



# Pumpkin Seed Oil Extracted From *Cucurbita maxima* Improves Urinary Disorder in Human Overactive Bladder

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## ABSTRACT

The pumpkin seed oil obtained from *Cucurbita pepo* has been shown to be useful for the treatment of nocturia in patients with urinal disorders in several western countries. In this study, we evaluated the effect of the pumpkin seed oil from *Cucurbita maxima* on urinary dysfunction in human overactive bladder (OAB). Forty-five subjects were enrolled in this study. An extract of pumpkin seed oil from *C. maxima* (10 g of oil/day) was orally administrated for 12 weeks. After 6 and 12 weeks, urinary function was evaluated using Overactive Bladder Symptom Score (OABSS). Pumpkin seed oil from *C. maxima* significantly reduced the degree of OABSS in the subjects. The results from our study suggest that pumpkin seed oil extracts from *C. maxima* as well as from *C. pepo* are effective for urinary disorders such as OAB in humans.

**Key words:** *Cucurbita maxima*, Overactive bladder, Pumpkin seed oil

## INTRODUCTION

The prevalence of urinary disorders such as nocturia and associated symptoms gradually increases with age, and has a great influence on the quality of life.<sup>[1,2]</sup> Elderly people with nocturia are at great risk for bone fracture and mortality.<sup>[3]</sup> Thus, prevention and treatment of urinary disorders are expected to improve this problem. Overactive bladder (OAB), a common urinary disorder, is well known and defined by the International Continence Society (ICS) as a syndrome with urgency, with or without urge incontinence, usually with frequency and nocturia.<sup>[1]</sup> OAB symptoms are commonly observed in patients with dysfunction of the lower urinary tract. Recently, the Overactive Bladder Symptom Score (OABSS) was developed and

validated by Homma *et al.* as a useful assessment tool specifically for evaluating OAB symptoms.<sup>[4]</sup> OABSS scores are based on answers to self-assessed questions.

Pumpkin is an edible fruit found in the American and European continents and is grown in Asia and Africa. The extract of the seed is a rich source of vitamins, linoleic acid, oleic acid, and microelements. Especially, the oil extracted from *Cucurbita pepo* has been useful for the treatment of urinary disorders. In previous reports, the effect of the pumpkin seed oil from *C. pepo* has been investigated in clinical trials involving over 2000 men suffering from benign prostate hypertrophy (BPH).<sup>[5]</sup> The oil significantly improved their urinary dysfunction. In an animal study, Gossell-Williams *et al.* demonstrated that oil from the pumpkin seed of *C. pepo* inhibited testosterone-induced hyperplasia of the prostate of rats.<sup>[6]</sup> Rats treated with 0.3 mg/100 g body weight of

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testosterone showed an increase of prostate size ratio, but administration of 2.0 or 4.0 mg/100 g body weight of pumpkin seed oil from *C. pepo* inhibited the prostate size ratio in rats treated with testosterone. These previous studies have clarified the effect of pumpkin seed oil extracted from *C. pepo*, but there has been no clinical investigation on urinary disorder treatment using any other kind of pumpkin seed oil.

In Japan, especially in Hokkaido, *Cucurbita maxima* is the main pumpkin species grown for food. Thus, numerous pumpkin seeds are available here. Ojiako *et al.* have analyzed the composition of seeds of *C. maxima* as having various fatty acids, proteins, carbohydrates, and minerals.<sup>[7]</sup> Recently, we have developed a product extracted from the pumpkin seed oil of *C. maxima*, and we herein evaluated the effect of the product on urinary disorders in volunteers suffering from OAB symptom.

## MATERIALS AND METHODS

### Subject and study design

Forty-five volunteers (male: female = 25:20; age 41-80 years) were enrolled in this study. Subjects were excluded if they were pregnant or had severe or acute diseases (e.g. cancer, infection, and acute organic failure such as heart or hepatic failure). All were older than 20 years of age. Ten grams of the pumpkin seed oil extracted from *C. maxima* was daily and orally administered in the subjects for 12 weeks. Analytical results of the composition of the pumpkin seed oil with regard to nutrients, vitamins, fatty acids, and sterols are provided in Table 1. All protocols in this study were approved by the Ethical Committee of Hokkaido Information University, and written informed consent was obtained from all participating subjects. Demographic and medical data were obtained from the medical records and interviews at study entry. Blood samples were obtained in the morning after overnight fasting, and biochemical data concerning lipids were measured.

### Diagnosis and evaluation of OAB

To diagnose and evaluate OAB, the subjects completed the OABSS questionnaire for evaluation of daytime frequency, nighttime frequency, urgency, and urgency incontinence, as described previously.<sup>[4]</sup>

### Statistical analysis

Values are expressed as means  $\pm$  standard deviation (SD). All statistical analyses were conducted using IBM SPSS Statistic 19 (IBM, Armonk, NY, USA). The statistical differences in the results of OABSS were analyzed by Wilcoxon signed-rank test, and those in the biochemical data were analyzed using Tukey's multiple comparison test.  $P < 0.05$  were considered statistically significant.

## RESULTS

### Demographic characteristics and physical and biochemical examination

All males enrolled in this study were not diagnosed as BPH in the hospital and did not receive the treatment of BPH.

Moreover, the levels of serum prostate-specific antigen (PSA) in all males were within normal range. Four subjects quit the entry on their own, and three subjects were excluded because of inadequate intake of the oil. The characteristics of the enrolled subjects are summarized in Table 2. Six and 12 weeks after the initial administration of the pumpkin seed oil, the average levels of high density lipoprotein-cholesterol (HDL-cholesterol) and low density lipoprotein-cholesterol (LDL-cholesterol) and triglyceride were essentially unchanged [Table 2]. There was no significant difference in the laboratory data between pre- and post-administration of the pumpkin seed oil in various age and body weight groups [Table 2].

### Improvement of OABSS in subjects given pumpkin seed oil

Serial changes of total score and sub-scores of OABSS are summarized in Table 3. Six and 12 weeks after the initial administration of pumpkin seed oil from *C. maxima*, the total scores were significantly decreased compared to those on day 0 [Table 3]. In detail, the scores on all parts of the questionnaire (daytime frequency, nighttime frequency, urgency, and urgency incontinence) significantly improved in the subjects administered pumpkin seed oil from *C. maxima* [Table 3].

## DISCUSSION

OAB symptoms are found in more than 15% of humans aged 40 and over, and are thought to increase with advancing age.<sup>[1]</sup> OABSS, a self-assessment of OAB symptoms, is recognized as a standard tool for diagnosis and evaluation of the severity

**Table 1.** Component of the pumpkin seed oil extracted from *Cucurbita maxima* per 100 g

|                              |      |
|------------------------------|------|
| Nutrition                    |      |
| Calories (kcal)              | 900  |
| Fat (g)                      | 99.9 |
| Vitamin                      |      |
| $\beta$ -carotene ( $\mu$ g) | 500  |
| Vitamin D ( $\mu$ g)         | 2    |
| Vitamin E (mg)               | 5.7  |
| $\alpha$ -tocopherol (mg)    | 0.2  |
| $\gamma$ -tocopherol (mg)    | 5.5  |
| Vitamin K-1 ( $\mu$ g)       | 10   |
| Fatty acid (g)               |      |
| C14:0                        | 0.1  |
| C16:0                        | 10.9 |
| C16:1                        | 0.1  |
| C17:0                        | 0.1  |
| C18:0                        | 6.0  |
| C18:1                        | 38.6 |
| C18:2                        | 37.8 |
| C18:3                        | 0.2  |
| C20:0                        | 0.5  |
| C22:0                        | 0.1  |
| C24:0                        | 0.1  |
| Sterol                       |      |
| Sitosterol (mg)              | 150  |

**Table 2.** Clinical characteristics and biochemical data

|                           | Day 0      | 6 weeks    | 12 weeks   |
|---------------------------|------------|------------|------------|
| Body mass index           | 24.73±2.86 | 24.98±2.80 | 24.97±2.76 |
| Body weight (kg)          | 62.98±8.24 | 63.62±8.17 | 63.63±8.15 |
| Total cholesterol (mg/dl) | 207.5±29.7 | 211.2±28.9 | 216.4±29.8 |
| HDL-cholesterol (mg/dl)   | 67.9±17.7  | 70.6±18.0  | 71.8±17.9  |
| LDL-cholesterol (mg/dl)   | 127.2±30.6 | 126.9±29.1 | 131.0±27.2 |
| Triglyceride (mg/dl)      | 116.8±58.9 | 114.7±66.5 | 119.9±78.5 |
| Urea nitrogen (mg/dl)     | 14.7±3.5   | 15.0±2.7   | 14.6±3.4   |
| Creatinine (mg/dl)        | 0.8±0.2    | 0.8±0.2    | 0.9±0.2    |

**Table 3.** Changes in obstructive bladder scoring system (OABSS) in all subjects given the extract of pumpkin seed oil (*Cucurbita maxima*)

|                           | Day 0 (0 week) | 6 weeks  | 12 weeks  |
|---------------------------|----------------|----------|-----------|
| Total score               | 4.4±2.2        | 3.5±2.1* | 2.7±2.2** |
| Q1 (daytime frequency)    | 0.7±0.5        | 0.6±0.5  | 0.4±0.5** |
| Q2 (nighttime frequency)  | 1.6±0.8        | 1.4±0.9  | 1.1±1.0** |
| Q3 (urgency)              | 1.5±1.2        | 1.1±1.1* | 0.1±1.3** |
| Q4 (urgency incontinence) | 0.7±0.9        | 0.4±0.7  | 0.3±0.6*  |

Values are expressed as means±SD. \* $P<0.05$ , \*\* $P<0.01$  versus the level of OABSS on day 0, OABSS: Obstructive bladder scoring system

of OAB, and has been used in clinical studies.<sup>[4]</sup> Furthermore, OABSS is useful for determining the effect of treatment on urinary disorders.<sup>[8,9]</sup> In this study, we investigated the effect of pumpkin seed oil from *C. maxima* by OABSS. The OABSS was remarkably reduced in subjects given pumpkin seed oil extracted from *C. maxima*. The effect of pumpkin seed oil obtained from *C. pepo* has been tested in urinary disorders and this oil is now being developed for self-medication in western countries. Friederich *et al.* have demonstrated that the pumpkin seed extract obtained from *C. pepo* improves abnormal urinary function in patients with BPH.<sup>[5]</sup> Oral administration of 500-1000 mg/day of this extract for 12 weeks caused International Prostate Symptom Scores to decrease by 41.4%. Moreover, more than 96% of the patients had no undesired side effect due to treatment with the oil. In our study, consistent with the results of a previous study, there was no severe side effect caused by the pumpkin seed oil from *C. maxima* (data not shown). These results suggest that the seed extract from *C. maxima* is safe and well tolerated in the treatment of urinary disorders such as OAB and BPH. In our lab, biochemical analysis has been carried out to identify the molecules responsible in the pumpkin seed oil to alleviate urinary tract problems, but it remains to be elucidated to date. Although the molecular mechanism of the seed oil for improvement of urinary tract disorders is not well understood from the current study, based on a previous report, it is speculated that sitosterols contained in the seed oil are responsible to alleviate these disorders.<sup>[5]</sup> As for the study design, it was an open-labeled trial because of excessive amount of oil volume required for encapsulation. To confirm the current results, we plan to perform a placebo-controlled, double-blind clinical trial when we identify the potential molecules, which would enable

us to downsize the test or placebo sample volume good enough for encapsulation.

Although we demonstrated the beneficial effects of pumpkin seed oil from *C. maxima*, our results are limited in several ways. Ours was not a randomized, double-blind, and placebo-controlled study design. Recently, OABSS has been recognized as the standard system of evaluation in urinary function,<sup>[5]</sup> but the system involves evaluation by self-assessment. Furthermore, the sample size in our study was small. Thus, further double-blind, randomized controlled study is needed to confirm the effect of pumpkin seed oil obtained from *C. maxima*.

## CONCLUSION

Although the results in our study are preliminary and further study is needed, our results suggest that pumpkin seed oil extracted from *C. maxima* has the potential for prevention or treatment of urinary disorders including OAB.

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