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# Antioxidant Effects of Lycopene in African American Men with Prostate Cancer or Benign Prostate Hyperplasia: A Randomized Controlled Trial

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## Abstract

Consumption of tomato products is associated with a decreased risk of prostate cancer, and lycopene, the red carotenoid in the tomato, is a potent antioxidant that might contribute to this chemoprevention activity. A double-blind, randomized, placebo-controlled trial of 105 African American men veterans, recommended for prostate biopsy to detect cancer was carried out to investigate whether oral administration of lycopene increases lycopene levels in blood and prostate tissue and lowers markers of oxidative stress. Urology patients were randomly assigned to receive 30 mg/d of lycopene as a tomato oleoresin or placebo for 21-days prior to prostate biopsy for possible diagnosis of prostate cancer. A total of 47 men were diagnosed with prostate cancer and 58 were diagnosed with benign prostate hyperplasia. Diet, smoking, and drinking habits were assessed. For the men receiving lycopene, the mean lycopene concentration increased from 0.74 ± 0.39 to 1.43 ± 0.61 μmol/L in plasma ($P$ <0.0001) and from 0.45 ± 0.53 to 0.59 ± 0.47 pmol/mg in prostate tissue ($P$ = 0.005). No significant changes in the DNA oxidation product 8-oxo-deoxyguanosine or the lipid peroxidation product malondialdehyde were observed in prostate tissue or plasma, respectively, as a result of lycopene administration.

### Keywords

prostate cancer; lycopene; chemoprevention; clinical trial; African American men

## Introduction

A dietary carotenoid without provitamin A activity, lycopene occurs in tomato, watermelon and pink grapefruit (1). Among the more than 600 naturally occurring carotenoids, lycopene is the most efficient antioxidant in terms of quenching singlet oxygen. Lycopene is twice as

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effective as β-carotene and 10-fold more active than α-tocopherol as an antioxidant (1). Since oxidative stress has been associated with prostate cancer risk (2), the potent antioxidant lycopene was investigated as a possible chemoprevention agent .

The most compelling evidence for the chemoprevention activity of lycopene has been in the prevention of prostate cancer. In a dietary assessment with follow-up of 51,529 male health professionals, 773 of whom developed prostate cancer over a 6-yr period, Giovannucci *et al.* (3) reported that higher intake of lycopene and tomato products was associated with lower risk of prostate cancer. Giovannucci (4) reaffirmed these results in a review of the epidemiological evidence. Gann *et al*. (5) and Giovannucci *et al.* (6) confirmed these results in a prospective study of this same cohort of male health professionals during a period of 12 yr. During this time, 2,481 cases of prostate cancer occurred in the study group, and these prospective epidemiological analyses confirmed the inverse correlation between prostate cancer and the consumption of tomato products. Clinton *et al*. (7) measured lycopene in a variety of tissues and found that lycopene is concentrated in the human prostate; an observation which supports the hypothesis that lycopene is a chemoprevention agent in the tomato.

In preparation for our study, a preliminary whole foods intervention was carried out in which 32 men with prostate cancer received tomato sauce containing 30 mg/day lycopene (8). Serum and prostate lycopene levels increased 1.97-fold and 2.93-fold, respectively, total serum prostate specific antigen (PSA) decreased 17.5%, and 8-oxodG (a marker of oxidative stress) decreased 21.3% in leukocytes. The aim of our present study was to determine the effects of lycopene supplementation on prostate tissue levels relative to those in plasma, and its effects on the oxidative stress intermediate endpoint markers DNA oxidation and lipid peroxidation. This was a randomized, double-blind, placebo controlled phase II clinical investigation of the effect of lycopene supplementation on lipid peroxidation in plasma and on DNA oxidation in prostate tissue of African American men recommended for prostate biopsy to detect cancer. Previous studies involved fewer subjects and were not blinded, not placebo controlled, and/or not randomized.

## Materials and Methods

### Participants

This was a randomized, double-blind, placebo-controlled study of African American veterans. The Institutional Review Board of the University of Illinois Medical Center, the Institutional Review Board of the Jesse Brown VA Hospital, the University of Illinois Cancer Center, and the General Clinical Research Center at the University of Illinois Medical Center approved the study protocol. All participants gave written informed consent. The study was registered on-line at Clinicaltrials.gov as protocol NCT00416390.

African American men from 50 to 83 years of age were recruited from June 2000 until June 2005 from among urology patients at the Jesse Brown VA Hospital and the University of Illinois Medical Center, who were being scheduled for prostate biopsy due to elevated total prostate specific antigen (PSA >4.0 ng/mL) and abnormality detected during digital rectal examination and/or ultrasound. Since prostate biopsies for the possible diagnosis of prostate cancer were being scheduled three to four weeks in advance, this provided an opportunity for a 21-day intervention without interfering with the usual care of these patients.

Subjects were excluded who had a history of chronic diseases associated with oxidative stress, such as previously diagnosed heart disease, inflammatory bowel disease or cancer. Men with known hypersensitivity to tomato products were also excluded, since a tomato extract was administered to study participants. Subjects currently suffering from alcoholism

or substance abuse were excluded as well as those who were taking dietary supplements containing lycopene or more than 2-times the recommended daily allowance of vitamin E, vitamin C or β-carotene.

### Randomization and Blinding

Each subject was assigned a computer-generated pseudo-random number that corresponded to placebo or lycopene. Numbers were printed on labels which were affixed to bottles of placebo or lycopene by the study pharmacist. Identical in size, color and shape, lycopene and placebo were formulated as gel capsules and placed in bottles that were identical in appearance. Neither the investigators nor the participants knew which numbered bottles contained lycopene or placebo. Subjects were enrolled by the study manager.

### Intervention

Each participant received 30 mg/day lycopene or placebo for 21 days prior to scheduled prostate biopsy in the form of two gel capsules per day (LycoRed; Beer-Sheva, Israel; lot number MSC-3742). The dose of 30 mg/day was selected because it approximates the amount that can be ingested in a single day by eating foods rich in tomato sauce such as spaghetti and pizza (8). Each lycopene gel cap contained a tomato oleoresin extracted from a tomato variety of high lycopene content and was standardized to 15 mg lycopene per gel capsule. In addition to 6.2% lycopene, the oleoresin contained 90% triglycerides, 2% plant sterols, 1.5% tocopherols, 1.0% phytoene and phytofluene, and 0.2% β-carotene. Placebo gel capsules contained soybean oil. Subjects were instructed to take 2 gel capsules per day with a meal to aid in the absorption of the extract, since lycopene is absorbed more efficiently with dietary lipids (9).

At baseline and at 21 days, fasting blood samples (3-5 mL each) were drawn from each subject by venipuncture in tubes containing EDTA. Plasma and blood cells were separated by centrifugation at 3000*g* at 4°C for 15 min, and then plasma aliquots were stored in 1.5 mL Eppendorf tubes at -80°C until analysis. Prostate biopsy specimens were collected by transrectal-ultrasound/prostate needle biopsy. In addition to six diagnostic needle biopsies obtained for pathology, one extra biopsy was obtained for lycopene measurement and another extra biopsy was obtained for the assessment of DNA oxidation. The needle biopsy specimens were frozen in 0.9% saline and stored at -80°C until analysis.

Dietary intakes of lycopene and other carotenoids and nutrients at baseline and during the study were determined based on five 24 h dietary recalls (one at baseline and four during the intervention) and nutritional analysis of the dietary records using Nutritional Data System for Research software (University of Minnesota; Minneapolis, MN). Demographic information was also collected that included age, ethnicity, height, weight, alcohol consumption, smoking habits, and current medications. Body mass index (BMI) was calculated for each subject based on recorded height and weight.

### Measurements

Lycopene levels in plasma, prostate tissue and in the gel capsules were measured using liquid chromatography-tandem mass spectrometry as described previously (10) but with the following modifications. One prostate tissue needle biopsy core per subject was homogenized and saponified prior to hexane extraction, and echinenone was used as an internal standard. Using an established liquid chromatography-tandem mass spectrometry assay incorporating stable isotopically labeled 8-oxo-dG as a surrogate standard (11), the DNA oxidation product 8-oxodeoxyguanosine (8-oxo-dG) was measured in another prostate biopsy core from each subject. DNA was prepared from tissue as described previously (8). An assay using liquid chromatography-tandem mass spectrometry was developed for the

quantitative analysis of the lipid peroxidation product malondialdehyde in support of this study (12). This assay was based on the widely used reaction of 1,3-diethyl-2-thiobarbituric acid with malondialdehyde, but the reaction product was detected selectively using liquid chromatography-tandem mass spectrometry to avoid interference from substances such as proteins, sucrose, and urea.

### Adherence

Each participant was provided with a calendar to record when capsules were consumed, and unused capsules were counted during the final visit to the General Clinical Research Center. Participants were reminded to take their capsules during four telephone calls for 24-h dietary recalls that occurred during the intervention period. Based on this information, compliance was estimated to be ~99%.

### Statistical Analysis

The primary endpoints for this study were plasma and prostate tissue levels of lycopene and their relationship to levels of the DNA oxidation product 8-oxo-dG. A secondary endpoint was the effect of lycopene on plasma levels of malondialdehyde. The study was originally intended to detect at least 0.75 SDs with power at least 0.8 ($\alpha$=0.05, two-sided tests, n1=n2=30). In the worst case (n1=23,n2=28), the obtained sample sizes are sufficient to detect at least 0.8 SDs with power greater or equal to 0.8 ($\alpha$=0.05, two-sided tests).

The differences in mean lycopene and biomarker values between groups were evaluated by analysis of variance allowing for controlling factors or covariates. For prostate tissue data analysis, *P*-values were calculated using the non-parametric Mann-Whiney test. In a few cases, parametric tests were confirmed using the Kruskal-Wallis one-way analysis of variance. Since smokers were included in this study, the possible effects of smoking on the primary endpoints were investigated. In addition, diet recall data were evaluated to determine whether intake of carotenoids, tocopherols, triglycerides, total lipids, etc., affected the outcomes.

Mean and SDs in this study are reported as mean ± SD, and *P*-values as *P*=0.xx. Values $P<0.05$ were considered statistically significant. Conversely, if $P>0.05$, results were reported as statistically not significant.

## Results

### Subject recruitment and demographics

Out of the 614 urology patients who were screened, 131 were randomized to either the placebo (62) or the lycopene (69) intervention group (see flow diagram in Fig. 1). A majority of the patients who were screened (409 subjects) declined to participate in the clinical trial. Among the 48 subjects who did not meet the inclusion criteria of the study, 40 men were already taking dietary supplements containing lycopene, β-carotene and/or α-tocopherol, four were actively abusing alcohol or other substances, and four were being treated for existing cancers other than prostate cancer. No washout period was allowed for men already taking dietary supplements containing antioxidants such as lycopene, since this would have delayed the diagnostic prostate biopsies in these patients. A group of 26 qualified subjects were screened and agreed to participate, but deferred enrollment since they had recently had prostate biopsies, were not diagnosed with cancer, and were currently engaged in a “watchful waiting” program and would enter the study if their serum PSA increased. However, the study was closed before these deferred subjects returned for randomization.

Among the 131 participants who were randomized, a total of 116 participants completed the study (Fig. 1). Eleven subjects withdrew consent before completing the study without giving any explanation, two complained of gastrointestinal disturbances and dropped out of the study, one subject refused the prostate biopsy, and one subject was withdrawn by the investigators because of a new diagnosis of colon cancer which was among the exclusion criteria. Except for gastrointestinal complaints raised by two subjects who withdrew from the study, no adverse effects were observed.

After receiving oral doses of lycopene or placebo for three weeks, all subjects underwent prostate needle biopsy for the diagnosis of BPH or prostate cancer, and two extra biopsies were obtained for measurement of lycopene and DNA oxidation, respectively. The pathology reports indicated that 51 men were diagnosed with prostate cancer and 65 men were diagnosed with BPH. Within the BPH group, 32 men received placebo while the remaining 33 were randomized to receive lycopene. Among the prostate cancer diagnosis group, 23 men received placebo and 28 men received lycopene. Since more than 90% of the men completing the study were African American veterans (105 out of 116), only the African Americans were included in the data analysis. This information is summarized in Fig. 1.

The demographic characteristics of the 105 African American subjects included in the analysis, each intervention group (lycopene or placebo), and each intervention group by diagnosis (prostate cancer or BPH) are shown in Table 1. The subjects ranged in age from 50 to 83 years with a mean age of 66.9 ± 7.5 years, and their mean body mass index (BMI) was 28.5 ± 5.3 kg/m$^2$. Approximately 30% of the subjects were current smokers and 46% consumed alcohol regularly. There were no significant differences between the two intervention groups with respect to age, BMI, smoking status, consumption of alcohol, or consumption of dietary carotenoids, lipids and total energy. Comparing the BPH and prostate cancer diagnosis groups (Table 1), there were no significant differences in age, BMI, smoking status or consumption of alcohol. When comparing the men with a diagnosis of BPH with respect to randomization into placebo or lycopene intervention groups, there were again no significant differences in regard to age, BMI, smoking, or alcohol intake. Although the groups of men diagnosed with prostate cancer who had been randomized to receive either placebo or lycopene (Table 1) were similar with respect to age ($P = 0.56$), BMI ($P = 0.59$) and alcohol consumption ($P = 0.93$), there was a significant difference in the smoking status of these two groups ($P = 0.009$). Whereas 23.8% of the men diagnosed with prostate cancer and randomized to the placebo group were current smokers, 42.3% of the men with prostate cancer who had been randomized to receive lycopene were current smokers (Table 1). For comparison, 26.7% of the men with BPH who received placebo were smokers, and 28.6% of the men diagnosed with BPH were randomized to the lycopene group.

## Lycopene response

The plasma concentrations of lycopene were determined using LC-MS-MS for each subject at the start of the intervention (time 0) and at the end of the 21-day intervention period. Since prostate biopsies were obtained only at the end of the 21-day intervention period, there were no baseline prostate tissue biopsies, and lycopene levels in tissue were measured only at day 21. These data are summarized in Table 2 for all subjects receiving either placebo or lycopene. Table 3 shows the lycopene results for the subsets of subjects according to diagnosis of prostate cancer or BPH. When comparing the plasma lycopene concentrations at baseline for both treatment groups and for both diagnosis groups, no significant differences were observed. Furthermore, no significant differences were observed in the mean changes in plasma lycopene concentration (day 0 vs. day 21) between smokers and non-smokers or between men who did or did not consume alcohol.

Men who received lycopene at 30 mg/day for 21 days showed a significant increase in mean plasma lycopene concentration (mean difference 0.69 ± 0.59 μM) compared with the placebo group (mean difference -0.013 ± 0.260 μM) ($P < 0.0001$). Mean plasma lycopene concentration increased 1.93-fold in the lycopene intervention group from 0.741 ± 0.388 μM at day 0 to 1.428 ± 0.613 μM at day-21 ($P < 0.0001$). In the placebo group, the mean lycopene concentration was essentially unchanged (Table 2) between baseline (0.599 ± 0.373 μM) and day 21 (0.588 ± 0.392 μM). For subjects who were diagnosed with prostate cancer or BPH (Table 3), plasma lycopene concentrations also increased approximately 2-fold in the lycopene intervention group but not in the placebo group, and these differences were also significant ($P < 0.0001$).

Lycopene levels in prostate biopsy tissue from men who received lycopene for 21-days were compared with prostate biopsy tissue from men who received placebo (Table 2). Lycopene levels in prostate tissue were significantly higher in the lycopene intervention group compared with the placebo group (Table 2; $P = 0.005$). This was confirmed using non-parametric, Kruskal-Wallis one-way analysis of variance. When changes in lycopene levels in prostate biopsy tissue due to lycopene supplementation were compared for the prostate cancer group or for the BPH group (Table 3), lycopene still increased in men who received 30 mg/day lycopene, but the differences between the treatment and placebo control groups were less significant due to the smaller sample size.

## Antioxidant biomarkers

Levels of the DNA oxidation biomarker 8-oxo-dG were measured in prostate tissue as an indication of oxidative stress in the prostate, and the lipid peroxidation product malondialdehyde was measured in plasma as an indication of systemic oxidative stress. The mean levels of 8-oxo-dG were determined in prostate tissue biopsies obtained at the end of the 21-day intervention with lycopene or placebo. The mean concentration of 8-oxo-dG for the entire study group of African Americans was 35% lower in the lycopene treatment group (125 ± 83 8-oxo-dG/$10^6$ dG) compared with the placebo group (193 ± 341 8-oxo-dG/$10^6$ dG), but this difference was not significant ($P = 0.22$) (Table 2).

The levels of 8-oxo-dG in prostate tissue of men diagnosed with BPH (Table 3) were 48% lower in the men receiving 30 mg/d lycopene for 21 days (117 ± 89 8-oxo-dG/$10^6$ dG) compared with the placebo group (245 ± 425 8-oxo-dG/$10^6$ dG). Although not significant ($P = 0.15$), this difference suggested a trend of lower 8-oxo-dG levels in men diagnosed with BPH receiving lycopene intervention. In the men diagnosed with prostate cancer (Table 3), levels of 8-oxo-dG in prostate tissue were essentially identical in men receiving lycopene or placebo for 21 days. Possible differences in prostate 8-oxo-dG levels due to smoking were investigated, but there were no significant differences observed between men who smoked and those who did not smoke.

The mean concentrations of malondialdehyde in the entire study group before and after intervention with lycopene are shown in Table 2. Since the concentrations of malondialdehyde did not follow a normal distribution, the values were log-transformed for statistical evaluation. At baseline, there was no difference between the subjects randomized to receive placebo and those randomized to lycopene, and after 21-day intervention with 30 mg/day lycopene, there was no significant change in plasma malondialdehyde levels in the placebo or the lycopene groups (Table 2).

Among the men diagnosed with BPH, mean malondialdehyde levels in plasma decreased 5.1% (from 0.195 ± 0.140 μM to 0.185 ± 0.152 μM) after treatment with lycopene but were unchanged after receiving placebo for 21 days (Table 3). However, these differences were not significant. Although mean malondialdehyde levels increased 34.8% in the plasma of

men diagnosed with prostate cancer and randomized to the placebo group (from 0.132 ± 0.097 μM to 0.178 ± 0.136 μM) but only increased 5.1% in men receiving lycopene (from 0.235 ± 0.150 μM to 0.247 ± 0.159 μM), this difference was also not significant ($P$= 0.34).

Smoking did not affect malondialdehyde levels in the placebo group or in the lycopene treatment group. Smoking also did not alter the variation of malondialdehyde levels in either the BPH diagnosis group or the prostate cancer diagnosis group. No effects of alcohol consumption were observed in these groups.

## Discussion

The increase in lycopene plasma concentration observed following supplementation with lycopene capsules at 30 mg/day was in close agreement with the whole-food dietary intervention of Chen *et al.* (8) who administered 30 mg/day of lycopene for 21 days in the form of tomato sauce. The dietary intervention of Chen *et al.* produced an increase of serum lycopene levels of 1.97-fold, from 0.638 μM to 1.26 μM. Human lycopene supplementation studies by Bohm and Bitsch (13), Richelle *et al.* (14), Hoppe *et al.* (15), and Bunker *et al.* (16), also produced similar increases in plasma or serum lycopene concentration. The results of these studies indicate that similar increases of plasma lycopene concentration can be achieved whether lycopene is administered at identical levels in capsules or in food.

Compared with previous studies of lycopene supplementation, our study is unusual with respect to the study population of African American men. African American men are at higher risk for prostate cancer, are less likely to participate in prostate cancer clinical trials (17) and are more likely to drop out of clinical trials than are Caucasian men (18). Most prostate cancer prevention or treatment studies involving human lycopene supplementation or dietary intervention with tomato products have not reported the ethnicity of the subjects. Among the few lycopene studies that reported the ethnicity of the subjects, the Prostate Cancer Prevention Trial included fewer than 5% African Americans (19), Vaishampayan *et al.* (20) included ~30% African Americans, and Bunker *et al.* (16) studied Afro-Caribbean men.

Few human intervention studies have reported prostate tissue levels of lycopene after lycopene supplementation. In a study of 32 men with prostate cancer, Chen *et al.* (8) reported that prostate levels of lycopene were approximately 3-fold higher in men who consumed tomato sauce containing 30 mg/day of lycopene for 21-days compared with tissue from men not in the study. However, the study by Chen was not placebo controlled or blinded. In a study with only 8 men diagnosed with prostate cancer (5 receiving lycopene capsules at 30 mg/day and 3 receiving placebo) which was too few to have valid conclusions, Kucuk *et al.* (21) reported no significant differences in lycopene levels in prostate tissue between the groups. Therefore, our study is unique in that it is randomized, placebo controlled, double-blind, and of sufficient power to provide statistically significant measurements showing an increase in prostate lycopene levels in prostate tissue due to supplementation with a tomato extract.

Neither plasma malondialdehyde nor 8-oxo-dG in prostate tissue was reduced significantly as a result of lycopene supplementation at 30 mg/day. There was an inverse correlation between malondialdehyde and lycopene concentrations in plasma, and there was a trend in reduction of 8-oxo-dG in men with BPH but not prostate cancer. Although lycopene supplementation did not significantly reduce the biomarkers of oxidative stress measured in this investigation, lycopene did not function as a prooxidant either, even in smokers. This is important in view of a clinical trial in Finland involving β-carotene supplementation in men

who were heavy smokers that found an increased risk of lung cancer in men receiving β-carotene compared to placebo (22).

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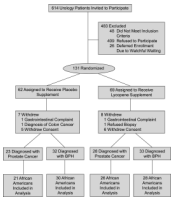


**Figure 1.**
Study Design and Flow Diagram

**Table 1**

Demographic characteristics of all study subjects included in the analyses, the subjects by intervention group and the subjects by both intervention and diagnosis groups.

| Characteristic | Total (N=105) | Placebo (N=51) | Lycopene (N=54) | BPH (N=58) | Prostate cancer (N=47) | BPH (N=58) | | Prostate cancer (N=47) | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Placebo (N=30) | Lycopene (N=28) | Placebo (N=21) | Lycopene (N=26) |
| Age (years) | 66.9 ± 7.5[1] | 69.4 ± 7.1 | 64.6 ± 7.2 | 67.6 ± 6.8 | 66.0 ± 8.3 | 69.5 ± 6.7 | 65.6 ± 6.4 | 69.2 ± 7.8 | 63.4 ± 8.0 |
| Height (cm) | 175.7 ± 7.2 | 175.5 ± 7.1 | 175.8 ± 7.4 | 175.8 ± 7.1 | 175.4 ± 7.4 | 175.1 ± 7.4 | 176.5 ± 6.9 | 176.1 ± 6.7 | 174.9 ±8.0 |
| Weight (kg) | 86.5 ± 16.4 | 83.7 ± 14.8 | 88.9 ± 17.4 | 86.7 ± 13.4 | 86.3 ± 19.8 | 83.1 ± 11.7 | 89.8 ± 14.2 | 84.6 ± 18.4 | 87.7 ±21.3 |
| Body mass index (kg/m$^2$) | 28.5 ± 5.3 | 27.8 ± 4.8 | 29.3 ± 5.6 | 28.5 ± 3.9 | 28.6 ± 6.7 | 27.9 ± 3.7 | 29.1 ± 4.0 | 27.6 ± 6.1 | 29.5 ± 7.2 |
| Ethnicity (%) | | | | | | | | | |
| African-American | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| Smoking status (%) | | | | | | | | | |
| yes | 30.5 | 25.5 | 35.2 | 27.6 | 34.0 | 26.7 | 28.6 | 23.8 | 42.3 |
| former/no | 69.5 | 74.5 | 64.8 | 72.4 | 66.0 | 73.3 | 71.4 | 76.2 | 57.7 |
| Alcohol consumption (%) | | | | | | | | | |
| yes | 43.8 | 49.0 | 38.9 | 41.4 | 46.8 | 50.0 | 32.1 | 47.6 | 46.2 |
| former/no | 56.2 | 51.0 | 61.1 | 58.6 | 53.2 | 50.0 | 67.9 | 52.4 | 53.8 |

[1] Mean ± SD

*Cancer Prev Res (Phila)*. Author manuscript; available in PMC 2012 May 1.

**Table 2**

Clinical outcomes of the entire study group.

| Biomarker | Placebo | | | Lycopene | | | |
|---|---|---|---|---|---|---|---|
| | **Baseline (mean ± SD)** | **End of intervention (mean ± SD)** | **Difference (mean ± SD)** | **Baseline (mean ± SD)** | **End of intervention (mean ± SD)** | **Difference (mean ± SD)** | ***P*** |
| **plasma lycopene (μmol/L)** | 0.599 ± 0.373 N=49 | 0.588 ± 0.392 N=48 | -0.013 ±0.260 N=48 | 0.741 ± 0.388 N=52 | 1.428 ± 0.613 N=57 | 0.69 ± 0.59 N=57 | <0.0001[1] |
| **prostate tissue lycopene (pmol/mg tissue)** | | 0.446 ± 0.530 N=46 | | | 0.593 ± 0.472 N=49 | | 0.005[2] |
| **prostate tissue 8-oxo-dG/$10^6$ dG** | | 193 ± 341 N=41 | | | 125 ± 82.8 N=47 | | 0.22[2] |
| **plasma malondialdehyde (MDA) (μM)** | 0.196 ± 0.145 N=49 | 0.216 ±0.180 N=45 | 0.012 ± 0.127 N=45 | 0.214 ± 0.145 N=52 | 0.214 ± 0.157 N=49 | -0.008 ± 0.145 N=49 | 0.49[1] |

[1] *P*-value determined by comparing the mean of differences between baseline and end of intervention for the placebo vs. lycopene-treatment groups

[2] *P*-value determined by comparing the mean of placebo vs. lycopene-treatment groups using the Mann-Whitney test

**Table 3**

Clinical outcomes of the prostate cancer and BPH groups.

| | Biomarker | Placebo | | | Lycopene | | | |
|---|---|---|---|---|---|---|---|---|
| | | Baseline (mean ± SD) | End of intervention (mean ± SD) | Difference (mean ± SD) | Baseline (mean ± SD) | End of intervention (mean ± SD) | Difference (mean ± SD) | *P* |
| **Prostate cancer** | **plasma lycopene (μmol/L)** | 0.58 ± 0.40 N=21 | 0.58 ± 0.43 N=21 | -0.001 ± 0.270 N=21 | 0.74 ± 0.37 N=25 | 1.43 ± 0.65 N=24 | 0.707 ± 0.602 N=24 | <0.0001[1] |
| | **prostate tissue lycopene (pmol/mg tissue)** | | 0.52 ± 0.66 N=18 | | | 0.71 ± 0.60 N=24 | | 0.06[2] |
| | **prostate tissue 8-oxo-dG/$10^6$ dG** | | 113 ± 103 N=16 | | | 134 ± 76 N=22 | | 0.51[2] |
| | **plasma malondialdehyde (MDA) (μM)** | 0.132 ± 0.097 N=20 | 0.178 ± 0.136 N=19 | 0.040 ± 0.107 N=19 | 0.235 ± 0.150 N=25 | 0.247 ± 0.159 N=23 | -0.001 ± 0.159 N=23 | 0.34[1] |
| **BPH** | **plasma lycopene (μmol/L)** | 0.613 ± 0.355 N=28 | 0.593 ± 0.360 N=27 | -0.025 ± 0.266 N=27 | 0.734 ± 0.409 N=27 | 1.42 ± 0.58 N=27 | 0.691 ± 0.593 N=27 | <0.0001[1] |
| | **prostate tissue lycopene (pmol/mg tissue)** | | 0.39 ± 0.42 N=28 | | | 0.464 ± 0.428 N=25 | | 0.048[2] |
| | **prostate tissue 8-oxo-dG/$10^6$ dG** | | 245 ± 425 N=25 | | | 117 ± 89 N=25 | | 0.15[2] |
| | **plasma malondialdehyde (MDA) (μM)** | 0.240 ± 0.157 N=29 | 0.243 ± 0.205 N=26 | -0.009 ± 0.138 N=26 | 0.195 ± 0.140 N=27 | 0.185 ± 0.152 N=26 | -0.014 ± 0.135 N=26 | 0.90[1] |

[1] *P*-value determined by comparing the mean of differences between baseline and end of intervention for the placebo vs. lycopene-treatment groups

[2] *P*-value determined by comparing the mean of placebo vs. lycopene-treatment groups using the Mann-Whitney test