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Research Article

Prostatic Tissue Level of Some Major and Trace Elements in Patients with BPH

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Abstract

Background: Several studies have supposed the role of age-related deficiency of some essential chemical elements in the etiology of benign prostatic hyperplasia (BPH).

Aim: The objective of this exploratory study was to evaluate whether significant deficiencies in the prostatic tissue levels of zinc (Zn), calcium (Ca), magnesium (Mg), iron (Fe), copper (Cu) and some other chemical elements exist in patients with BPH.

Material and Methods: We prospectively evaluated prostatic tissue levels of 17 chemical elements in 32 patients with BPH and 32 healthy male inhabitants (control group). Measurements were performed using two analytical methods: instrumental neutron activation analysis with high resolution spectrometry of short-lived radionuclides and inductively coupled plasma atomic emission spectrometry.

Results: In the hyperplastic prostates we observed a significant increase in levels of K (potassium) and Sr (strontium) in comparison with the histologically normal prostates. It was not found a significant difference of prostatic tissue levels of Zn, Ca, Mg, Fe, and Cu between group of BPH patients and control group. Correlations between the prostatic chemical element mass fractions indicated that there is a great disturbance of prostatic chemical element relationships with a hyperplasia of prostate tissue.

Conclusion: Our finding of prostatic tissue levels of chemical element and correlation between chemical element contents indicates that there is a disturbance of chemical element metabolism in BPH tissue in comparison with the normal prostate tissue. However, the potential role of age-related Zn, Ca, Mg, Fe, and Cu deficiency in the prostate has not been confirmed as being involved in the etiology of BPH. Thus, our findings cast doubts on a beneficial effect of the Zn, Ca, Mg, Fe, and Cu supplementations on BPH prevention and treatment.

Keywords: Benign Prostate Hyperplasia; Prostatic Trace Element Contents; Trace Element Supplementations

Abbreviations

BPH: Benign Prostatic Hyperplasia;

INAA-SLR: Instrumental Neutron Activation Analysis with high resolution Spectrometry of Short-lived Radionuclides;

ICP-AES: Inductively Coupled Plasma Atomic Emission Spectrometry

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Introduction

Benign prostatic hyperplasia (BPH) represents the most common urologic age-related disease. BPH is histologically defined as an overgrowth of the epithelial and stromal cells in prostate gland [1]. The prevalence of histological BPH is found in approximately 50-60% of males age 40-50, in over 70% at 60 years old and in greater than 90% of men over 70 [2]. To date, we still have no precise knowledge of the cellular and biochemical processes underlying the etiology and pathogenesis of BPH [3]. There are a few hypotheses on the subject but the most common concept is based on the differentiating and growth-promoting actions of androgens [4].

In our previous studies it was shown that the levels of Zn, Ca, Mg, K and some other chemical elements in prostate tissue are the androgen-dependent parameters and play an important role in prostate functions [5-10]. Moreover, it is well known that Zn, Ca, Mg, K, Fe, Cu, and some other chemical element play important roles in cell proliferation, differentiation, and transformation and are essential for the regulation of DNA synthesis, mitosis and apoptosis [11]. Due to lifestyle, eating and dietary habits, and physiological effects of aging, the elderly male population is normally predisposed to conditions of chemical elements deficiency [12,13], which can increase this population's susceptibility to BPH [14]. According to the proponents of dietary supplemental chemical element usage, in the absence of such supplements, cellular chemical element uptake will be depressed and chemical element levels in prostate tissue will be reduced [14,15].

The chemical element contents in tissue of the non-hyperplastic [6,9,16-33] and hyperplastic [19,23-25,34-42] prostate have been studied, producing contradictory results. Data obtained in the majority of studies are based on measurements of processed tissue. The most frequently used digestion procedures have been the traditional dry ashing and wet digestion that allow destruction of organic matter of the sample. Moreover, in many studies before digestion procedures prostate samples have been treated with solvents (distilled water, ethanol etc) and then dried at a high temperature for many hours. Sample preparation, including sample digestion and other kinds of treatment tissue samples before measurement, is a critical step in elemental analysis due to risk of contamination and analyses loss, contributing for the uncontrolled analysis errors [43-47]. Moreover, only a few of these studies employed quality control using certified reference materials for determination of the chemical element mass fractions. Thus, the questions about the differences between chemical element contents in intact and BPH tissue remained open.

This work had four aims. The first was to assess the chemical element mass fractions in BPH tissue using nondestructive instrumental neutron activation analysis with high resolution spectrometry of short-lived radionuclides (INAA-SLR) combined with inductively coupled plasma atomic emission spectrometry (ICP-AES). The second aim was to compare the results for BPH tissue with the levels of chemical elements in the non-hyperplastic prostate gland of age-matched health subjects, who had died suddenly. The third aim was to estimate the inter-correlations between trace element mass fractions in hyperplastic prostate and to compare these results with data for non-hyperplastic gland. The final aim was to compare the results obtained in this work with data from the literature.

All studies were approved by the Ethical Committee of the Medical Radiological Research Center, Obninsk.

Materials and Methods

All patients studied (n=32) were hospitalized in the Urological Department of the Medical Radiological Research Centre. In all cases the diagnosis of BPH has been confirmed by clinical and morphological results obtained during studies of biopsy and resected materials. None of the patients were taking a trace element supplement known to affect prostate chemical element contents. The age of patients with BPH ranged from 46 to 78 years (1 in age before 50 years, 7 in age range 51-60 years, 15 in age range 61-70 years, and 9 in age above 70 years), the mean being 65±6 years (M±SD). Using a titanium scalpel resected materials were divided into two portions to permit morphological study of prostatic tissue and to estimate their chemical element contents.

Intact prostates were removed at necropsy from 32 men aged from 44 to 87 years (10 in age before 50 years, 10 in age range 51-60 years, 8 in age range 61-70 years, and 4 in age above 70 years, mean M±SD age 60±11 years) who had died suddenly (age-matched control group). The majority of deaths were due to trauma. The available clinical data were reviewed for each subject. None of the subjects had a history of an intersex condition, endocrine disorder, neoplasm or other chronic disease that could affect the normal development of the prostate. None of the subjects were receiving medications known to affect prostate morphology or chemical element content. All prostate glands were collected within 2 days of death and divided (with an anterior-posterior cross-section) into two portions using a titanium scalpel. One tissue portion was reviewed by an anatomical pathologist while the other was used for the chemical element content determination. A histological examination was used to control the age norm conformity as well as to confirm the absence of any microadenomatosis and/or latent cancer.

After the samples intended for chemical element analysis were weighed, they were freeze-dried and homogenized. The pounded sample weighing about 100 mg was used for chemical element measurement by INAA-SLR. The samples for INAA-SLR were sealed separately in thin polyethylene films washed with acetone and rectified alcohol beforehand. After INAA-SLR investigation the prostate samples were taken out from the polyethylene ampoules, decomposed in autoclaves and used for

ICP-AES. Information detailing with the INAA-SLR and ICP-AES methods used and other details of the analysis was presented in our previous publication [6,8,26,30].

For quality control, ten subsamples of the certified reference materials IAEA H-4 Animal muscle from the International Atomic Energy Agency (IAEA), and also five sub-samples INCT-SBF-4 Soya Bean Flour, INCT-TL-1 Tea Leaves and INCT-MPH-2 Mixed Polish Herbs from the Institute of Nuclear Chemistry and Technology (INCT, Warszawa, Poland) were analyzed simultaneously with the investigated prostate tissue samples. All samples of CRM were treated in the same way as the prostate tissue samples. Detailed results of this quality assurance program were presented in earlier publications [6,8,26,30].

A dedicated computer program for INAA mode optimization was used [48]. The mean values of chemical element mass fractions were taken into account in final calculation for elements measured by both INAA-SLR and ICP-AES methods. Using Microsoft Office Excel software, arithmetic mean (M), standard deviation (SD), and standard error of mean (SEM) was calculated for chemical element mass fractions. The reliability of difference in the results between non-hyperplastic and hyperplastic prostate glands was evaluated by the parametric Student's t-test and values of $p<0.05$ were considered to be statistically significant.

Results

Table 1 presents basic statistical parameters (arithmetic mean, standard deviation, standard error of mean, minimal and maximal values, median, percentiles with 0.025 and 0.975 levels) for aluminum (Al), boron (B), barium (Ba), bromine (Br), Ca, Cu, Fe, K, lithium (Li), Mg, manganese (Mn), sodium (Na), phosphorus (P), sulphur (S), silicon (Si), Sr, and Zn mass fraction in BPH and non-hyperplastic prostate tissue.

The ratios of means and the reliability of difference between mean values of Al, B, Ba, Br, Ca, Cu, Fe, K, Li, Mg, Mn, Na, P, S, Si, Sr, and Zn mass fraction in BPH and normal prostate tissue are presented in Table 2.

To estimate the effect of age on the Al, B, Ba, Br, Ca, Cu, Fe, K, Li, Mg, Mn, Na, P, S, Si, Sr, and Zn mass fractions in BPH tissue we examined two age groups: the first comprised persons with ages ranging from 56 to 65 years (mean age 62±3 years, n=18) and the second comprised those with ages ranging from 66 to 87 years (mean age 70±5 years, n=14). The means, the ratios of means and the reliability of difference between mean values of chemical element mass fractions in two age groups are presented in Table 3.

Tables 4 and 5 present intercorrelations (r – the Pearson correlation coefficient) of pairs of the chemical element mass fractions in normal and BPH prostate glands, respectively.

Tissue	**El**	**Mean**	**SD**	**SEM**	**Min**	**Max**	**Med.**	**P 0.025**	**P 0.975**
BPH n=32	Al	24.4	10.2	3.2	8.4	38.2	25.6	10	38.2
	B	1.51	0.79	0.26	0.7	3.2	1.2	0.76	3.02
	Ba	1.22	0.68	0.2	0.42	2.32	0.97	0.468	2.24
	Br	30.7	17.2	3.4	5.5	77	26.2	5.75	63.8
	Ca	2032	547	165	1168	2762	1898	1173	2757
	Cu	9.86	3.96	1.25	6	18.9	8.3	6.25	17.9
	Fe	131	66	12	56.5	376	116	60.6	279
	K	14471	2454	740	11683	20519	13552	12025	19744
	Li	0.039	0.024	0.007	0.013	0.088	0.03	0.014	0.086
	Mg	1201	276	83	687	1585	1263	749	1552
	Mn	1.19	0.31	0.09	0.8	1.8	1.2	0.8	1.73
	Na	11612	2882	869	7762	15503	10564	7893	15400
	P	7907	1385	418	6279	11780	7547	6512	10888
	S	8787	1616	487	7671	13507	8289	7726	12401
	Si	141	79	24	72.1	333	102	73.1	307
	Sr	3.69	1.84	0.45	1.6	8.3	3.4	1.76	7.66
	Zn	1297	725	119	312	4432	1173	325	2642
Normal n=32	Al	34.2	18.1	3.7	9.6	73.3	28.9	11.9	70.9
	B	1.04	0.86	0.18	0.3	3	0.7	0.3	2.89
	Ba	1.54	1	0.21	0.38	4.33	1.18	0.422	3.75
	Br	33.8	17.5	3.7	12.5	80.7	28.3	12.9	71.3
	Ca	2437	1255	242	1180	6893	2210	1196	5603
	Cu	9.88	4.76	1.02	4.1	22.2	7.9	4.94	19.9
	Fe	132	39	7	62	218	134	72.4	212
	K	11574	2346	443	6325	18198	11401	7315	15586
	Li	0.043	0.027	0.006	0.015	0.101	0.03	0.016	0.1
	Mg	1078	415	78	447	2060	1040	517	1959
	Mn	1.3	0.42	0.09	0.75	2.8	1.3	0.833	2.25
	Na	11012	2191	407	6415	15300	10934	6708	15156
	P	7617	1879	384	5969	14838	7210	6015	11870
	S	8632	1292	264	5662	12567	8555	6638	11416
	Si	100	56	12	32.3	235	94.1	36.8	206
	Sr	2.38	1.88	0.39	0.87	8.1	1.54	0.914	6.51
	Zn	1094	971	172	223	5868	1016	247	2717

El element *M* arithmetic mean, *SD* standard deviation, *SEM* standard error of mean, *Min* minimum value, *Max* maximum value, *Med.* median, *P0.025* percentile with 0.025 level, *P0.975* percentile with 0.975 level.

Table 1. Basic statistical parameters of the Al, B, Ba, Br, Ca, Cu, Fe, K, Li, Mg, Mn, Na, P, S, Si, Sr, and Zn mass fraction (mg/kg, on dry mass basis) in the hyperplastic (BPH) and non-hyperplastic prostate tissue (Normal)

Median, minimum and maximum value of means of Al, B, Ba, Br, Ca, Cu, Fe, K, Li, Mg, Mn, Na, P, S, Si, Sr, and Zn mass fraction in BPH and normal prostate tissue according to data from the literature in comparison with our results (mg/kg, dry mass basis) are shown in Table 6. When our results were compared with data of literature a number of values for trace element mass fractions were not expressed on a dry mass basis by the authors of the cited references. However, we calculated these values using the medians of published data for water – 83% [49] and ash – 1% [50] on wet mass basis contents in non-hyperplastic prostate of adult men, and also for water – 80% in BPH tissue [40].

Element	**Prostatic tissue**			**Ratio BPH /Normal**
	BPH 56-78 year (n=32)	**Normal 44-87 year (n=32)**	**Student's t-test $p \le$**	
Al	24.4±3.2	34.2±3.7	0.054 (NS)	0.71
B	1.51±0.26	1.04±0.18	0.160 (NS)	1.45
Ba	1.22±0.20	1.54±0.21	0.297 (NS)	0.79
Br	30.7±3.4	33.8±3.7	0.529 (NS)	0.91
Ca	2032±165	2437±242	0.175 (NS)	0.83
Cu	9.86±1.25	9.88±1.02	0.992 (NS)	1.00
Fe	131±12	132±7	0.942 (NS)	0.99
K	14471±740	11574±443	0.0036	1.25
Li	0.0385±0.0073	0.0425±0.0057	0.667 (NS)	0.91
Mg	1201±83	1078±78	0.290 (NS)	1.11
Mn	1.19±0.09	1.30±0.09	0.391 (NS)	0.92
Na	11612±869	11012±407	0.541 (NS)	1.05
P	7907±418	7617±384	0.614 (NS)	1.04
S	8787±487	8632±264	0.784 (NS)	1.02
Si	141±24	100±12	0.147 (NS)	1.41
Sr	3.69±0.45	2.38±0.39	0.035	1.55
Zn	1297±119	1094±172	0.337 (NS)	1.19

M arithmetic mean, *SEM* standard error of mean, *NS* not significant difference.

Table 2. Comparison of mean values (M±SEM) of the Al, B, Ba, Br, Ca, Cu, Fe, K, Li, Mg, Mn, Na, P, S, Si, Sr, and Zn mass fraction (mg/kg, dry mass basis) in BPH and normal prostate tissue.

Element	**BPH**			**Ratio Age group 2/Age group 1**
	Age group 1 56-65 year (n=18)	**Age group 2 66-78 year (n=14)**	**Student's t-test $p \le$**	
Al	24.8±5.4	24.1±4.1	0.981 (NS)	1.03
B	1.60±0.47	1.47±0.35	0.831 (NS)	1.09
Ba	1.24±0.32	1.21±0.29	0.950 (NS)	1.02
Br	33.8±5.8	28.3±4.1	0.446 (NS)	1.19
Ca	2104±277	1972±217	0.717 (NS)	1.07
Cu	7.88±0.54	11.8±2.2	0.146 (NS)	0.67
Fe	145±21	118±12	0.287 (NS)	1.23
K	15438±1584	13666±221	0.328 (NS)	1.13
Li	0.041±0.013	0.036±0.009	0.776 (NS)	1.14
Mg	1255±112	1156±127	0.574 (NS)	1.09
Mn	1.16±0.15	1.22±0.13	0.795 (NS)	0.95
Na	11494±1620	11712±1008	0.912 (NS)	0.98
P	8445±840	7458±283	0.317 (NS)	1.13
S	9504±1016	8189±156	0.267 (NS)	1.16
Si	183±45	105±13	0.157 (NS)	1.74
Sr	3.34±0.34	3.83±0.62	0.498 (NS)	0.87
Zn	1143±107	1477±223	0.191 (NS)	0.77

M arithmetic mean, *SEM* standard error of mean, *NS* not significant difference.

Table 3. Differences between mean values (M±SEM) of the Al, B, Ba, Br, Ca, Cu, Fe, K, Li, Mg, Mn, Na, P, S, Si, Sr, and Zn mass fraction (mg/kg, dry mass basis) in hyperplastic prostate glands of two age groups.

Element	**B**	**Ba**	**Br**	**Ca**	**Cu**	**Fe**	**K**	**Li**
Al	-0.31	0.30	-0.01	-0.28	-0.23	0.12	0.24	0.43
B	**1.00**	0.22	-0.25	-0.16	0.07	-0.06	0.02	0.11
Ba	0.22	**1.00**	-0.07	-0.06	0.07	-0.12	-0.01	0.55[a]
Br	-0.25	-0.07	**1.00**	0.58[a]	0.27	0.06	-0.44	0.14
Ca	-0.16	-0.06	0.58[a]	**1.00**	0.22	0.07	-0.22	-0.10
Cu	0.07	0.07	0.27	0.22	**1.00**	0.25	-0.09	-0.08
Fe	-0.06	-0.12	0.06	0.07	0.25	**1.00**	-0.02	0.01
K	0.02	-0.01	-0.44	-0.22	-0.09	-0.02	**1.00**	-0.18
Li	0.11	0.55[a]	0.14	-0.10	-0.08	0.01	-0.18	**1.00**
Mg	0.03	0.18	-0.10	-0.04	0.41	-0.02	0.22	-0.04
Mn	0.08	0.17	-0.07	-0.22	0.41	0.33	0.07	0.13
Na	-0.38	0.05	-0.28	-0.12	0.15	0.23	0.24	0.08
P	-0.03	0.24	-0.10	0.19	0.37	0.05	0.21	-0.14
S	-0.07	0.35	-0.31	-0.28	0.13	0.21	0.67[b]	0.02
Si	-0.03	0.29	-0.35	-0.28	-0.25	-0.12	0.31	0.44
Sr	-0.16	0.25	0.70[b]	0.60[b]	-0.03	-0.21	-0.40	0.46
Zn	-0.15	0.13	0.02	-0.05	0.43	0.04	-0.01	-0.17
Element	**Mg**	**Mn**	**Na**	**P**	**S**	**Si**	**Sr**	**Zn**
Al	-0.15	0.23	0.06	0.24	0.29	0.68[b]	0.03	-0.14
B	0.03	0.08	-0.38	-0.03	-0.07	-0.03	-0.16	-0.15
Ba	0.18	0.17	0.05	0.24	0.35	0.29	0.25	0.13
Br	-0.10	-0.07	-0.28	-0.10	-0.31	-0.35	0.70[b]	0.02
Ca	-0.04	-0.22	-0.12	0.19	-0.28	-0.28	0.60[b]	-0.05
Cu	0.41	0.41	0.15	0.37	0.13	-0.25	-0.03	0.43
Fe	-0.02	0.33	0.23	0.05	0.21	-0.12	-0.21	0.04
K	0.22	0.07	0.24	0.21	0.67[b]	0.31	-0.40	-0.01
Li	-0.04	0.13	0.08	-0.14	0.02	0.44	0.46	-0.17
Mg	**1.00**	0.16	0.52[a]	0.71[b]	0.55[a]	-0.09	-0.22	0.53[a]
Mn	0.16	**1.00**	0.10	-0.04	0.21	0.15	-0.15	-0.02
Na	0.52[a]	0.10	**1.00**	0.15	0.50	0.21	-0.19	0.21
P	0.71[b]	-0.04	0.15	**1.00**	0.35	-0.13	-0.24	0.85[b]
S	0.55[a]	0.21	0.50	0.35	**1.00**	0.23	-0.29	0.09
Si	-0.09	0.15	0.21	-0.13	0.23	**1.00**	0.16	-0.19
Sr	0.22	-0.15	-0.19	0.24	-0.29	0.16	**1.00**	-0.31
Zn	0.53[a]	-0.02	0.21	0.85[b]	0.09	-0.19	-0.31	**1.00**

Statistically significant difference: [a] - p≤0.01, [b] - p≤0.001.

Table 4. Intercorrelations (r – coefficient of correlation) of pairs of the Al, B, Ba, Br, Ca, Cu, Fe, K, Li, Mg, Mn, Na, P, S, Si, Sr, and Zn mass fractions in normal prostate tissue.

Element	**B**	**Ba**	**Br**	**Ca**	**Cu**	**Fe**	**K**	**Li**
Al	0.07	0.61	-0.23	0.28	0.151	-0.47	0.69	0.30
B	**1.00**	-0.27	0.08	-0.15	-0.35	0.22	-0.39	-0.68
Ba	-0.27	**1.00**	0.04	0.43	0.36	0.08	0.58	0.15
Br	0.08	0.04	**1.00**	-0.36	-0.40	0.16	-0.23	-0.31
Ca	-0.15	0.43	-0.36	**1.00**	0.45	0.04	0.01	-0.23
Cu	-0.35	0.36	-0.40	0.45	**1.00**	-0.17	0.01	0.20
Fe	0.22	0.08	0.16	0.04	-0.17	**1.00**	-0.08	-0.20
K	-0.39	0.58	-0.23	0.01	0.01	-0.08	**1.00**	0.59
Li	-0.68	0.15	-0.31	-0.23	0.20	-0.20	0.59	**1.00**
Mg	-0.46	0.32	-0.47	0.57	0.41	-0.37	0.55	0.48
Mn	0.14	0.59	0.34	0.10	-0.12	0.35	0.06	-0.07
Na	-0.16	-0.15	-0.11	-0.25	0.18	-0.13	0.26	0.59
P	0.34	0.50	-0.04	-0.14	-0.22	0.30	0.75[a]	0.44
S	-0.02	0.35	-0.16	-0.17	-0.23	0.07	0.85[b]	0.60
Si	-0.25	0.39	-0.31	0.07	-0.16	-0.12	0.92[b]	0.53
Sr	0.13	0.29	0.32	0.35	0.16	0.03	0.54	0.10
Zn	-0.35	0.62	0.03	0.28	0.51	-0.14	-0.08	-0.10
Element	**Mg**	**Mn**	**Na**	**P**	**S**	**Si**	**Sr**	**Zn**
Al	0.62	0.12	-0.15	0.69	0.53	0.75[a]	0.10	0.27
B	-0.46	0.14	-0.16	0.34	-0.02	-0.25	0.13	-0.35
Ba	0.32	0.59	-0.15	0.50	0.35	0.39	0.29	0.62
Br	-0.47	0.34	-0.11	-0.04	-0.16	-0.31	-0.32	0.03
Ca	0.57	0.10	-0.25	-0.14	-0.17	0.07	0.35	0.28
Cu	0.41	-0.12	0.18	-0.22	-0.23	-0.16	0.16	0.51
Fe	-0.37	0.35	-0.13	0.30	0.07	-0.12	0.03	-0.14
K	0.55	0.06	0.26	0.75[a]	0.85[b]	0.92[b]	0.54	-0.08
Li	0.48	-0.07	0.59	0.44	0.60	0.53	0.10	-0.10
Mg	**1.00**	-0.17	0.38	0.22	0.45	0.63	0.40	0.04
Mn	0.17	**1.00**	-0.21	0.56	0.27	-0.01	-0.18	0.61
Na	0.38	-0.21	**1.00**	0.19	0.32	0.15	0.31	-0.20
P	0.22	0.56	0.19	**1.00**	0.93[b]	0.73[a]	0.34	-0.02
S	0.45	0.27	0.32	0.93[b]	**1.00**	0.89[b]	0.36	-0.18
Si	0.63	-0.01	0.15	0.73[a]	0.89[b]	**1.00**	0.46	-0.22
Sr	0.40	-0.18	0.31	0.34	0.36	0.46	**1.00**	-0.32
Zn	0.04	0.61	-0.20	-0.02	-0.18	-0.22	-0.32	**1.00**

Statistically significant difference: [a] - p≤0.01, [b] - p≤0.001.

Table 5. Intercorrelations (r – coefficient of correlation) of pairs of the Al, B, Ba, Br, Ca, Cu, Fe, K, Li, Mg, Mn, Na, P, S, Si, Sr, and Zn mass fractions in BPH tissue.

Tissue	Element	Published data [Reference]			This work result
		Median of means (n^a)	Minimum of means M or M±SD, (n^b)	Maximum of means M or M±SD, (n^b)	M±SD
Normal	Al	34.0 (9)	13±66 (50) [16]	80±98 (16) [9]	34±18
	B	0.97 (8)	<0.47 (50) [16]	5.9±17.2(16) [9]	1.04±0.86
	Ba	1.75 (9)	0.1 (50) [16]	102±82 (10) [17]	1.54±1.00
	Br	30.0 (14)	14±9 (4) [18]	50±32 (10) [19]	34±18
	Ca	1990 (20)	427±117 (21) [20]	7500±12300 (57) [21]	2437±1255
	Cu	9.6 (27)	1.37 (-) [22]	1488±47 (10) [23]	9.9±4.8
	Fe	118 (30	5.7±0.1 (5) [24]	1224±76 (10) [23]	132±39
	K	11800 (18)	4360±70 (27) [25]	13000±660 (16) [6]	11574±2346
	Li	0.041 (6)	0.040±0.024 (64) [26]	0.064±0.049 (16) [9]	0.043±0.027
	Mg	1120 (19)	498±172 (13) [21]	2056±476 (21) [20]	1078±415
	Mn	1.48 (21)	<0.47 (12) [27]	106±18 (5) [28]	1.30±0.42
	Na	10500 (14)	23±26 (13) [21]	13700±3500 (4) [29]	11012±2191
	P	7120 (14)	2060±690 (13) [21]	11600 (12) [27]	7617±1879
	S	8810 (5)	5300±750 (57) [21]	9040±990 (10) [30]	8632±1292
	Si	100 (5)	51 (1) [31]	111±64 (64) [26]	100±56
	Sr	1.46 (11)	0.75±0.09 (48) [16]	2.61±3.07(27) [32]	2.4±1.9
	Zn	525 (71)	101 (1) [33]	3218±41 (10) [23]	1094±971
BPH	Al	-	-	-	24±10
	B	-	-	-	1.51±0.79
	Ba	-	-	-	1.22±0.68
	Br	23.3 (2)	18±9 (27) [25]	21.5±13 (9) [34]	31±17
	Ca	3100 (6)	1000 (34) [35]	5100±3200 (9) [36]	2032±547
	Cu	15 (12)	3±1 (7) [37]	885±80 (10) [23]	9.9±4.0
	Fe	197 (10)	5.9±0.4 (8) [24]	1345±95 (27) [25]	131±66
	K	7400 (5)	1010±100 (27) [25]	12800±1900 (43) [38]	14471±2454
	Li	-	-	-	0.039±0.024
	Mg	820 (7)	566±130 (25) [39]	1560±50 (10) [40]	1201±276
	Mn	9 (4)	6.5 (-) [41]	23±13 (27) [25]	1.19±0.31
	Na	7800 (1)	7800 (34) [35]	7800 (34) [35]	11612±2882
	P	7600 (3)	7590±1120 (43) [38]	19300±14300 (9) [36]	7907±1385
	S	37400 (1)	37400±2100 (9) [36]	37400±2100 (9) [36]	8787±1616
	Si	-	-	-	141±79
	Sr	4.4 (2)	3.8±0.6 (43) [34]	5.0±3.0 (10) [19]	3.7±1.8
	Zn	725 (39)	55±25 (23) [42]	3218±41 (10) [23]	1297±119

M arithmetic mean, *SD* standard deviation, "–"no data, ^{a} Number of all references, ^{b} Number of samples.

Table 6. Median, minimum and maximum value of means of the Al, B, Ba, Br, Ca, Cu, Fe, K, Li, Mg, Mn, Na, P, S, Si, Sr, and Zn mass fractions (mg/kg, on dry mass basis) in BPH and normal prostate glands of adults according to data from the literature in comparison with our results.

Discussion

The INAA-SLR and ICP-AES allowed determine the mean mass fractions of 6 (Br, Ca, K, Mg, Mn, and Na) and 16 (Al, B, Ba, Ca, Cu, Fe, K, Li, Mg, Mn, Na, P, S, Si, Sr, and Zn) trace elements, respectively, in the tissue samples of BPH and normal prostate glands. Thus, the use two analytical methods one by one allowed us to estimate the mass fractions of 17 trace elements. Moreover, good agreement was found between the mean values of the Ca, K, Mg, Mn, and Na mass fractions determined by both INAA-SLR and ICP-AES indicating complete digestion of the prostate tissue samples (for ICP-AES techniques) and correctness of all results obtained by the two methods. The fact that the elemental mass fractions (M±SD) of the certified reference materials obtained in the present work were in good agreement with the certified values and within the corresponding 95 % confidence intervals [8,30] suggests an acceptable accuracy of the measurements performed on the prostate tissue samples.

In the hyperplastic prostates, we have observed an increase in mass fraction of B, K, Mg, Si, Sr and Zn in comparison with the histologically normal prostates (Tables 1 and 2). However, a significant higher level of K ($p<0.0036$) and Sr ($p<0.035$) mass fraction was only found in BPH tissue (Table 2). For example, in prostate glands of patients with BPH the K mass fraction was 25% greater than in controls. It is well known that K is the major action of the intracellular fluid and also that cells are the main pools of this electrolyte in human body [51]. Thus, because the major characteristic of BPH is an overgrowth of the prostatic cells, becomes clear why an increase in the prostatic K mass fraction has respect to a hyperplastic transformation. The real reason behind the high level of Sr mass fraction in BPH tissue requires further study for a more complete understanding.

No statistically significant differences between the mean values of all other chemical element mass fractions determined in this study (Al, B, Ba, Br, Ca, Cu, Fe, Li, Mg, Mn, Na, P, S, Si, and Zn) for BPH and normal prostates were found (Table 2). This finding agrees well with data of some other known studies for Ca, Fe, Mg, Na, and Zn [23,35,38,39].

In our previous publications [26,30, 52-55] it was shown that in the histologically normal prostates of males in the sixth to ninth decades, the magnitude of chemical element mass fractions were maintained at near constant levels. No age-related differences in chemical element mass fraction in the hyperplastic prostate glands of men aged from 56 to 78 years were found in this study (Table 3).

In normal prostate glands a statistically significant direct correlation was found, for example, between the prostatic Zn and Mg ($r = 0.53$), and Zn and P ($r = 0.85$), between the prostatic Mg and Na ($r = 0.52$), Mg and P ($r = 0.71$), Mg and S ($r = 0.55$), and Mg and Zn ($r = 0.53$), between the prostatic Ca and Br ($r = 0.58$), and also Ca and Sr ($r = 0.60$), between the prostatic K and S ($r = 0.67$), between the prostatic Si and Al ($r = 0.68$), and between the prostatic Sr and Br ($r = 0.60$) (Table 4). If some positive correlations between the elements were predictable (e.g., Ca–Sr), the interpretation of other observed relationships requires further study for a more complete understanding.

In BPH tissue significant correlations between chemical elements found in the control group are no longer evident, for example, correlations for pairs with Zn, Mg, Ca, correlation between K and S, etc. (Table 5). Thus, if we accept the levels and relationships of chemical element mass fraction in prostate glands of males in the control group as a norm, we have to conclude that with a hyperplasia the levels and relationships of chemical elements in prostate significantly changed. No published data referring to correlations between chemical elements mass fractions in hyperplastic prostate tissue were found.

The obtained values for Al, B, Ba, Br, Ca, Cu, Fe, K, Li, Mg, Mn, Na, P, S, Si, Sr, and Zn mass fractions in intact and histologically normal prostate tissue, as shown in Table 6, agree well with median of means cited by other researches for the non-hyperplastic prostate glands of adult males, including samples received from persons who died from various diseases. For BPH tissue the means for Br, K and Na are somewhat higher than the maximum mean value of previously reported data. The means of this work for Mn and S are almost 5 times lower, than previously reported minimal results. No published data referring to Al, B, Ba, Li, and Si mass fractions in BPH tissue were found.

Conclusion

This work revealed that there are the significantly elevated levels of K and Sr mass fractions in hyperplastic prostates in comparison with those in the histologically normal prostates. In the sixth to eighth decades the mass fractions of all chemical elements investigated in BHP tissue were maintained at approximately stable levels. Our finding of correlation between pairs of prostatic chemical element mass fractions indicates that there is a great disturbance of prostatic chemical element relationships with a hyperplasia of prostate tissue.

However, our data also revealed that there are no any differences between Zn, Ca, Mg, Fe and Cu mass fraction in the prostate tissue of healthy individuals and patients with BPH. Thus, the potential role of age-related Zn, Ca, Mg, Fe, and Cu deficiency in the prostate has not been confirmed as being involved in the etiology of BPH. Moreover, our findings cast doubts on a beneficial effect of the Zn, Ca, Mg, Fe, and Cu supplementations on BPH prevention and treatment.

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