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The effectiveness of dried cranberries (*Vaccinium macrocarpon*) in men with lower urinary tract symptoms

Ales Vidlar[1], Jitka Vostalova[2]*, Jitka Ulrichova[2], Vladimir Student[1], David Stejskal[3], Richard Reichenbach[4], Jana Vrbkova[5], Filip Ruzicka[6] and Vilim Simanek[1]

[1]*Department of Urology, University Hospital, Olomouc, Czech Republic*
[2]*Department of Medical Chemistry and Biochemistry, Faculty of Medicine and Dentistry, Palacky University, Olomouc, Czech Republic*
[3]*Department of Laboratory Medicine, Central Moravian Hospital, Prostejov Hospital, Prostejov, Czech Republic*
[4]*WALMARK a.s., Trinec-Oldrichovice, Czech Republic*
[5]*Department of Mathematical Analysis and Applications of Mathematics, Faculty of Science, Palacky University, Olomouc, Czech Republic*
[6]*Department of Microbiology, Faculty of Medicine, Masaryk University, Brno, Czech Republic*

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Lower urinary tract symptoms (LUTS) are a common condition in older men. The objective of the present study was to evaluate the efficacy and tolerability of cranberry (*Vaccinium macrocarpon*) powder in men at risk of prostate disease with LUTS, elevated prostate-specific antigen (PSA), negative prostate biopsy and clinically confirmed chronic non-bacterial prostatitis. Forty-two participants received either 1500 mg of the dried powdered cranberries per d for 6 months (cranberry group; *n* 21) or no cranberry treatment (control group; *n* 21). Physical examination, International Prostate Symptom Score, quality of life (QoL), five-item version of the International Index of Erectile Function (IIEF-5), basic clinical chemistry parameters, haematology, Se, testosterone, PSA (free and total), C-reactive protein (CRP), antioxidant status, transrectal ultrasound prostate volume, urinary flow rate, ultrasound-estimated post-void residual urine volume at baseline, and at 3 and 6 months, and urine *ex vivo* anti-adherence activity were determined in all subjects. In contrast to the control group, patients in the cranberry group had statistically significant improvement in International Prostate Symptom Score, QoL, urination parameters including voiding parameters (rate of urine flow, average flow, total volume and post-void residual urine volume), and lower total PSA level on day 180 of the study. There was no influence on blood testosterone or serum CRP levels. There was no statistically significant improvement in the control group. The results of the present trial are the first firm evidence that cranberries may ameliorate LUTS, independent of benign prostatic hyperplasia or C-reactive protein level.

***Vaccinium macrocarpon*: Cranberries: Urinary tract disorders: Prostatitis: Prostate-specific antigen**

Prostate diseases are a major health concern for the male population throughout the Western world. Benign prostatic hyperplasia (BHP) and chronic prostatitis (CP), two of the most common medical conditions affecting older men (aged over 40 years), are associated with lower urinary tract symptoms (LUTS) which can have a negative impact on the quality of life (QoL). LUTS are divided into irritative and obstructive symptoms. The former include frequency, urgency and nocturia. The latter consist of slow urine stream and incomplete bladder emptying. Recently, a significant association between the serum levels of C-reactive protein (CRP) and irritative LUTS in both men and women was found[1,2]. On the other hand, CRP levels were not significantly associated with obstructive LUTS, or prostate-specific antigen (PSA) levels[3]. Untreated BHP and CP can lead to a number of medical complications, such as acute urinary retention, gross haematuria, repeated urinary tract infections, obstructive uropathy and cystolithiasis. The current standard of preventive care for men at risk of BHP and/or CP is treatment with α-adrenergic receptor blockers, 5-α-reductase inhibitors or antibiotics[4]. In recent years, there has been increasing interest in dietary supplements in the prevention of prostate diseases[5–8]. The proposed active components of these preparations include Se, vitamin E, vitamin D, lycopene, plant oils, *n*-3 fatty acids, phytosterols, terpenoids, lectins, polysaccharides, flavonolignans, flavonols and isoflavones. Some important dietary supplements for prostate health are complex extracts from green tea leaf

Abbreviations: BHP, benign prostatic hyperplasia; CFP, cranberry fruit powder; CP, chronic prostatitis; CRP, C-reactive protein; IIEF-5, five-item version of the International Index of Erectile Function; IPSS, International Prostate Symptom Score; LUTS, lower urinary tract symptoms; PSA, prostate-specific antigen; PSA_{free}, free prostate-specific antigen; PSA_{tot}, total prostate-specific antigen; Q_{max}, maximal urinary flow rate; QoL, quality of life.

* **Corresponding author:** Dr Jitka Vostalova, fax +420 585 632 302, email psotova@tunw.upol.cz

Table 1. Baseline demographics and clinical characteristics
(Mean values and standard deviations)

	Overall (*n* 42)		Control group (*n* 21)		Cranberry group (*n* 21)	
Variable	Mean	SD	Mean	SD	Mean	SD
Age (years)	63·0	5·5	64·0	5·4	62·0	5·4
BMI (kg/m^2)	26·46	3·04	24·91	2·09	28·00*	3·09
QoL	1·36	0·91	1·29	0·72	1·43	1·08
IPSS	10·48	5·95	10·86	5·88	10·10	6·14
PSA_{tot} (μg/l)	6·82	4·61	5·80	4·18	7·85	4·89
PSA_{free}:PSA_{tot}	0·22	0·04	0·18	0·02	0·21	0·07
Q_{max} (ml/s)	14·26	5·04	16·56	4·38	11·97*	4·68
Se (μmol/l)	1·12	0·67	0·97	0·53	1·27	0·77

QoL, quality of life questionnaire; IPSS, International Prostate Symptom Score; PSA_{tot}, total prostate-specific antigen; PSA_{free}, free prostate-specific antigen; Q_{max}, maximal urinary flow rate.
* Mean value was significantly different from that of the control group ($P<0·05$).

(*Camellia sinensis*), saw palmetto berry (*Serenoa repens*), milk thistle seed (*Silybum marianum*), pumpkin seed (*Cucurbita pepo*) and stinging nettle root (*Urtica dioica*). Cranberry (*Vaccinium macrocarpon*) is a source of organic and phenolic acids, flavonoids, flavonoid glycosides, anthocyanins, proanthocyanidins and triterpenoids of the ursane type with beneficial effects on the urinary tract[9,10]. Cranberry preparations are used as natural treatments for urinary tract infections, may reduce the ability of *Helicobacter pylori* to cause gastrointestinal ulcers and display anti-plaque activity[11–13]. The medicinal effectiveness and safety of intact cranberry fruits, juice and extracts have been critically evaluated recently[14]. Among recently reported effects of cranberry are its anti-inflammatory action through reduced cyclo-oxygenase-2 expression, suppression of IκBα degradation in human colon cancer cells[15] and inhibition of the growth and proliferation of several types of tumour cells including prostate[16]. However, to date there has been no published clinical study assessing whether cranberry reduces LUTS in men at risk of developing prostate diseases.

The aim of the present study was to evaluate the effect on urinary tract function of a 6-month daily consumption of 1500 mg cranberry fruit powder (CFP) in men with LUTS based on the International Prostate Symptom Score (IPSS), elevated PSA, BHP and histopathologically confirmed non-bacterial CP.

Table 2. International Prostate Symptom Score (IPSS), quality of life (QoL) score and International Index of Erectile Function (IIEF-5) in control and cranberry groups
(Mean values and standard deviations)

	Difference between answer							
	(Day 90 − day 0)				(Day 180 − day 0)			
	Control group		Cranberry group		Control group		Cranberry group	
Score	Mean	SD	Mean	SD	Mean	SD	Mean	SD
IPSS	0·00	2·39	−2·95*	2·48	1·43	4·09	−4·48*	3·74
Irritation questions	0·14	1·15	−1·14*	1·53	0·86	2·15	−1·62*	1·86
Obstruction questions	−0·14	1·68	−1·81*	1·94	0·57	2·38	−2·86*	2·52
Incomplete emptying: Over the past month how often have you had a sensation of not emptying your bladder completely after you had finished urinating?	0·14	1·28	−0·24	1·04	0·29	1·52	−0·38	0·92
Frequency: Over the past month how often have you had to urinate again less than 2 h after you finished urinating?	−0·14	0·65	−0·57	1·03	0·29	1·06	−0·76*	1·18
Intermittency: Over the past month how often have you found you stopped and started again several times when you urinated?	0·00	0·77	−0·38	1·12	0·14	0·85	−0·76*	1·22
Urgency: Over the last month how difficult have you found it to postpone urination?	0·29	0·72	−0·33*	0·73	0·29	1·06	−0·48*	1·03
Weak stream: Over the past month how often have you had a weak urinary stream?	−0·14	0·65	−0·67*	1·24	0·14	1·15	−1·19*	1·40
Straining: Over the past month how often have you had to push or strain to urinate?	−0·14	0·36	−0·52	0·75	0·00	0·52	−0·52*	0·93
Nocturia: Over the past month how many times did you most typically get up to urinate from the time you went to bed until the time you got up in the morning?	0·00	0·55	−0·24	0·70	0·29	0·72	−0·38*	0·86
QoL	−0·14	0·65	−0·52	0·68	0·00	0·77	−0·81*	0·75
IIEF-5	0·57	1·33	0·48	2·79	−0·71	2·17	0·05	1·88

* Mean value was significantly different from that of the control group ($P<0·05$).

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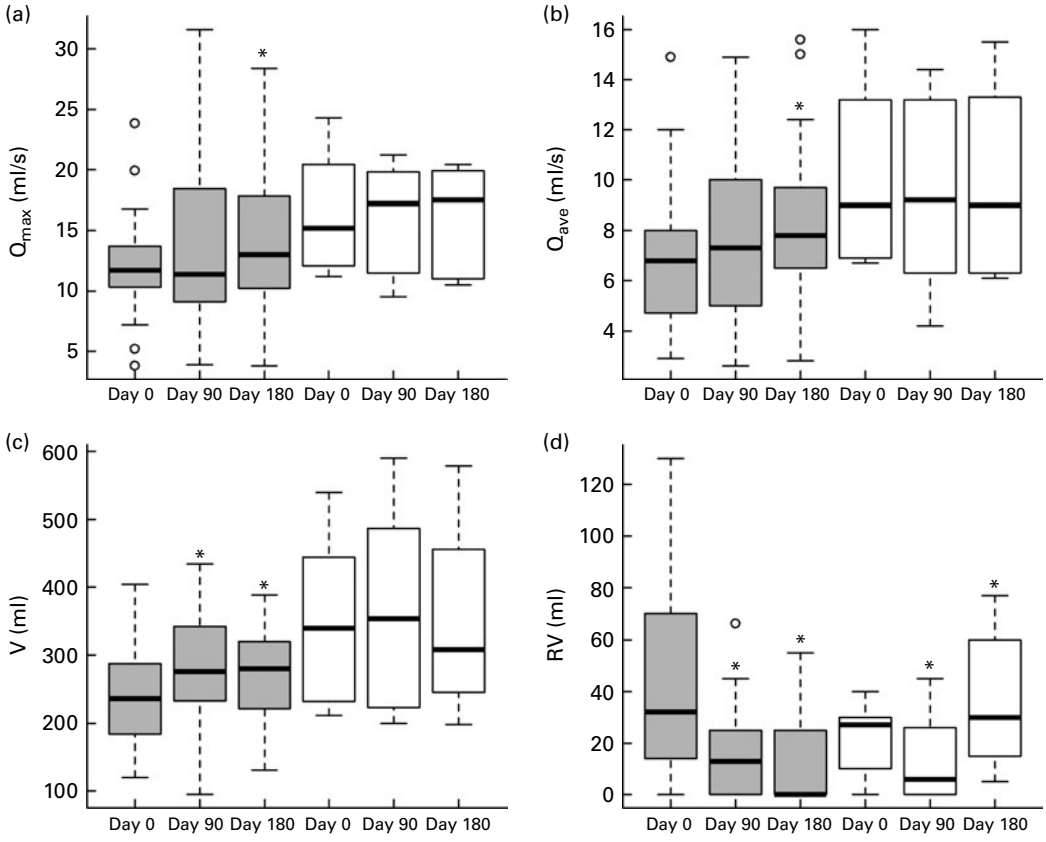

Fig. 1. Effect of cranberry (*Vaccinium macrocarpon*) on uroflowmetry parameters of maximal urinary flow rate (Q_{max}; a), average urinary flow rate (Q_{ave}; b), prostate bladder voiding volume (V; c) and post-void residual urine volume (RV; d) during 6 months of treatment. (■), Cranberry group; (□), control group. The box-and-whisker graphs show the median as the middle line. The box extends from the 25th to the 75th percentile and the whiskers extend from the lowest value to the highest. ○, Outside values. * Median was significantly different from that of the control group ($P<0·05$).

Materials and methods

Cranberry fruit powder characterisation

CFP (lot 070306-B/07-0659 supplied by Decas Botanical Synergies, LLC, Carver, MA, USA), containing 14·85 % (w/w) organic acids, 15·5 % sugars, 0·11 % anthocyanins, 1·95 % condensed tannins, 3·49 % total phenolics, was used for the clinical part of the study. One gelatine capsule contained 500 mg CFP.

Study subjects and data collection

The study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving human subjects/patients were approved by the Ethics Committee of the University Hospital and Faculty of Medicine and Dentistry, Palacky University in Olomouc, Czech Republic. Written informed consent was obtained from all participants. A 6-month randomised controlled trial was conducted from October 2008 to November 2009 at the Department of Urology of the University Hospital.

Study subjects

We invited forty-two men, aged 45 to 70 years (mean age 63 (SD 5·5) years), to participate in the study. All subjects entering the study had LUTS, elevated PSA and/or BHP. Other inclusion criteria were histological findings of acute or chronic non-bacterial prostatitis, normal urinary sediment and negative bacterial cultivation of urine. The diagnosis was asymptomatic inflammatory prostatitis category IV according to the National Institute of Health classification system[17]. Exclusion criteria were no supplements such as Se, vitamins E and D, lycopene or herbal products with possible effects on prostate health, a diet rich in isoflavones, antibiotics, anti-inflammatory drugs, α-blockers or 5α-reductase inhibitors, food allergies, chronic liver or kidney diseases, gastrointestinal or metabolic disorder or any other chronic health condition such as diabetes, all identified from interview. Participants were randomly divided into two groups: control (*n* 21; mean age 64·0 (SD 5·4) years) and cranberry (*n* 21; mean age 62·0 (SD 5·4) years). In the cranberry group, three capsules (1500 mg CFP per d) were taken at approximately equal intervals daily throughout the day for the 6-month period. The size of the daily dose was based on our double-blind study in young women[18]. They were instructed not to consume food rich in phenolics, especially anthocyanin-containing fruits, and to make no other dietary or lifestyle changes during the study. The control group received the same instructions as the cranberry group but no cranberry supplementation.

Data collection

Each case report form included: (i) a detailed medical history; (ii) assessment of all concurrent medical drugs and therapies;

(iii) digital rectal examination; (iv) dietary habits; (v) IPSS, QoL and the abridged five-item version of the International Index of Erectile Function (IIEF-5)[19]; (vi) urinanalysis; (vii) uroflowmetry with post-voidal residual urine; (viii) kidney and bladder ultrasound; (ix) transrectal ultrasound prostate volume; (x) a complete blood laboratory analysis. The following data were also collected at baseline and at 3 and 6 months in all subjects: Se; testosterone; free PSA (PSA_{free}); total PSA (PSA_{tot}); CRP; antioxidant status; urine *ex vivo* anti-adherence activity.

Lower urinary tract symptoms

All participants completed the IPSS including each of the seven areas (feeling of incomplete emptying, frequency, intermittency, urgency, weak stream, hesitancy and nocturia), QoL and five-item version of the International Index of Erectile Function (IIEF-5) questionnaires. Uroflowmetry data – maximal urinary flow rate (Q_{max}) and average urinary flow rate (Q_{ave}) – were measured using the FlowMic (Medkonsult, Olomouc, Czech Republic). Prostate bladder voiding volume (V) and post-void residual urine volume (RV) were assessed using the BK Medical Viking 2400 (BK Medical World Headquarters, Herlev, Denmark) with abdominal probe 3–7 MHz. V and RV were calculated using the formula for a prolate ellipsoid (width × length × height × 0·523). Histopathological examination of prostate tissue was done using ultrasound-guided prostate biopsy (BK Medical Viking 2400, transrectal probe 5–12 MHz; BK Medical World Headquarters) in all subjects.

Clinical biochemistry and haematology

Basic biochemical and haematological parameters were determined in all samples: Na, K, chlorides, total cholesterol, LDL, HDL, TAG, apoA, apoB, CRP, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, γ-glutamyl transpeptidase, lactate dehydrogenase, urea, creatinine, and testosterone were quantified in serum using a Hitachi Modular Evo P Analyzer (Hitachi, Tokyo, Japan). PSA (PSA_{tot} and PSA_{free}) in serum was determined using an Architect type LEIA Analyzer (Abbott Laboratories, Abbott Park, IL, USA). Analysis of selected parameters, i.e. total antioxidant capacity and total thiol (SH) groups in plasma, lipid peroxidation products such as malondialdehyde in plasma and erythrocytes, advanced oxidation protein products in serum, glutathione, glutathione peroxidase, catalase, glutathione reductase, glutathione transferase, and superoxide dismutase in erythrocytes was carried out as described by Psotova *et al.*[20]. Se in plasma was determined by atomic absorption spectrometry using the AA6300 instrument (Shimadzu, Kyoto, Japan). Hb, packed cell volume, erythrocytes, thrombocytes and leucocytes were measured in Na_2EDTA blood.

Urinanalysis

Urine samples were collected from a midstream clean catch and analysed by the IQ200 Automated Urinanalysis System (IRIS International, Inc., Chatsworth, CA, USA).

Table 3. Values of uroflowmetry in control and cranberry groups
(First quartiles, medians and third quartiles)

	Cranberry group								Control group							
	Day 0			Day 90			Day 180		Day 0			Day 90			Day 180	
Parameter	1st quartile	Median	3rd quartile	1st quartile	Median	3rd quartile	1st quartile	Median	3rd quartile	1st quartile	Median	3rd quartile	1st quartile	Median	3rd quartile	1st quartile	Median	3rd quartile
Q_{max} (ml/s)	10·3	11·7	13·7	9·1	11·4	18·4	10·2	13*	17·8	12·1	15·2	20·4	11·5	17·2	19·8	11	17·5	19·9
Q_{ave} (ml/s)	4·7	6·8	8	5	7·3	10	6·5	7·8*	9·7	6·9	9	13·2	6·3	9·2	13·2	6·3	9	13·3
V (ml)	184	236	288	233	276*	342	221	280*	320	232	340	444	223	354	487	245	308	456
RV (ml)	14	32	70	0	13*	25	0	0*	25	10	27	30	0	6*	26	15	30*	60

Q_{max}, maximal urinary flow rate; Q_{ave}, average urinary flow rate; V, prostate bladder voiding volume; RV, post-void residual urine volume.
*Median was significantly different from that at day 0 ($P<0.05$).

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Table 4. Markers of haematology and clinical chemistry in control and cranberry groups
(First quartiles, medians and third quartiles)

	Cranberry group									Control group								
	Day 0			Day 90			Day 180			Day 0			Day 90			Day 180		
Parameter	1st quartile	Median	3rd quartile	1st quartile	Median	3rd quartile	1st quartile	Median	3rd quartile	1st quartile	Median	3rd quartile	1st quartile	Median	3rd quartile	1st quartile	Median	3rd quartile
Hb (g/l)	143	149	159	142	152	156	142	152	159	143	152	160	141	149	156	140	150	155
Erythrocytes (10^{12}/litre)	4·84	4·97	5·22	4·92	5·09	5·28	4·90	5·06*	5·31	4·41	4·94	5·30	4·48	4·95	5·14	4·45	4·94	5·25
Leucocytes (10^9/litre)	6·10	6·98	7·68	6·25	7·20	8·19	6·37	7·23	8·02	5·83	6·20	7·21	5·92	6·54	7·04	6·20	6·43	7·04
Thrombocytes (10^9/litre)	187	225	267	181	223	254	201	220	245	194	207	235	188	192*	217	184	190	242
Packed cell volume (litres)	0·43	0·45	0·46	0·42	0·44	0·46	0·43	0·44	0·46	0·40	0·44	0·46	0·40	0·44	0·45	0·40	0·44	0·46
Na (mmol/l)	139	140	140	137	138	141	139	140	142	136	137	139	140	142*	142	137	140*	143
K (mmol/l)	4·13	4·26	4·38	4·07	4·28	4·51	4·11	4·36	4·67	3·98	4·06	4·22	4·17	4·30*	4·58	4·11	4·46*	4·65
Cl (mmol/l)	102	103	104	102	104	107	102	106	106	100	104	104	103	106*	108	101	103	106
Urea (mmol/l)	4·7	6·3	6·8	4·9	5·7	7·7	5·4	6·0	7·0	4·0	5·0	66	4·2	6·7*	70	4·0	5·0	70
Creatinine (μmol/l)	69	82	89	71	79	92	73	79	95	6	76	83	6·4	73	80	5·6	71	83
Bilirubin (μmol/l)	5	6	9	6	8*	10	6	8	9	6	9	10	7	10*	13	10	13*	14
ALT (μkat/l)	0·40	0·47	0·59	0·35	0·45	0·55	0·39	0·44	0·59	0·29	0·33	0·40	0·24	0·37	0·48	0·33	0·34*	0·71
AST (μkat/l)	0·42	0·45	0·51	0·39	0·44	0·48	0·39	0·47	0·53	0·38	0·43	0·45	0·38	0·40*	0·43	0·40	0·49*	0·53
ALP (μkat/l)	1·30	1·56	1·84	1·26	1·46	1·81	1·27	1·57	1·74	1·35	1·59	1·76	1·41	1·54	2·12	1·55	1·75*	2·14
GMT (μkat/l)	0·37	0·46	0·54	0·35	0·49	0·66	0·38	0·44	0·61	0·20	0·27	0·52	0·24	0·40	0·55	0·24	0·33*	0·61
LD (μkat/l)	2·52	2·73	3·05	2·74	3·04*	3·31	2·67	3·04*	3·42	2·48	2·74	3·05	2·70	2·78	2·89	2·47	2·57	2·80
CRP (mg/l)	1	2	3	1	2	3	1	2	3	1	1	1	1	1*	2	1	1*	3
Cholesterol (mmol/l)	4·23	4·90	5·61	4·51	4·78	5·46	4·64	5·00	5·68	4·92	5·49	6·23	4·02	5·09*	5·97	4·61	5·45	6·28
TAG (mmol/l)	1·30	1·65	2·28	1·23	1·87	2·21	1·40	1·72	2·65	1·21	1·34	2·34	0·98	1·31	2·59	1·41	1·61	2·11
HDL (mmol/l)	1·24	1·35	1·48	1·21	1·29	1·49	1·19	1·25	1·46	1·09	1·13	1·54	1·05	1·20	1·34	1·10	1·19	1·29
LDL (mmol/l)	2·15	2·71	3·47	2·28	2·85	3·33	2·48	2·91	3·18	2·99	3·83	4·02	2·23	3·12*	3·66	2·78	3·72	4·51
ApoA1 (g/l)	1·43	1·48	1·58	1·41	1·50	1·60	1·39	1·52	1·66	1·30	1·48	1·88	1·36	1·50	1·94	1·38	1·46	1·92
ApoB (g/l)	0·73	0·86	1·09	0·73	0·93	1·05	0·79	0·93	1·06	0·83	1·04	1·15	0·69	0·93	1·21	0·78	0·94	1·23
PSA_{tot} (μg/l)	4·20	6·18	11·40	3·76	5·59*	7·10	3·53	4·53	7·54	2·99	3·99	11·25	2·70	4·24	10·20	3·43	5·37	9·80
PSA_{free} (μg/l)	0·87	1·03	1·18	0·77	0·91*	1·09	0·73	0·90*	1·36	0·66	0·73	0·82	0·50	0·69	0·93	0·69	0·73	0·76
TST (nmol/l)	10·7	14·2	16·2	11·4	14·4	16·5	12·6	15·9	17·5	12·8	17·6	22·4	16·9	20·4	28·0	10·9	18·7	24·1
Se (μmol/l)	0·89	1·13	1·37	0·91	1·02	1·34	0·82	1·04	1·29	0·49	0·84	1·11	0·71	0·78	0·85	0·68	0·91	1·20

ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; GMT, γ-glutamyl transpeptidase; LD, lactate dehydrogenase; CRP, C-reactive protein; PSA_{tot}, total prostate-specific antigen; PSA_{free}, free prostate-specific antigen; TST, testosterone.
* Median was significantly different from that at day 0 ($P<0·05$).

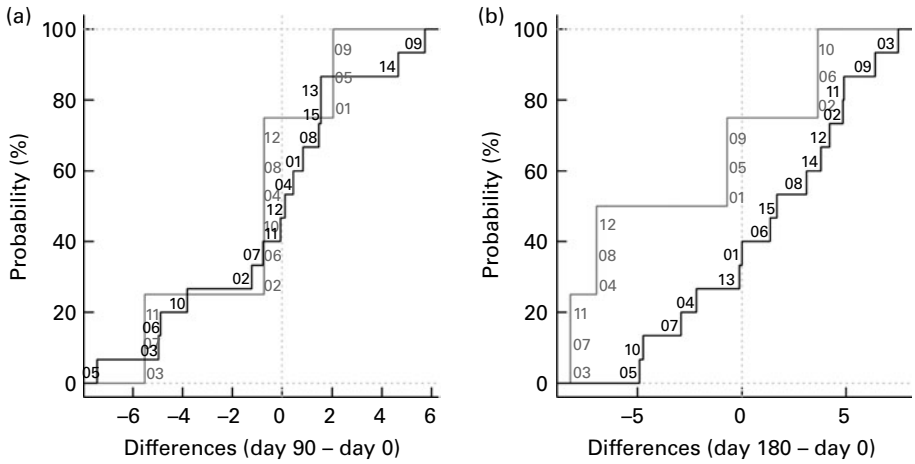

Fig. 2. Effect of cranberry (*Vaccinium macrocarpon*) on free prostate-specific antigen:total prostate-specific antigen ratio after 90 and 180 d of consumption. The values are expressed as difference values based on day 90 and day 0 (a) and day 180 and day 0 (b) of study. (—), Cranberry group; –, control group. * $P<0{\cdot}05$ *v.* control. The numbers near to the lines correspond with the number of each participant.

Anti-adherence activity of urine

Four biofilm-positive micro-organisms were used: *Escherichia coli* FB42, *Enterococcus faecalis* FB16 and *Candida parapsilosis* BC 12 (clinical strain; Collection of the Department of Microbiology, Faculty of Medicine, Masaryk University, Brno, Czech Republic) and *Staphylococcus epidermidis* CCM 7221 from the Czech Collection of Micro-organisms (CCM; Faculty of Sciences, Masaryk University, Brno, Czech Republic). The bacteria were stored in cryotubes at −76°C. The biofilm formation was detected using a modification of the adherence assay[21]. The experiment was repeated three times.

Statistical analysis

The data were analysed using the non-parametric Wilcoxon two-tailed tests (paired-samples and independent-samples) to test the statistical significance of differences in all parameters on days 0, 90 and 180. The level of significance was 5 %. Values are presented as 1st quartile, median and 3rd quartile or mean value and standard deviation. Box and empirical cumulative distribution plots were used as graphic illustration of significant differences in progression over 3 and 6 months between the groups.

Results

At baseline both groups had similar clinical and demographic characteristics except for significant differences in BMI and Q_{max} values (Table 1). The daily dose of CFP contained 223 mg organic acids, 1·65 mg anthocyanins, 29·5 mg condensed tannins and 52 mg total phenols. Patients who received cranberry for 6 months had a statistically significant lower IPSS and QoL score than controls. A lower IPSS score reflected improvement in the irritative and obstructive symptoms (Table 2). All parameters of urination (Q_{max}, average urinary flow rate (Q_{ave}), prostate bladder voiding and post-void residual urine volumes) were significantly improved in at least 70 % of participants of the cranberry group (Fig. 1); in the control group, the tested parameters did not change with the exception of post-void residual urine volume where a statistically significant deterioration was found (Table 3). Haematology values were unchanged with the exception of a significant increase in erythrocytes in the cranberry group, which, however, was within physiological limits (Table 4). PSA_{tot} decreased in approximately 80 % of patients in the cranberry group while, in contrast, the PSA_{free}:PSA_{tot} ratio mostly increased (Table 4; Fig. 2). Although changes in the values of several 'safety' markers were statistically significantly different, after 6 months for both groups, the fluctuation was within normal physiological limits. From this point of view, the cranberry group compared with the control group stabilised and this might be true for oxidative stress markers as well (Table 5). Differences in urine adherence *ex vivo* in both groups were not significantly different. No adverse events were recorded.

Discussion

Plant extracts for urinary tract disorders have long been used in traditional medicine. Today, botanical diuretics, antimicrobials and anti-adherence agents, renal protectives and herbs for patients with LUTS or BHP are requested by patients, even though accepted only with reservation by urologists[22,23]. Cranberry fruit and juice are noted for their ability to inhibit the binding of pathogenic *E. coli* strains and other microbes to the bladder epithelium. This effect has been attributed to proanthocyanidins (condensed tannins), even if a more simple explanation might be the direct antibacterial action of hippuric acid[14]. Cranberry prophylaxis is also recommended to women with recurrent urinary tract infection. In a recent publication, for example, the antibiotic Trimethoprim was shown to have minimal advantage over cranberry extract in the prevention of recurrent urinary tract infections in women and had side effects[24]. LUTS refer to a complex of irritative and obstructive voiding symptoms that are common in both ageing women and men. Prostate enlargement and BPH affect primarily older men. The incidence of LUTS associated with BPH increases dramatically with advancing age[25]. Unfortunately, no trials have yet been published assessing the effect of cranberry components on men with indicated

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Table 5. Markers of oxidative stress in control and cranberry groups

(First quartiles, medians and third quartiles)

	Cranberry group									Control group								
	Day 0			Day 90			Day 180			Day 0			Day 90			Day 180		
Parameter	1st quartile	Median	3rd quartile	1st quartile	Median	3rd quartile	1st quartile	Median	3rd quartile	1st quartile	Median	3rd quartile	1st quartile	Median	3rd quartile	1st quartile	Median	3rd quartile
PMDA (nmol/g protein)	49·11	60·46	76·40	50·54	74·31	77·40	50·40	57·80	76·60	51·23	60·55	70·45	47·10	51·20*	63·87	47·67	61·79	69·77
SHG_{tot} (μmol/g protein)	3·06	3·65	4·06	2·40	4·10	4·93	2·83	3·72	4·21	3·10	3·52	3·56	3·01	3·13	3·43	3·00	3·40	3·74
AOPP (μmol/l)	189·9	199·0	231·2	160·6	202·4	257·5	161·2	203·2	240·5	159·0	222·3	302·7	145·3	180·4*	274·3	139·9	155·3*	286·5
TAC (nA)	4·92	5·72	6·64	5·08	6·01	6·50	5·29	5·82	6·29	4·41	5·39	6·19	4·35	5·72	6·50	4·51	4·72	6·36
MDA (nmol/g Hb)	0·31	0·37	0·44	0·32	0·34	0·41	0·33	0·39	0·44	0·29	0·35	0·42	0·25	0·36	0·41	0·25	0·41*	0·48
GSH (μmol/g Hb)	10·29	10·82	11·91	10·24	11·45	12·15	10·86	11·13	12·14	8·69	10·10	11·44	9·43	10·25	11·41	9·72	11·25	11·77
SOD (U/g Hb)	1·78	2·17	2·31	1·97	2·08	2·34	2·07	2·14	2·25	1·57	1·88	2·05	1·18	1·66	2·01*	1·50	1·95	2·06
GPX (μmol/min per g Hb)	22·58	27·09	29·12	22·26	26·76	29·14	23·28	25·08	29·87	21·23	22·77	26·52	18·89	19·89	27·36	23·77	24·41*	29·05
CAT (μmol/min per g Hb)	39·11	96·62	121·56	39·80	108·49	134·13	40·53	102·30	129·31	95·43	101·04	123·74	98·36	115·93*	117·98	111·21	117·60*	124·08
GST (μmol/min per g Hb)	36·01	44·42	53·46	39·23	46·08	59·58	40·48	46·46	56·54	16·43	51·17	60·47	16·95	51·05	61·31	18·05	49·10	62·94
GSR (μmol/min per g Hb)	4·35	5·62	6·25	5·09	6·08	7·69	5·09	6·53	7·13	2·26	4·58	5·74	2·84	4·81	5·33	1·86	4·87*	6·38

PMDA, plasma malondialdehyde; SHG_{tot}, total thiol groups; AOPP, advanced oxidation protein products; TAC, total antioxidant capacity; MDA, malondialdehyde; GSH, glutathione; SOD, superoxide dismutase, GPX, glutathione peroxidase; CAT, catalase; GST, glutathione transferase; GSR, glutathione reductase.

* Median was significantly different from that at day 0 ($P<0·05$).

LUTS and/or increased PSA levels. Recently published results have demonstrated that CP might be linked to a higher prostate cancer risk[26]. The present study was focused on men with diagnosed LUTS, increased PSA level, and histologically confirmed non-bacterial prostatitis. We selected cranberry whole fruit powder in preference to cranberry extract for the present study. Our previous work had shown equivalent efficacy between CFP and two different cranberry extracts[27]. The daily dose of 1500 mg dried cranberries was based on our double-blind study in young women[18]. This dose elicited urine anti-adherence activity but had no adverse effects. In participants taking cranberry for 6 months there was, in addition to a marked improvement in all urodynamic parameters (Fig. 1), a statistically significant decrease in the IPSS score, and an increase in the quality of life evaluated by the QoL questionnaire (Table 2). Taking cranberry affected the value of PSA (Table 4). In the cranberry group, both a decrease in the PSA value and an increase in the PSA_{free}: PSA_{tot} ratio (Fig. 2) without affecting CRP or testosterone levels were recorded. The use of selective 5-α-reductase inhibitors has often been linked to hormone changes associated with unpleasant sexual side effects, in particular, erectile dysfunction and decreased libido[28,29]. The treatment approach in patients with elevated PSA and histologically confirmed prostatitis is rather complicated and may involve long-term antibiotics with the expectation of lowering the PSA level. The decrease in PSA in the cranberry group demonstrates that prophylaxis by cranberry may be as effective as antibiotic treatment but without the risk of antimicrobial resistance and a minimum of adverse effects. The diuretic effects of cranberries may also have contributed to the reduction in LUTS in the cranberry group[30]. Cranberries contain several structurally different groups of compounds that modulate various cellular pathways in man including the urinary tract and the prostate. However, phenolics, as phenolic acids, anthocyanins and proanthocyanidins, that are metabolised mainly to hippuric acid, are assumed to be the active components. The synergistic effects of cranberry constituents may improve their bioactivity. Use of the whole berries may be more beneficial than single components and with minimal adverse effects.

Conclusions

Our trial is the first to evaluate cranberry in the treatment of LUTS specifically in men with BHP, elevated PSA levels and non-bacterial prostatitis. The present results show that dried cranberries improve prostate health very effectively both in men with elevated PSA in histologically proven prostatitis and for improving voiding dysfunction. In the cranberry group, no associations were found between dried powdered berry consumption and CRP levels. Unlike currently used medication for prostatitis and LUTS, cranberry has no adverse effects. Our findings may assist men suffering from LUTS, and also their clinicians, to decide on a treatment that is both inexpensive and natural, like cranberry. The limitations of the present study include the relatively small number of men. Given the probability that some responses on the IPSS and QoL questionnaires in the cranberry group may have been secondary to a placebo effect, there is a need to control for this in future clinical trials.

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There is no conflict of interest.

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