Published in final edited form as:
*Complement Ther Med*. 2008 June ; 16(3): 147–154.

# A DETAILED SAFETY ASSESSMENT OF A SAW PALMETTO EXTRACT

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## Abstract

**Background—**Saw palmetto is commonly used by men for lower urinary tract symptoms. Despite its widespread use, very little is known about the potential toxicity of this dietary supplement.

**Methods—**The Saw palmetto for Treatment of Enlarged Prostates (STEP) study was a randomized clinical trial performed among 225 men with moderate-to-severe symptoms of benign prostatic hyperplasia, comparing a standardized extract of the saw palmetto berry (160mg twice daily) with a placebo over a one-year period. As part of this study, detailed data were collected on serious and non-serious adverse events, sexual functioning, and laboratory tests of blood and urine. Between-group differences were assessed with mixed-effects regression models.

**Results—**There were no significant differences observed between the saw palmetto and placebo-allocated participants in the risk of suffering at least one serious adverse event (5.4% vs. 9.7%, respectively; $p = 0.31$) or non-serious symptomatic adverse event (34.8% vs. 30.1%; $p = 0.48$). There were few significant between-group differences in sexual functioning or for most laboratory analyses, with only small differences observed in changes over time in total bilirubin ($p = 0.001$), potassium ($p = 0.03$), and the incidence of glycosuria (0% in the saw palmetto group vs. 3.7% in the placebo group, $p = 0.05$).

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ClinicalTrials.gov Registration # NCT00037154

Conflict of Interest Statement: None of the authors had any financial or personal relationships with any other individuals or organizations that could inappropriately influence this work.

The study sponsors played no role in the study design; the collection, analysis, and interpretation of the data; in the writing of the manuscript; and in the decision to submit a manuscript for publication.

**Conclusions—**Despite careful assessment, no evidence for serious toxicity of saw palmetto was observed in this clinical trial. Given the sample size and length of this study, however, these data do not rule out potential rare adverse effects associated with the use of saw palmetto.

## Introduction

Herbal therapies are one of the most widely used alternative modalities in the U.S. with sales exceeding $18 billion in 2005 (1). Among the most commonly used phytotherapeutics is an extract of the berry of the saw palmetto plant, a dwarf palm tree native to the southeastern U.S. (2,3). Saw palmetto extracts are generally used to relieve symptoms associated with benign prostatic hyperplasia (BPH), a non-malignant enlargement of the prostate gland affecting the majority of men over the age of 50 (4). Because saw palmetto extracts are sold without prescription, it is difficult to determine the numbers of men who take the extract regularly, but it is estimated that the number of regular users is approximately 2.5 million adults in the U.S (5).

The efficacy of saw palmetto (also known as *serenoa repens*) is currently the subject of active investigation by several research groups. An updated systematic review of saw palmetto for BPH found that most, but not all, published studies showed some modest benefit in overall lower-urinary tract symptoms and nocturia, but that much of the available research suffered from serious methodologic problems (6). We recently reported the efficacy results of a year-long clinical trial of a saw palmetto extract in men with at least moderately severe BPH that addressed many of the shortcomings of earlier studies. This trial, the Saw palmetto Trial for Enlarged Prostates (STEP) study, found no evidence of efficacy of saw palmetto for either BPH symptoms or objective measures of urinary function (7).

Despite the substantial quantity of clinical research performed on saw palmetto, there are few data regarding potential adverse effects associated with its use. Most trials were of short duration; few described any systematic attempt to assess adverse effects, and with rare exception (8), laboratory testing was not performed to test for asymptomatic toxicities of saw palmetto (9). This information is of great public-health consequence given the large numbers of men who self-medicate with saw palmetto for extended periods of time. Since it is well known that most individuals who take dietary supplements do not inform their physicians about their use of these products (10–14), most men who take saw palmetto will not be monitored for potential adverse effects. Understanding the risks of using saw palmetto, therefore, is of great importance for patients, clinicians, and regulatory authorities.

A major goal of the STEP study was a detailed assessment of potential toxicity of saw palmetto, including both symptomatic adverse effects, as well as asymptomatic laboratory abnormalities. A summary of the major adverse-event data from this trial has been published previously (7). This report provides comprehensive information on the adverse-event data from the STEP trial, including detailed information about laboratory measurements.

## METHODS

### Study Design and Participants

The STEP study was a single-center double-blind placebo-controlled randomized clinical trial of an extract of the saw palmetto berry. Inclusion criteria included age at least 50 years, a mean score of at least 8 on the American Urological Association Symptom Inventory (AUASI) on two measurements prior to randomization, a peak urine flow between 4 and 15 ml/sec, a post-void residual volume <250 ml, and a prostate-specific antigen (PSA) <4.0 ng/ml (or a PSA <10ng/ml with a negative prostate biopsy for malignancy). Potential participants were excluded if they had a creatinine >2.0 mg/dl, prior prostate surgery, a history of prostate cancer, a

neurologic condition affecting urination, severe concomitant illness, or were taking a medication with androgenic or antiandrogenic properties. The STEP study was funded by the National Institutes of Health (co-funded by the National Institute of Diabetes, Digestive, and Kidney Diseases and the National Center for Complementary and Alternative Medicine) and was conducted under an Investigational New Drug exemption from the U.S. Food and Drug Administration. All study procedures were approved by the institutional review boards at the University of California, San Francisco and the Kaiser Foundation Research Institute.

Participants underwent two eligibility screening visits, a one-month, singleblind run-in period, and were seen for follow-up visits at one, three, six, nine, and twelve months after randomization.

## Intervention

Participants were randomized to a saw palmetto berry extract, 160mg twice daily, for one year or a placebo capsule. The saw palmetto preparation was produced by Indena, USA (Seattle, WA) and contained 92.1% total fatty acids. The extract was packaged in gelatin capsules by Cardinal Health (formerly RP Scherer, Inc (St. Petersburg, Florida)) and supplied to the trial by Rexall-Sundown, Inc, (Boca Raton, FL).

The identical-appearing placebo capsules contained 200mg of polyethylene-glycol 400, colored to match the saw palmetto extract.

## Outcomes

At each post-randomization visit, all participants were asked if they had experienced “any significant medical illness since the last study visit.” Those who responded affirmatively to this global question were then asked to complete a symptom checklist that included open-ended fields (15). Serious adverse events (SAE's) were recorded and verified with medical records, where possible. Non-serious adverse events were recorded and categorized by organ system.

Twenty-two laboratory tests were obtained at baseline and at one, six, and twelve months after randomization (Table 5). Most baseline laboratory values were obtained at the randomization visit, except the serum prostate-specific antigen test and the prothrombin time (international normalized ratio) were obtained at the first screening visit (approximately six weeks prior to randomization), as these were part of the eligibility screening process.

The effect of saw palmetto on sexual functioning was measured with the O’Leary Brief Sexual Function Inventory (16) at randomization, the 6-month visit and at the one-year closeout visit. Scores for each domain were calculated as the sum of scores for each of the items in that domain; each item was scored on a 0-to-4 Likert-like scale. The domains assessed (and the number of items included and the range of scores for that domain) were: sexual drive (2 items, range 0 – 8), erectile function (3 items, range 0 – 12), ejaculation (2 items, range 0 – 8), perceptions of problems (3 items, range 0 – 12), and overall sexual satisfaction (1 item, range 0 – 4).

## Statistical Analyses

The frequencies of symptomatic adverse events (both serious and non-serious) were tabulated and the proportions of participants in each treatment group who reported at least one event were compared with Fisher’s exact tests.

Comparisons between the active-treatment and placebo arms for the laboratory and sexual-functioning outcomes were made with mixed-effects regression models to account for the repeated measures (17), which included a random intercept and terms to describe change in

outcomes over time within each group. The test of the group-by-time interaction terms provided the primary test of significance between the two treatment arms. This test assesses the statistical significance of the differences between the two groups for each continuous variable over the duration of the study. The time variable was treated as fully categorical (the individual time points (three for the sexual functioning outcome and four for the laboratory values) were modeled with indicator variables) as several variables showed significant departures from linear or quadratic models. The tables show the model-derived predicted mean values and standard errors for the baseline and closeout timepoints. Also shown are the differences between these assessments with confidence intervals derived using the standard error of the group-by-time (closeout value) interaction term from the mixed model, with the test of significance derived from the mixed-effects models. All analyses were consistent with the principle of intention-to-treat in that all data for all participants were used; no data were imputed.

## RESULTS

Overall, 225 men were randomized to either the saw palmetto extract or a placebo; demographic characteristics were similar between the two groups (Table 1). Adherence to both the study visit schedule and medication regimen was excellent: 96% of randomized participants completed the study and 91.6% of all study medication was consumed (as measured by capsule counts at each visit) (7); there was no difference in adherence between the two trial arms.

### Serious Adverse Events

As described previously, a total of 26 serious adverse events among 17 participants were reported during the study (Table 2) (7). While the majority of these events (18 events) occurred in participants randomized to placebo, several of these events occurred in the same participant, so that the likelihood of suffering at least one SAE was not significantly different between the two treatment arms: 5.4% in the saw palmetto group and 9.7% in the placebo group ($p = 0.31$).

Most of the events were cardiovascular incidents, elective musculoskeletal procedures, or serious gastrointestinal problems. Three incident cancer cases occurred, of which two were in the placebo group. None of the serious adverse events were assessed as probably related to the study medicine and no deaths occurred.

### Non-Serious Adverse Events

The risk of suffering at least one non-serious adverse event was similar between the two groups (34.8% in the saw palmetto group and 30.1% in the placebo group, $p = 0.48$). Events were distributed widely over many organ systems, with musculoskeletal, respiratory, and gastrointestinal problems being most commonly reported (Table 3).

### Sexual Functioning

No statistically significant differences were observed between the saw palmetto and placebo groups in the measured domains of sexual functioning with the exception of the perception-of-sexual-problems domain which showed a small but significantly greater improvement in the placebo group (Table 4).

### Laboratory Test Results

A large number of serum laboratory tests were performed at baseline, one month, six months and one year after randomization (Table 5). Only the between-group differences in total bilirubin and potassium achieved conventional levels of statistical significance (Table 5). The magnitude of the differences for each of these variables was judged to be small from a clinical

standpoint. In addition, there were no significant differences in most urine tests, including pH ($p = 0.50$), specific gravity ($p = 0.37$), and the proportions of saw-palmetto-assigned participants *vs*. placebo-assigned participants whose closeout urine samples had evidence of hematuria (2.9% *vs*. 6.5%, $p = 0.22$), proteinuria (1.0% *vs*. 4.6%, $p = 0.11$), ketonuria (2.9% *vs*. 2.8%, $p = 0.95$), or bilirubinuria (0% *vs*. 1.0%, $p = 0.33$); patients randomized to placebo were significantly more likely to develop glycosuria (0% *vs*. 3.7%, $p = 0.05$). Of note, we found no significant effect of saw palmetto on serum prostate-specific antigen levels, consistent with other studies (8,18–20).

## DISCUSSION

Because many men choose to take saw palmetto extracts, the potential adverse effects of this dietary supplement must be ascertained so that these individuals can make informed decisions about their use of this product. The STEP study provided a unique opportunity to make detailed assessments about potential toxicities of saw palmetto, having obtained extensive data on both symptomatic side effects as well as asymptomatic laboratory abnormalities and included a placebo group which allowed for comparison with an untreated control condition.

Overall, we found no evidence that consumption of this saw palmetto extract, at a dose of 160mg twice daily over a period of one year, was associated with any clinically important adverse effects. Relatively few participants suffered serious adverse events, and these were more common in the placebo-allocated participants. Non-serious adverse events were nearly equally distributed between the saw palmetto and placebo groups, both in total number and in the proportion of participants who suffered at least one adverse event. Only one of the five domains on the O'Leary sexual-functioning instrument (the perception-of-problems domain) showed a significant difference between treatment groups; however, this difference was small (approximately 1/3 of a point difference on a 12-point scale). Finally, we found little evidence of toxicity of saw palmetto among the laboratory analyses performed: while there were a small number of significant results, the large number of tests conducted would be expected to generate a small number of significant differences due to chance. Further evidence suggesting that these differences are most likely due to chance is the fact that no other liver-function tests besides the total bilirubin showed significant differences and that the greater source of the observed difference in potassium levels was due to a small decline in the placebo group, not a rise in the saw palmetto group (Table 5); the significant difference in glycosuria was due to an increase in urine glucose in placebo-allocated participants. Recent laboratory evidence also suggests that saw palmetto does not have serious hepatic toxicity (21).

With the growing popularity of dietary supplements, it is imperative that better data on their potential toxicities be generated. Several dietary supplements have been shown to have serious toxic effects and have been removed from the market in the U.S. and some European countries. There is a compelling need to better understand potential adverse effects of other widely used dietary supplements, so that consumers can make more informed decisions about risks and benefits.

The efficacy of saw palmetto extracts for the treatment of BPH is still a matter of controversy and higher-quality studies of this phytotherapeutic are now beginning to appear. Regardless of the ultimate outcomes of these studies, saw palmetto extracts will likely continue to be used widely by men who feel that they benefit from its use (22). Prior studies suggested that side effects of saw palmetto may include headache, dizziness, nausea, and constipation but assessment of adverse effects of saw palmetto has often been incomplete and unsystematic (23). The STEP trial data are reassuring in that no important toxicities of this extract were identified among the group of patients studied.

These reassuring results, however, must be viewed within the context of the study limitations. The statistical power to detect important clinical differences was limited for some variables, given the sample size of the study. The follow-up phase was one year, so no conclusions regarding use over a longer time period can be made. Whether the favorable safety profile of the extract used in this study is typical of other extracts cannot be determined, as there is variation in the extraction techniques and final product composition among the marketed products (24). Finally, rare but serious adverse effects of saw palmetto cannot be assessed in a trial of this size and, like pharmaceutical agents, will require large-scale post-marketing studies to adequately assess this possibility. While case reports do not establish causality, there are case reports suggesting that serious idiosyncratic toxicity of saw palmetto may exist: one patient developed cholestasis after taking an herbal blend that contained saw palmetto (25), another developed transient hepatitis and pancreatitis (26), and one patient suffered excessive intra-operative bleeding and prolonged bleeding time from saw palmetto (27).

Overall, the data from the STEP trial do not support the concern of serious clinical adverse effects of this saw palmetto extract over a period of one year. While these results are reassuring, further data are needed to more definitively address toxicity issues and will likely emerge from ongoing investigations of saw palmetto as well as population-based toxicity studies.

**Acknowledgments**

the authors wish to thank Bertina Lee and Arleen Sakamoto, R.N. for their outstanding assistance during the study, Dr. Henry Leung for management of the study medication, and Dr. Howard Leong for assistance with the laboratory assays.

Financial Support: supported by a grant from the National Institute of Diabetes, Digestive, and Kidney Diseases (#R01 DK56199) and the National Center for Complementary and Alternative Medicine (#K08 AT001338).

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**Table 1**

Baseline characteristics of study sample by treatment group.

| Characteristic | Saw Palmetto (N=112) | Placebo (N=113) |
|---|---|---|
| Age – N (%) | | |
| 50–59 years | 45 (40%) | 42 (37%) |
| 60–69 years | 46 (41%) | 48 (42%) |
| 70–79 years | 21 (18%) | 23 (20%) |
| Race or ethnic group – N (%) | | |
| White | 94 (84%) | 89 (79%) |
| Black | 4 (4%) | 8 (7%) |
| Asian or Pacific Islander | 7 (6%) | 8 (7%) |
| Hispanic | 6 (5%) | 5 (4%) |
| Other | 1 (1%) | 2 (2%) |
| American Urological Association Symptom Index | | |
| Mean (S.D.) | 15.7 (5.7) | 15.0 (5.3) |
| Prostate Volume – ml | | |
| Mean (S.D.) | 34.7 (13.9) | 33.9 (15.2) |
| Maximal Urinary Flow Rate – ml/s | | |
| Mean (S.D.) | 11.4 (3.5) | 11.6 (4.3) |
| Post-void Residual Volume – ml | | |
| Mean (S.D.) | 80.0 (51.9) | 84.5 (63.8) |

Abbreviations: N = number of participants, S.D. = Standard Deviation

**Table 2**

Summary of serious adverse events during STEP trial.

| SAE* | ID† | Adverse Event | Treatment Group |
|---|---|---|---|
| 1 | A | Hernia repair | Placebo |
| 2 | B | Hypotension | Placebo |
| 3 | B | Hematoma | Placebo |
| 4 | B | Bradycardia | Placebo |
| 5 | B | Coronary artery stent re-occlusion | Placebo |
| 6 | B | Coronary artery stent re-occlusion | Placebo |
| 7 | B | Superficial femoral artery occlusion | Placebo |
| 8 | B | Congestive heart failure | Placebo |
| 9 | C | Colon cancer | Placebo |
| 10 | D | Elective hip replacement | Placebo |
| 11 | E | Localized prostate cancer | Placebo |
| 12 | F | Total knee arthroplasty | Placebo |
| 13 | G | Syncope, possible seizure | Placebo |
| 14 | H | Gastrointestinal bleeding | Placebo |
| 15 | I | Shortness of breath | Placebo |
| 16 | J | Resection of bladder carcinoma | Placebo |
| 17 | J | Rhabdomyolysis | Placebo |
| 18 | K | Hip revision | Placebo |
| 19 | L | Lumbar laminectomy | Saw palmetto |
| 20 | L | Gastrointestinal bleeding | Saw palmetto |
| 21 | M | Vertigo | Saw palmetto |
| 22 | N | Bleeding gastric ulcer | Saw palmetto |
| 23 | O | Shoulder surgery | Saw palmetto |
| 24 | P | Atrial fibrillation | Saw palmetto |
| 25 | P | Elective laminectomy | Saw palmetto |
| 26 | Q | Melanoma removal | Saw palmetto |

*SAE = Serious adverse event

†ID = Study participant identification code

**Table 3**

Summary of non-serious adverse events during the STEP trial.

| Adverse Event | Saw palmetto (N=112) | Placebo (N=113) |
|---|---|---|
| **Cardiac** | | |
| Dysrrhythmia / palpitations | 0 | 2 |
| **Dermatologic** | | |
| Rash | 1 | 3 |
| Shingles | 0 | 2 |
| Skin cancer removal | 1 | 0 |
| Keratoses trunk | 0 | 1 |
| **Gastrointestinal** | | |
| Diarrhea | 2 | 2 |
| Heartburn | 0 | 3 |
| Abdominal pain | 2 | 1 |
| Nausea/vomiting | 2 | 0 |
| Hemorrhoids | 1 | 0 |
| Abdominal swelling | 1 | 0 |
| Liver cyst on ultrasound scan | 0 | 1 |
| Polyp removal | 1 | 0 |
| Blood in stool | 0 | 1 |
| **Genitourinary** | | |
| Nocturia | 0 | 2 |
| Discomfort in kidney | 1 | 0 |
| Pain in prostate area | 1 | 0 |
| Testicular pain | 0 | 1 |
| Kidney stone | 1 | 0 |
| Prostatitis | 1 | 0 |
| Urinary infection | 1 | 0 |
| **HEENT** | | |
| Headache | 1 | 0 |
| TMJ pain | 1 | 0 |
| Head and neck infection | 0 | 2 |
| Chemical conjunctivitis | 1 | 0 |
| Periodontal cyst | 1 | 0 |
| **Musculoskeletal** | | |
| Back pain | 4 | 4 |
| Gout | 2 | 2 |
| Joint pain/swelling | 3 | 2 |
| Trauma (fracture/bruise) | 4 | 2 |
| Myalgias | 0 | 1 |
| Soft tissue pain (e.g., tendonitis) | 3 | 0 |
| Infected digit | 0 | 2 |
| **Neurologic / Psychiatric** | | |
| Depression | 1 | 0 |
| **Pulmonary** | | |
| Upper respiratory tract infection | 12 | 10 |
| Cough | 1 | 2 |
| Collapsed lung | 1 | 0 |
| Sleep apnea | 1 | 0 |
| Walking pneumonia | 1 | 0 |
| **Miscellaneous / Other** | | |
| Fatigue | 0 | 2 |
| Inguinal hernia | 2 | 0 |
| Axillary abscess | 1 | 0 |
| Cyst removal | 0 | 1 |
| Fistula | 0 | 1 |
| Hypothyroidism | 0 | 2 |
| Tumor removal | 0 | 1 |
| Yeast infection | 1 | 0 |
| **Total Non-Serious AE's*** | **57** | **53** |

* AE's = Adverse events

**Table 4**

Baseline and 12-month closeout scores for the domains of the O'Leary Brief Sexual Function Inventory

| | Saw Palmetto | | Placebo | | | | |
|---|---|---|---|---|---|---|---|
| **Domain (Range)** | **Baseline** | **12 Months** | **Baseline** | **12 Months** | **Difference** | **95% CI** | ***p*-value*** |
| Sexual drive (0–8) | 4.29 ± 0.17 | 4.28 ± 0.18 | 4.26 ± 0.17 | 4.22 ± 0.18 | 0.03 | −0.35 to 0.41 | 0.99 |
| Erectile function (0–12) | 5.43 ± 0.16 | 5.71 ± 0.16 | 5.42 ± 0.16 | 5.61 ± 0.16 | 0.08 | −0.31 to 0.49 | 0.49 |
| Ejaculation (0–8) | 1.60 ± 0.22 | 1.55 ± 0.22 | 1.80 ± 0.22 | 1.90 ± 0.22 | −0.16 | −0.62 to 0.30 | 0.25 |
| Perception of problems (0–12) | 8.84 ± 0.33 | 8.79 ± 0.33 | 8.78 ± 0.33 | 8.38 ± 0.33 | 0.35 | −0.31 to 1.01 | 0.04 |
| Overall satisfaction (0–4) | 2.18 ± 0.10 | 2.12 ± 0.11 | 2.01 ± 0.10 | 2.08 ± 0.10 | −0.13 | −0.40 to 0.14 | 0.40 |

Mean values at baseline and the 12-month closeout visit and between-group differences (calculated as the change in the placebo group subtracted from the change in the saw palmetto group). Mean values are derived from the mixed-effects regression models. The *p*-values for the between-group differences are derived from the hypothesis test on the group-by-time interaction term from the linear mixed-effects model which tests for overall differences between groups at any time point; the confidence interval for the between-group differences are obtained from the difference between the estimated baseline and closeout values and does not consider interim time points.

* *p*-value for between-group differences in change in variable

CI = confidence interval

**Table 5**

Laboratory test data

| | Saw Palmetto | | Placebo | | | | |
|---|---|---|---|---|---|---|---|
| **Test** | **Baseline** | **12 Months** | **Baseline** | **12 Months** | **Difference** | **95% CI** | ***p*-value*** |
| Albumin (gm/dl) | 4.17 ± 0.02 | 4.08 ± 0.03 | 4.11 ± 0.02 | 4.04 ± 0.03 | −0.01 | −0.07 to 0.05 | 0.44 |
| Bilirubin: total (mg/dl) | 0.93 ± 0.03 | 0.88 ± 0.03 | 0.90 ± 0.03 | 0.96 ± 0.03 | −0.12 | −0.18 to −0.05 | 0.001 |
| Calcium (mg/dl) | 9.64 ± 0.03 | 9.60 ± 0.03 | 9.60 ± 0.03 | 9.59 ± 0.03 | −0.04 | −0.12 to 0.05 | 0.44 |
| Carbon dioxide (mmol/dl) | 29.59 ± 0.22 | 28.65 ± 0.22 | 29.17 ± 0.22 | 28.73 ± 0.22 | −0.50 | −1.10 to 0.10 | 0.20 |
| Chloride (mmol/dl) | 101.85 ± 0.27 | 102.94 ± 0.28 | 102.22 ± 0.27 | 103.03 ± 0.28 | 0.28 | −0.52 to 1.09 | 0.69 |
| Cholesterol, Total (mg/dl) | 206.22 ± 3.47 | 205.97 ± 3.53 | 204.70 ± 3.45 | 204.02 ± 3.48 | 0.44 | −7.22 to 8.10 | 0.91 |
| Creatine Kinase (CPK) (U/l)§ | 157.06 ± 9.82 | 154.01 ± 9.97 | 156.98 ± 9.80 | 143.19 ± 9.90 | 10.74 | −13.49 to 34.97 | 0.59 |
| Creatinine (mg/dl) | 1.03 ± 0.02 | 1.03 ± 0.02 | 1.03 ± 0.02 | 1.04 ± 0.02 | 0.001 | −0.03 to 0.03 | 0.46 |
| Glucose (mg/dl) | 96.04 ± 2.89 | 96.08 ± 2.93 | 97.87 ± 2.87 | 102.12 ± 2.89 | −4.21 | −11.19 to 2.77 | 0.55 |
| Hematocrit (%) | 44.34 ± 0.29 | 43.99 ± 0.29 | 43.77 ± 0.29 | 43.91 ± 0.29 | −0.48 | −1.07 to 0.11 | 0.43 |
| International Normalized Ratio (INR) (no units) | 0.93 ± 0.01 | 0.94 ± 0.01 | 0.92 ± 0.01 | 0.93 ± 0.01 | −0.01 | −0.02 to 0.003 | 0.40 |
| Platelet Count ($10^9$/L) | 241.88 ± 4.85 | 238.14 ± 4.89 | 246.83 ± 4.82 | 237.56 ± 4.85 | 5.53 | −3.16 to 14.22 | 0.53 |
| Potassium (mmol/dl) | 4.32 ± 0.03 | 4.35 ± 0.04 | 4.38 ± 0.03 | 4.33 ± 0.04 | 0.08 | −0.02 to 0.18 | 0.03 |
| Prostate Specific Antigen (PSA) (ng/ml) | 1.78 ± 0.14 | 1.85 ± 0.14 | 1.62 ± 0.14 | 1.77 ± 0.14 | −0.07 | −0.30 to 0.15 | 0.10 |
| SGOT (AST) (U/L) | 26.34 ± 1.23 | 25.22 ± 1.25 | 27.80 ± 1.23 | 28.69 ± 1.24 | −2.01 | −5.15 to 1.13 | 0.64 |
| SGPT (ALT) (U/L) | 27.28 ± 1.75 | 25.91 ± 1.77 | 30.25 ± 1.74 | 30.82 ± 1.75 | −1.94 | −5.65 to 1.76 | 0.56 |
| Sodium (mmol/dl) | 138.42 ± 0.21 | 138.15 ± 0.22 | 138.43 ± 0.22 | 138.09 ± 0.22 | 0.06 | −0.62 to 0.75 | 0.88 |
| Testosterone (ng/dl) | 372.97 ± 12.01 | 356.15 ± 12.10 | 376.48 ± 11.98 | 375.07 ± 11.99 | −15.40 | −39.49 to 8.69 | 0.06 |
| Triglycerides (mg/dl) | 152.97 ± 9.21 | 143.13 ± 9.32 | 168.90 ± 9.11 | 143.62 ± 9.17 | 15.44 | −3.69 to 34.58 | 0.11 |
| Urea nitrogen (BUN) (mg/dl) | 13.92 ± 0.42 | 14.82 ± 0.43 | 14.78 ± 0.42 | 14.75 ± 0.43 | 0.93 | −0.22 to 2.08 | 0.39 |
| White Blood Cells (WBC) ($10^9$/L) | 6.30 ± 0.15 | 6.08 ± 0.15 | 5.95 ± 0.15 | 6.00 ± 0.15 | −0.27 | −0.60 to 0.05 | 0.25 |

Mean laboratory values at baseline and the 12-month closeout visit and between-group differences (calculated as the change in the placebo group subtracted from the change in the saw palmetto group). Mean values are derived from the mixed-effects regression models. The *p*-values for the between-group differences are derived from the hypothesis test on the group-by-time interaction term from the linear mixed-effects model which tests for overall differences between groups at any time point; the confidence interval for the between-group differences are obtained from the difference between the estimated baseline and closeout values and does not consider interim time points.

* *p*-value for between-group differences in change in variable

§ excludes one placebo-randomized participant who developed a statin-induced rhabdomyolysis

CI = confidence interval