S by 8%, as well as a statistically significant increase in T concentrations by 11% if not divided by gender and

an 11.4% increase in men. A non-significant 0.2% reduction in T concentrations was observed in women.<sup>25</sup>

Kataria et al. studied the effects of ashwagandha on the hypothalamus using the clonal GnRH cell line from the rat hypothalamus cells.<sup>41</sup> The authors assessed GnRH expression and release in response to ashwagandha, and showed that it stimulated GnRH neuronal activity and increased GnRH release.

## Fenugreek

Fenugreek, a herb belonging to the legume family, grows in India and North Africa. The plant is used in the cooking and the food industry as the seeds can be eaten raw or cooked, are used as a spice due to their characteristic bitter taste, and have a high fiber content. Fenugreek is characterized by a high water-holding capacity and is used to produce jellies and spreads and as a thickener for soups, drinks and sauces. The plant is also sometimes added to flour to increase the fiber content of bread and to baked goods such as muffins and cakes due to its maple syrup-like aroma, while the leaves are used as a green leafy vegetable.

Fenugreek seeds are used in traditional Indian medicine to treat anorexia, in the postpartum period to increase lactation, and as a gastric stimulant, while Persians and Arabs traditionally used them to increase lean muscle mass in women.<sup>42</sup> Fenugreek is available as a standardized extract or tea for medical purposes, with its medicinal properties derived from high concentrations of glycosides and saponins, including diosgenin, tigogenin, gitogenin, neotigogens, and yamogenin. Diosgenin, the primary sapogenin, is a precursor for sex hormone synthesis and is believed to be the main mechanism responsible for fenugreek increasing T concentrations.<sup>42</sup> Since pharmaceutical T is obtained by chemical conversion of diosgenin (Fig. 1), regular intake of diosgenin is believed to increase T concentrations and enhance its effects.<sup>43,44</sup>

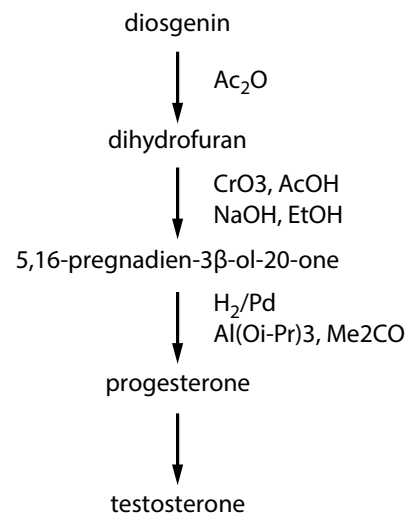


Fig. 1. Chemical conversion of diosgenin to testosterone

Diosgenin is also a precursor for the synthesis of other steroid hormones and metabolites, so its biological effect is not limited to increased T synthesis. Indeed, diosgenin and its metabolites may influence numerous physiological processes (having hypocholesterolemic, gastro- and hepato-protective, antioxidant, anti-inflammatory, and anti-diabetic properties) and diseases, including inhibiting the development of cancer (including prostate cancer, oral squamous cell carcinoma, laryngeal cancer, esophageal cancer, liver cancer, gastric cancer, lung cancer, cervical cancer, glioma, and leukemia), neurodegenerative and cardiovascular diseases, and many others.<sup>45–49</sup> The beneficial effects of the diosgenin found in fenugreek on metabolism and cancers common in men means they are indicated in situations where these conditions coexist with male hypogonadism.

The effect of fenugreek on T concentration in men has been studied in several randomized clinical trials. Wankhede et al. studied healthy men aged 18–35 administered 300 mg of fenugreek seed extract (Fenu-FG, a patented composition; details not shown) twice daily for 8 weeks alongside resistance training. The regimen increased free T concentration (from 17.76 ng/dL to 35.29 ng/dL).<sup>26</sup> Mokashi et al. studied the effects of fenugreek on T concentrations in healthy sedentary men aged 18–41 receiving a single dose (600 mg) of standardized fenugreek seed extract (IND9, a patented composition; details not shown) during two 10-h intervals. Despite the short duration, the results showed an increase in the total (from 405.5 ng/dL to 519.0 ng/mL) and free T (from 11.7 ng/dL to 13.5 pg/mL).<sup>27</sup> Rao and Grant assessed the effects of Fenu-FG on benign prostatic hyperplasia (BPH) symptoms in men aged 45–80 taking 300 mg of the extract twice a day for 3 months.<sup>28</sup> The results showed that fenugreek did not reduce BPH symptoms, and the concentrations of T, free T, SHBG, and prostate-specific antigen did not change significantly and remained within normal limits.<sup>28</sup> Another double-blind, randomized study by Rao et al. assessed the effects of Fenu-FG on androgen concentrations in healthy men aged 43–70 given 600 mg/day for 12 weeks. Total and free T concentrations increased significantly (1.3 nmol/L and 33 pmol/L, respectively), though no significant changes in DHEA-S, androstenedione, estradiol, SHBG, or PRL were observed in any group.<sup>29</sup>

Guo et al., in their double-blind placebo-controlled randomized clinical trial, investigated the effects of fenugreek extract enriched with 20% protodioscin (Furosap, patented, so composition not shown) in healthy male athletes aged 20–28 at a dose of 250 mg/day for 12 weeks. In the group receiving Furosap, a significant increase in total serum T concentration was observed (by 124 ng/dL).<sup>30</sup> The results of animal studies indicate that fenugreek extract caused degenerative changes in the structure of the testes, sperm parameters and concentrations of sialic acid in the epididymis and fructose in the seminal vesicle, and negatively affected the oxidative state in the testicles.<sup>50</sup>

## Limitations

In our work, we used realist synthesis as the best method. However, this was a limitation. Although there are reporting standards for realist synthesis, there are no specific standards for conducting a realist inquiry or protocol development frameworks. This allows for flexibility and inclusivity, but there is a risk of suboptimal data analyses due to a lack of prescriptive guidance. However, since the results of the synthesis focus on explaining to the reader why and how a specific supplement works and enable a conscious choice of its further use, this is the only method that allowed the implementation of the objectives of the work, despite its limitations.

## Conclusions

Based on the analysis of existing data on T-booster ingredients used to increase endogenous T concentrations, especially double-blind placebo-controlled randomized clinical trials, 2 herbal extracts with the best documented positive effects on T levels in men were selected, ashwagandha root and root extracts/leaves and fenugreek seed extracts. Both can significantly raise T concentrations in men, which may be useful in clinical practice. On the other hand, they may change the results of laboratory tests if they are not declared by the patients. Moreover, athletes need to be aware that taking these products can lead to positive results in doping control because of adulteration or unintentional contamination of commercial products with prohibited substances.<sup>51,52.</sup>

Ashwagandha and fenugreek show differences in their postulated mechanisms of action, with the literature demonstrating that ashwagandha extract inhibits C and PRL effects on the hypothalamic–pituitary–gonadal axis and perhaps directly affects the hypothalamus. Additionally, it improves the antioxidant potential of semen plasma by reducing oxidative stress. Fenugreek seeds increase T levels thanks to the active ingredient diosgenin, which is a precursor for sex hormone synthesis. Data from animal studies indicate that *Trigonella foenum-graecum* seed extract treatment caused degenerative changes in rodent testes and had a negative effect on rodent sperm parameters. The different mechanism of action determines other possible clinical indications for ashwagandha and fenugreek, with their influence on semen parameters one of the most critical factors to consider. In addition, clinical trials on ashwagandha used a standardized extract with a known composition, while the research on fenugreek employed patented preparations of unknown composition. For this reason, using fenugreek preparations other than those used in clinical trials is difficult as we do not know how the extracts were standardized.

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