Can a concentrated cranberry extract prevent recurrent urinary tract infections in women? A pilot study

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Abstract

\textbf{Background:} Urinary tract infections (UTIs) are extremely prevalent and despite treatment with antibiotics, recurrences are common causing frustration in the patient and the potential for developing antibiotic resistance. The use of cranberry products to prevent UTIs has recently become popular and more clinical studies are needed to explore this use.

\textbf{Objective:} This open label pilot study examined the ability of a concentrated cranberry preparation to prevent UTIs in women with a history of recurrent infections.

\textbf{Subjects:} Women between the ages of 25 and 70 years old were included with a history of a minimum of 6 UTIs in the proceeding year.

\textbf{Intervention:} The women took one capsule twice daily for 12 weeks containing 200 mg of a concentrated cranberry extract standardized to 30% phenolics.

\textbf{Design:} A questionnaire was used initially to determine the patient’s medical history and they were asked at monthly intervals if any of the information had changed. All of the women in the study had urinalysis within 24 h before starting on the study preparation and once a month after that for 4 months. Subjects were followed-up approximately 2 years later.

\textbf{Results:} All 12 subjects participated in the 12-week study and were available for follow up 2 years later. During the study none of the women had a UTI. No adverse events were reported. Two years later, eight of the women who continue to take cranberry, continue to be free from UTIs.

\textbf{Conclusion:} A cranberry preparation with a high phenolic content may completely prevent UTIs in women who are subject to recurrent infections.

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\textbf{Keywords:} Cranberry extract; Vaccinium macrocarpon; Urinary tract infections; Pilot study

Introduction

Urinary tract infections (UTIs) are extremely prevalent, especially in women, the elderly and in infants. UTIs are defined as the presence of a certain threshold number of bacteria in the urine (usually greater than 100,000 per ml). One in four women who develop a UTI will have a recurrence. The risk factors that predispose women to a recurrence include sexual intercourse, the use of contraception, antimicrobials, estrogen, genetics...
and the proximity of the urethra to the anus. UTIs are caused by microorganisms, principally Gram-negative bacteria, notably *Escherichia coli*. They are usually treated with antibiotics but recurrences frustrate the patient and may contribute to bacterial antibiotic resistance. Due to these concerns, research has begun to focus on prevention (Avon et al., 1994; Pelton, 2000; Lowe and Fragolman, 2001; Franco, 2005; Liu et al., 2006).

Cranberries are small, dark red fruits that are widely consumed as juice and sauce. They come from a shrub, *Vaccinium macrocarpon* Aiton [Ericaceae], native to eastern North America (Winston et al., 2002). The use of cranberry preparations to prevent UTIs became popular in the 1920s when American scientists demonstrated that the urine became more acidic after eating large amounts of cranberries (Blatherwick and Long, 1923). Subsequent studies have shown that the effectiveness of cranberry is not due to its ability to acidify the urine (Liu et al., 2006). As the first step in developing infections, bacteria must bind to the host cell and tissues. The *E. coli* strains that cause UTIs have proteinaceous macromolecules (fimbriae) that facilitate the adhesion of bacteria to uroepithelial cells in the urinary tract. In vitro and ex vivo studies indicate that cranberry products prevent adhesion of bacteria to the cell walls of the urinary tract, thus preventing UTIs (Di Martino et al., 2006; Liu et al., 2006).

Two types of compounds in cranberry have been identified as having anti-adhesion activity: fructose (a sugar) and proanthocyanidins (condensed tannins). Fructose, a common constituent of fruits, has been shown to inhibit adherence of *E. coli* with type I (mannose-sensitive) fimbriae to cells grown in tissue culture (Zafriri et al., 1989). Cranberry proanthocyanidins have been shown to inhibit adherence of *E. coli* with P-type fimbriae (Howell et al., 1998).

Proanthocyanidins are composed of oligomers (small chains) of flavanol units. The procyanidins in cranberry are unique from those in other fruits as the flavonol units are linked (A-type) in a manner that is different from those found in other fruits (B-type). Recent studies have determined that proanthocyanidins with this A-type linkage are more effective than those with B-type linkages in inhibiting the adherence of bacteria to cell surfaces (Howell et al., 2005). Further, biochemical studies have revealed that in addition to causing the fimbriae on the surface of the bacteria to become compressed, reducing their adhesion, the proanthocyanidins in cranberry may change the shape of the bacteria from rods to spheres and cause chemical changes to their surface membranes (Camesano, 2006).

Several clinical studies have been conducted on the use of cranberry preparations to prevent UTIs. A review published in 2004 found seven studies that met the criteria of randomized controlled studies. The effectiveness of cranberry juice (or cranberry–lingonberry juice) compared to placebo was evaluated in six studies and the effectiveness of cranberry tablets compared to placebo was evaluated in two studies (one study included both juice and tablets). Only two of the studies were considered good quality. These studies demonstrated that cranberry significantly reduced the incidence of UTIs after twelve months of treatment (RR 0.61; 95% CI: 0.40–0.91) in women compared to placebo. One study used 7.5 g cranberry concentrate in 50 ml. The other used a 1:30 concentrate in 250 ml juice or in tablet form. There was no significant difference between the effects due to the juice and the effects due to the tablets (Jepson et al., 2004). The authors of this review commented that the optimum dosage of cranberry or form of administration (e.g. juice or tablet) is not clear.

Typical cranberry preparations are dried and ground whole cranberries, or dried cranberry juices. The dried, ground berries commonly contain 0.5% total phenolic compounds, including proanthocyanidins. The dried juice concentrates commonly contain 3–5% total phenolics (private communication, R. Dietz, Eurofins Scientific data, 2006). Through selective extraction of the berries, Phenolics, LLC has produced an extract that contains 30% phenolics (US Patent nos. 6,780,442 and 6,960,360, and European Patent no. 1, 328,282). This extraction process concentrates the phenolic compounds and eliminates other compounds in the fruit such as oxalic acid and other small organic acids, as well as sugars. As this preparation concentrates the active proanthocyanidins, it might be more effective in preventing UTIs. The aim of this study is to test the effects of this concentrated extract on women with recurrent UTIs.

### Materials and methods

An open label pilot study of 4 months duration was conducted at Helios Integrated Medicine, PC in Boulder, CO. The study was conducted with women between the ages of 25 and 70 years of age with a history of a minimum of 6 UTIs in the past year. Women who were pregnant, currently using antibiotics, had a major illness or diseases other than UTIs were excluded.

The cranberry product used in this study was manufactured in the US according to the aforementioned-patented processes. It is currently being used by GNC as the ingredient in Cranberry Supreme™. The women took one capsule twice daily for 12 weeks. Each capsule contained 200 mg cranberry extract standardized to 30% total phenols (25% minimum proanthocyanidins). The total cranberry proanthocyanidin intake during the study was approximately 100 mg per day. Total phenols were determined according to the use of Folin–Ciocalteu method (Singleton and Rossi, 1965) as