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Short Communication

Inhibition of Testosterone-Induced Hyperplasia of the Prostate of Sprague-Dawley Rats by Pumpkin Seed Oil

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ABSTRACT The oil from the pumpkin (*Cucurbita pepo*) seed is claimed to be useful in the management of benign prostatic hyperplasia. This investigation seeks to examine the effect of pumpkin seed oil on testosterone-induced hyperplasia of the prostate of rats. Hyperplasia was induced by subcutaneous administration of testosterone (0.3 mg/100 g of body weight) for 20 days. Simultaneous oral administration of either pumpkin seed oil (2.0 and 4.0 mg/100 g of body weight) or corn oil (vehicle) was also given for 20 days. The weights of the rats were recorded weekly, and the influence of testosterone and pumpkin seed oil on the weight gain of the rats was examined. On day 21, rats were sacrificed, and the prostate was removed, cleaned, and weighed. The prostate size ratio (prostate weight/rat body weight) was then calculated. Neither testosterone nor pumpkin seed oil had any significant influence on the weight gain of the rats. Testosterone significantly increased prostate size ratio ($P < .05$), and this induced increase was inhibited in rats fed with pumpkin seed oil at 2.0 mg/100 g of body weight. The protective effect of pumpkin seed oil was significant at the higher pumpkin seed oil dose ($P < .02$). We conclude pumpkin seed oil can inhibit testosterone-induced hyperplasia of the prostate and therefore may be beneficial in the management of benign prostatic hyperplasia.

KEY WORDS: • ***benign prostatic hyperplasia*** • ***prostate*** • ***prostate size ratio*** • ***pumpkin seed oil***

BENIGN PROSTATIC HYPERPLASIA (BPH) is the result of gradual overgrowth of the prostate gland, a gland that lies at the base of the bladder and encircles the urethra.[1,2] The enlarged prostate impinges on the urethra, and therefore BPH is generally associated with impairment in urinary function. It is reported that 80% of men over 80 years will suffer from BPH.[3] Management of this condition has come to include many nutraceutical preparations including preparations containing pumpkin seed oil.

Pumpkin (species *Cucurbita*) is an edible fruit found on the American and European continents, as well as the Caribbean. The seeds are a rich source of vitamins A, B, and E, linoleic acid, oleic acid, zinc, selenium, carbohydrates, and phytosterols.[4]

The oil from *Cucurbita pepo* has been documented as being useful for the treatment of urinary problems associated with BPH. In previous reports of clinical trials involving over 2,000 men suffering from BPH, one or two capsules containing pumpkin seed oil from *C. pepo* produced significant improvement in their urinary function.[5] This action of pumpkin seed oil was also confirmed in other investigations.[6]

In the prostate, dihydrotestosterone is produced from testosterone by the enzyme 5α-reductase and is the more potent androgen that promotes growth of the prostate. Although the pathogenesis of BPH is not completely defined, these androgens have been identified as playing an integral part in the disease process of BPH.[2] Inhibition of the production or actions of dihydrotestosterone can results in the inhibition of the growth of the prostate gland. Studies have suggested that the actions of pumpkin seed oil may be attributed to the content of phytosterols, which are known to interfere with the actions of dihydrotestosterone.[7] Thus, the effectiveness of pumpkin seed oil in BPH may be the result of a direct influence on the prostate gland size and therefore improving urinary function.

Many preparations of pumpkin seed oil, mainly approved as dietary supplements, are sold in pharmacies and health stores. This investigation seeks to develop a rat model of BPH and to examine the ability of the pumpkin seed oil from one available nutraceutical preparation (containing oil from seeds of *C. pepo*) to inhibit the development of BPH in the animal model. The nutraceutical preparation selected was Good 'N Natural® pumpkin seed oil 1,000 mg (Good 'N

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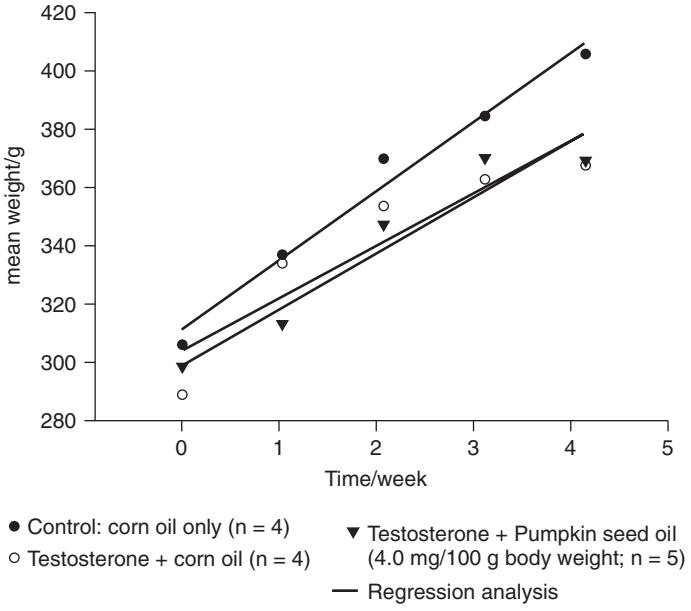

FIG. 1. Mean weight gain of each group of rats over the period of dosing. There was no significant difference in the slope of the lines. Therefore treatment with testosterone or pumpkin seed oil did not have any significant influence on the weight gain during the treatment period.

Natural Manufacturing Corp., Holbrook, NY), since this is the most common preparation available in Jamaica.

Pumpkin seed oil was collected from capsules manufactured by Good 'N Natural (pumpkin seed oil 1,000 mg) purchased from the local pharmacy. The bottle label indicated that each soft gel capsule contained 1,000 mg of oil from seeds of *C. pepo*. The oil was diluted with corn oil to obtain concentrations of 50 and 100 mg/mL.

Testosterone was given in the form of Sustanon® 100 mg/mL (N.V. Organon, Roseland, NJ), which contained 20 mg of testosterone propionate, 40 mg of testosterone phenylpropionate, and 40 mg of testosterone isocaproate. It was diluted to a concentration of 10 mg/mL.

The animal model used was adapted from methods previously described by Auger-Pourmarin *et al.*[8] Mature Sprague-Dawley male rats weighing 290–320 g (older than 13 weeks) were provided by the animal house at the University of the West Indies, Jamaica. Hyperplasia of the rat prostate was induced by a subcutaneous injection of testosterone at a dose of 0.3 mg/100 g of body weight/day for 20 days.

In the human study of Schielbel-Schlosser and Friederich,[6] 500–1,000 mg of pumpkin seed oil was given daily. For a 70-kg adult this calculates to approximately 7–14 mg/kg of body weight. Using 1,000 mg of pumpkin seed oil as the daily dose, rats were given an oral dose of 2.0 or 4.0 mg/100 g of body weight (20–40 mg/kg) once daily for 20 days. Control rats received an oral administration of corn oil (vehicle) for 20 days. The rats were placed in three groups to receive pumpkin seed oil, testosterone, and corn oil as follows: Group 1, simultaneous administration of testosterone and pumpkin seed oil (2.0 or 4.0 mg/100 g of body weight) for 20 days; Group 2, simultaneous administration of testosterone and corn oil for 20 days; and Group 3, corn oil only for 20 days. The 20-day dosing regimen was followed from Monday to Friday (no weekend dosing) for 4 weeks. Twenty days was considered adequate, since the clinical trials in men with BPH involving pumpkin seed oil showed significant improvement within 12 days.[5]

On day 21 rats were sacrificed with an intraperitoneal overdose of urethane. The abdominal cavity was then opened, and the prostate was removed. It was then cleaned, gently tapped dry, and weighed immediately. The Animal Ethics Committee of the University of the West Indies approved the protocol followed by this project.

The weight of each rat was measured weekly, and changes in weight over the period of dosing were examined using multiple linear regression analysis. The prostate of each rat was weighed, and the prostate size ratio (weight of prostate/body weight of the rat) was calculated. The mean weight and standard error for each group was calculated. Statistical significance was examined using the Mann–Whitney test.

Consumption of oil can produce increases in weight,[9] and therefore it was important to examine for differences in the gain of weight between the groups. Neither testosterone nor pumpkin seed oil administration had any significant influ-

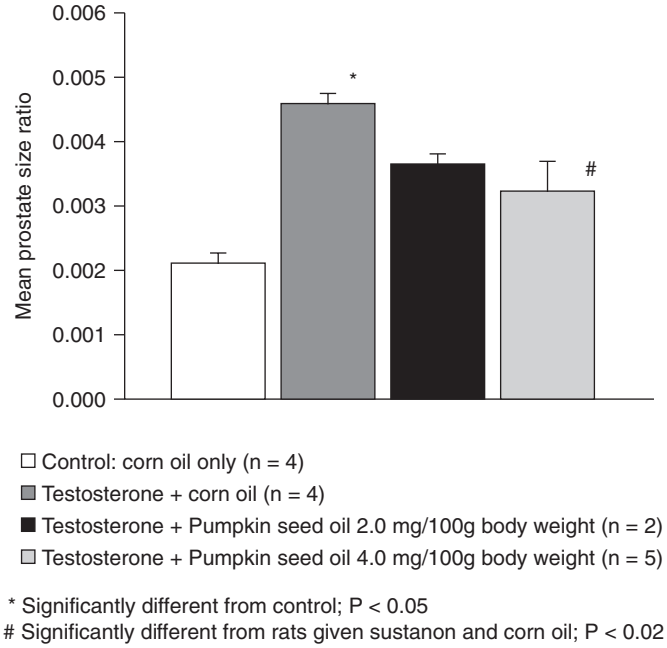

FIG. 2. Rats treated with testosterone (0.3 mg/100 g of body weight, $n = 4$) showed a significant increase in mean prostate size ratio ($P < .05$) compared with the control group ($n = 4$). This induced increase was inhibited at both 2.0 mg/100 g ($n = 2$) and 4.0 mg/100 g ($n = 5$). At the higher dose this inhibition was significant ($P < .02$).

ence of the weight gain of the rats, as all groups of rats produced regression slopes that were similar (Fig. 1); that is, the weight gain between the groups was similar.

Although BPH is not a condition known to develop in rats, the enlargement induced with testosterone in mature Sprague-Dawley rats less than 1 year of age has been accepted as a suitable model.[8,10] Significant hyperplasia of the prostate ($P < .01$, $n = 4$) was induced with testosterone, as the mean prostate size ratio of these rats was twice the value obtained for the control group (Fig. 2). The hyperplasia induced by testosterone was less in rats simultaneously given pumpkin seed oil along with testosterone, attaining significant protection when the pumpkin seed oil dose was increased to 4.0 mg/kg ($P < .02$, $n = 4–5$).

In conclusion, our investigations showed that pumpkin seed oil extracted from the seeds of *C. pepo* (obtained from "Good 'N Natural" pumpkin seed oil 1,000 mg) inhibited testosterone-induced hyperplasia of the rat prostate. The usefulness of pumpkin seed oil in the management of BPH may therefore involve a direct inhibition of growth of the prostate.

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