

**ORIGINAL ARTICLE**

**Tribulus terrestris** versus placebo in the treatment of erectile dysfunction: A prospective, randomized, double-blind study

C.A. Santos Jr. a, L.O. Reis a,b,*, R. Destro-Saade a, A. Luiza-Reis a, A. Fregonesi a

a Departamento de Cirugía (Urología), Facultad de Ciencias Médicas, Universidad Estatal de Campinas UNICAMP, Säo Paulo, Brazil
b Facultad de Medicina (Urología), Centro de Ciencias de la Vida, Universidad Católica de Campinas PUC-Campinas, Säo Paulo, Brazil

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**KEYWORDS**
Impotence; Sexual dysfunction; Herbal medicine; Alternative medicine; Testosterone; Libido; Placebo and Chinese medicine

**Abstract**

**Objectives:** To evaluate the possible effects of **Tribulus terrestris** herbal medicine in the erectile dysfunction treatment and to quantify its potential impact on serum testosterone levels.

**Design and methods:** A prospective, randomized, double-blind and placebo-controlled study including 30 healthy men selected from 100 patients who presented themselves spontaneously complaining of erectile dysfunction, ≥40 years of age, nonsmokers, not undergoing treatment for prostate cancer or erectile dysfunction, no dyslipidemia, no phosphodiesterase inhibitor use, and no hormonal manipulation, and if present, hypertension and/or diabetes mellitus should be controlled. International Index of Erectile Function (IIEF-5) and serum testosterone were obtained before randomization and after 30 days of study. The patients were randomized into two groups of fifteen subjects each. The study group received 800 mg of **Tribulus terrestris**, divided into two doses per day for 30 days, and the control group received placebo administered in the same way.

**Results:** The groups were statistically equivalent in all aspects evaluated. The mean (SD) age was 60 (9.4) and 62.9 (7.9) years, p = 0.36, for intervention and placebo groups, respectively. Before treatment, the intervention group showed mean IIEF-5 of 13.2 (5−21) and mean total testosterone 417.1 ng/dl (270.7−548.4 ng/dl); the placebo group showed mean IIEF-5 of 11.6 (6−21) and mean total testosterone 442.7 ng/dl (301−609.1 ng/dl). After treatment, the intervention group showed mean IIEF-5 of 15.3 (5−21) and mean total testosterone 409.3 ng/dl (216.9−760.8 ng/dl); the placebo group showed mean IIEF-5 of 13.7 (6−21) and mean total testosterone 466.3 ng/dl (264.3−934.3 ng/dl). The time factor caused statistically significant changes in both the groups for IIEF-5 only (p = 0.0004); however, there was no difference between the two groups (p = 0.7914).

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* Corresponding author.
E-mail addresses: reisleo@unicamp.br, reisleo.l@gmail.com (L.O. Reis).

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**Introduction**

*Tribulus terrestris* is a herb belonging to the family Zygophyllaceae, mostly from southern temperate zones of Europe. It has been used for centuries in traditional Chinese medicine, and also in Indian system of medicine, in order to improve libido and sexual performance. Some authors have confirmed this effect in rabbits and primates.

Studies also show an increase in the level of free testosterone in guinea pigs. These effects could be due to the presence of saponins and flavonoids in the compound, which would act on the fat-soluble steroids.

Dell’Agli et al. tested possible inhibitory effects on the enzyme phosphodiesterase-5. Rogerson et al. studied the possible increase in human skeletal muscle with supplementation of *Tribulus* for a period of five weeks. Other authors have attempted to confirm these effects in humans, but they were unsuccessful, possibly due to limitations in study design and sample size.

**Methods**

The local Ethics Committee approved this prospective, randomized, double-blind and placebo-controlled study. Data collection occurred from September 2009 to April 2010, in a urology outpatient clinic. The subjects were evaluated with history and physical examination directed to the genitals and femoral pulses bilaterally. No patient had abnormal physical examination.

Inclusion criteria were as follows:

- Male;
- Minimum age 40 years;
- Erectile dysfunction treatment-naive;
- Consenting to participate;

Exclusion criteria were as follows:

- Illiterate individuals;
- Smoking;
- Dyslipidemia (abnormal serum cholesterol or triglycerides);
- Uncontrolled diabetes mellitus (fasting glucose > 150 mg/dl);
- Uncontrolled hypertension (diastolic blood pressure > 90 mmHg);
- Prior pelvic radiotherapy;
- Previous pelvic surgery;
- Use of phosphodiesterase-5 inhibitor.

**Conclusions:** At the dose and interval studied, *Tribulus terrestris* was not more effective than placebo in improving symptoms of erectile dysfunction or serum total testosterone. © 2013 AEU. Published by Elsevier España, S.L. All rights reserved.
All subjects underwent determination of serum total testosterone, fasting glucose, triglycerides, and total cholesterol, and were subsequently weighed and had height measured in order to obtain the Body Mass Index (BMI). Additionally, the International Index of Erectile Function questionnaire (IIEF – 5) was also applied.12

Then, all the patients were randomized using a computer program into two groups of fifteen, the intervention (Tribulus terrestris) and control (placebo) groups. Researchers and individuals were blinded for the groups.

The intervention group received sixty capsules containing 400 mg of dry extract of Tribulus terrestris in each, being told to take one capsule in the morning, before breakfast, and another capsule after twelve hours without ingesting any food.

The control group received similar sixty capsules containing 400 mg of pharmaceutical talc (placebo) in each, with identical orientation of the herbal medicine.

At the end of the treatment, both groups were instructed to collect a new blood sample for total testosterone dosage, and again to respond to the IIEF-5 questionnaire. All were asked about the possible side effects that could have been associated with the treatment they had undergone.

All patients were instructed that they were free to leave the study at any time without any harm.

The Chi-square test or Fisher’s exact test was used to compare proportions, and the Mann–Whitney test for comparison of continuous measures between the two groups. The ANOVA was used for comparisons between the groups and times, as well as for repeated measures with post-transformation. The significance level was 5%.

**Results**

Among 100 patients screened in a urology outpatient clinic, 30 patients were enrolled and randomized: 15/15 for intervention and placebo groups.

The mean (SD) age was 60 (9.4) and 62.9 (7.9) years, p = 0.36, for intervention and placebo groups, respectively.

Regarding weight, subjects were divided into three groups based on their BMI: normal (18.6–25.0), overweight (25.1–30.0), and obese (>30.0). In the intervention group, four individuals presented normal weight (26.6%), six overweight (40.0%), and five obese (33.3%). In the placebo group, eight were normal (53.3%), five were overweight (33.3%), and two were obese (13.3%). Fisher’s test showed no significant difference (p = 0.2689). (Table 1).

Three patients in the intervention group (20.0%) and four in the placebo group (26.6%) had compensated diabetes mellitus. This difference was not significant (p = 1.0000).

Eight subjects in the intervention group (53.3%) and ten in the placebo group presented controlled hypertension (66.6%), with no significant difference using the Chi-square test (p = 0.4561). (Table 1).

Regarding the degree of erectile dysfunction (IIEF-5), patients were divided into four levels: Mild, Mild to Moderate, Moderate, and Severe. In the intervention group, we found three patients with mild (20.0%), nine with mild/moderate (60.0%), two with moderate (13.3%), and one with severe (6.6%) erectile dysfunction. In the placebo group, we found three with mild (20.0%), three with mild/moderate (20.0%), seven with moderate (46.6%), and two with severe (13.3%) erectile dysfunction. Applying the Fisher test, no significant difference was found between the groups (p = 0.0841) (Table 1).

In the intervention group, the results of the IIEF-5 were: mean 13.2, median 17.0, range 5.0–21.0 points. In the placebo group, we found the following data: mean 11.6, median 14.0, range 6.0–21 points. The groups were homogeneous prior to treatment (p = 0.2463) (Table 2).

After treatment, the results of the IIEF-5 were as follows:

- Intervention group: mean 15.3, median 18.0, range 5.0–21.0 points.
- Placebo group: mean 13.7, median 16.0, range 6.0–21.0 points.

The time factor was significant and caused statistically significant changes in both the groups, and in both the groups the response was better in the second IIEF-5 questionnaire (p = 0.0004). When comparing the responses between the two groups, they were not different (p = 0.7914) (Table 2).

Regarding the initial serum total testosterone, the intervention group showed: mean 417.1 ng/dl, median 404.7 ng/dl, range 270.7 ng/dl – 548.4 ng/dl. The placebo group obtained mean 442.7 ng/dl, median 419.9 ng/dl, range 301.0 ng/dl – 609.1 ng/dl. The Mann–Whitney test showed no statistical difference (p = 0.4306) (Table 3).

After treatment, testosterone in the intervention group showed an average of 409.3 ng/dl, median 410.6 ng/dl, range 216.9 ng/dl – 760.8 ng/dl. In the placebo group, the average was 466.3 ng/dl, median 421.5 ng/dl, range

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**Table 1** Patients baseline characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Intervention (%)</th>
<th>Placebo (%)</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>Normal weight</td>
<td>26.6</td>
<td>53.3</td>
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<tr>
<td>Overweight</td>
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<td>33.3</td>
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<td>Obese</td>
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<td>13.3</td>
<td>0.2689</td>
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<tr>
<td>Diabetes (+)</td>
<td>20.0</td>
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<tr>
<td>Diabetes (−)</td>
<td>80.0</td>
<td>73.4</td>
<td>1.000</td>
</tr>
<tr>
<td>Hypertension (+)</td>
<td>53.3</td>
<td>66.6</td>
<td></td>
</tr>
<tr>
<td>Hypertension (−)</td>
<td>46.6</td>
<td>33.3</td>
<td>0.4561</td>
</tr>
<tr>
<td>Mild ED</td>
<td>20.0</td>
<td>20.0</td>
<td></td>
</tr>
<tr>
<td>Mild/moderate ED</td>
<td>60.0</td>
<td>20.0</td>
<td></td>
</tr>
<tr>
<td>Moderate ED</td>
<td>13.3</td>
<td>46.6</td>
<td></td>
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<tr>
<td>Severe ED</td>
<td>6.6</td>
<td>13.3</td>
<td>0.0841</td>
</tr>
</tbody>
</table>

**Table 2** Erectile function (IIEF-5).

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Median</th>
<th>Min</th>
<th>Max</th>
<th>p</th>
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<tbody>
<tr>
<td>Intervention baseline</td>
<td>13.2</td>
<td>17.0</td>
<td>5.0</td>
<td>21.0</td>
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<tr>
<td>Placebo baseline</td>
<td>11.6</td>
<td>14.0</td>
<td>6.0</td>
<td>21.0</td>
<td>0.2463</td>
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<tr>
<td>Intervention final</td>
<td>15.3</td>
<td>18.0</td>
<td>5.0</td>
<td>21.0</td>
<td></td>
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<tr>
<td>Placebo final</td>
<td>13.7</td>
<td>16.0</td>
<td>6.0</td>
<td>21.0</td>
<td>0.7914</td>
</tr>
</tbody>
</table>
Table 3  Serum testosterone.

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Median</th>
<th>Min.</th>
<th>Max.</th>
<th>p</th>
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<tbody>
<tr>
<td>Intervention</td>
<td>417.1</td>
<td>404.7</td>
<td>270.7</td>
<td>548.4</td>
<td></td>
</tr>
<tr>
<td>baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>442.7</td>
<td>419.9</td>
<td>301.0</td>
<td>609.1</td>
<td>0.4306</td>
</tr>
<tr>
<td>baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>409.3</td>
<td>410.6</td>
<td>216.9</td>
<td>760.8</td>
<td></td>
</tr>
<tr>
<td>final</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>466.3</td>
<td>421.5</td>
<td>264.3</td>
<td>934.3</td>
<td>0.3551</td>
</tr>
<tr>
<td>final</td>
<td></td>
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</table>

264.3 ng/dl – 934.3 ng/dl. There was no difference between the groups (p = 0.3551) (Table 3).

Regarding testosterone, there was no statistically significant difference between the groups before and after treatment (p = 0.7775) and no significant time effect either (p = 0.3993).

Discussion

Despite the great advances made in the treatment of erectile dysfunction after the introduction of phosphodiesterase-5 inhibitors and the increasing knowledge gained about the androgen dysfunction of the aging male, many individuals still seek and believe in the effects of natural and herbal aphrodisiac products.

In this scenario, *Tribulus terrestris* is a plant of the Zygophyllaceae family, native of tropical regions of southern Europe, southern Asia, Africa, and northern Australia. It can thrive even in desert climates and poor soils.12

Tribulus has been used for centuries in traditional Chinese medicine and Indian medicine to improve libido and sexual performance.9 Tuncer et al. demonstrated a reduction in lipid levels and also a possible recovery of endothelial dysfunction caused by hyperlipidemia in rabbits fed with a diet rich in *Tribulus*.14

Aggarwal et al. using experimental models suggest that Tribulus is able to reduce calcium oxalate nucleation and crystal growth in the kidney.15,16

Kim et al. demonstrated that the plant extract blocks proliferation and induces apoptosis in human hepatic cancer cells, suggesting that this extract can be used in the treatment of hepatocellular carcinoma.17

Its effect is attributed to the presence of a substance called protodioscin.9 Protodioscin (5,6-dihydroprotodioscin, neoprotodioscin)18 is a saponin that can be found in different concentrations in the aerial part of the plant, depending on the place where it is grown.19

Additionally, protodioscin may act in improving erection function by being converted into dehydroepiandrosterone (DHEA).20 Adaikan et al. showed in an experimental study that protodioscin increased by 24% the relaxation response of rabbit cavernous tissue to stimulation with acetylcholine and nitroglycerin when fed with 5 mg/kg of *Tribulus terrestris*.21

Gauthaman et al. reported a significant increase in the intracavernous pressure (PI) of animals receiving *Tribulus terrestris*. They also described improvement in the sexual behavior of animals through breeding parameters, intromission, ejaculatory latency, and post-ejaculatory interval. The authors concluded that the increase in PI was due to the possible effects of pro-erectile protodioscine and the improvement of other parameters could be linked to pro-androgenic effects.22 The same authors conducted a study describing that castrated animals that received testosterone and Tribulus showed a statistically significant increase in intracavernosal pressure measurement, in prostate weight and in intromission and mounts.4

However, Dell’Agli et al. have not demonstrated the inhibitory effect of *Tribulus terrestris* on the enzyme phosphodiesterase-5,8 which contradicts a possible pro-erectile effect.

In the present study, we observed an improvement in the response of both the groups compared with scores obtained in the first IEF-5, before receiving the capsules, p-value = 0.0004. This result, in our opinion, is due to the strong power of the placebo effect when treating individuals with erectile dysfunction.

Although *Tribulus terrestris* is the target of numerous experimental studies with favorable results, with several suggested actions from anti-neoplastic, anti-lithiasis to stimulating libido and erection, these data do not have confirmation in well-conducted clinical trials yet.

In the context of male sexual dysfunction, the present study demonstrated only placebo effect for *Tribulus terrestris* at the studied dose and interval when treating patients with erectile dysfunction.

Although it is a prospective, randomized, double-blinded, and placebo-controlled study using a validated questionnaire to assess sexual function, and accounting for serum testosterone, the present study is preliminary, including a relatively small number of patients.

Future studies are warranted, including more patients and also evaluating those with normal erectile function.

Conflict of interest

The authors declare that they have no conflict of interest.

References