



A Systematic Review of the Trace Element Concentrations in the Prostate Fluid of Normal Gland

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Abstract

Background: The prostate gland is subject to various disorders. The etiology and pathogenesis of these diseases are not well understood. Moreover, despite technological advancements, the differential diagnostics of prostate disorders has become progressively more complex and controversial. It was suggested that the measurement of Trace Elements (TEs) levels in Expressed Prostatic Fluid (EPF) may be useful as a biomarker. This suggestion promoted more detailed studies of the TEs concentrations in the EPF of healthy subjects.

Objective: The present study evaluated by systematic analysis the published data for concentration of TEs analyzed in EPF of normal gland.

Methods: The present systematic analysis included 1885 studies, all of which were published in the years from 1942 to 2019 and selected by searching the databases Scopus, PubMed, MEDLINE, ELSEVIER-EMBASE, Cochrane Library, and the Web of Science. The articles were analyzed and "Median of Means" and "Range of Means" were used to examine heterogeneity of TE concentrations in EPF of apparently healthy men. The objective analysis was performed on data from the 26 studies, with about 900 subjects.

Results: The median of concentration means for such TEs as Bromine (Br), Cadmium (Cd), Coper (Cu), Iron (Fe), Rubidium (Rb), Strontium (Sr), and Zinc (Zn) in EPF of apparently healthy men were (mg/L): Br-2.86, Cd-0.146, Cu-0.416, Fe-8.3, Rb-1.13, Sr-1.22, and Zn-501.

Conclusion: The study has demonstrated that the human prostatic secretion is a target fluid of human body for Cd, Fe, Sr, and Zn. Because of small sample size and high data heterogeneity, we recommend other primary studies.

Keywords: Prostate; Prostatic fluid; Biomarkers; Trace elements; Bromine; Cadmium; Coper; Iron; Rubidium; Strontium; Zinc

Abbreviations : PSA: Prostate-specific antigen; Zn : Zinc; Rb: Rubidium; TE: Trace Element; EPF : Expressed Prostatic Fluid; Cd : Cadmium; Cu : Coper; Fe : Iron; Sr : Strontium; FES : Flame Emission Spectrophotometry; AAS : Atomic Absorption Spectrophotometry; EDXRF : Energy Dispersive X-ray Fluorescent Microanalysis

Introduction

The prostate gland is subject to various disorders and of them chronic prostatitis, benign prostatic hyperplasia, and prostate cancer are the extremely common diseases of ageing men [1-3]. The etiology and pathogenesis of these diseases are not well understood. Moreover, despite technological advancements, the differential diagnostics of prostate disorders has become progressively more complex and controversial. This is particularly concerned with prostate cancer where the limitations and potential harms associated with the use of Prostate-Specific Antigen (PSA)

as a diagnostic marker. The situation stimulates significant investigation of numerous novel biomarkers that demonstrate varying capacities to detect prostate cancer and can decrease unnecessary biopsies [4].

In our previous studies the significant involvement of Zinc (Zn), Rubidium (Rb) and some other Trace Elements (TEs) in the normal physiology of the prostate was found [5-30]. It was also found a great deformation of TE concentrations in affected prostate and was demonstrated that the changes of some TEs content, as well

as levels of some TE ratios in the prostate tissue can be used as the biomarkers of prostate diseases [31-41] and global environmental contamination [42]. Moreover, it was shown that levels of some TEs in prostate tissue play a very important role in carcinogenesis of the gland [43-45].

One of the main functions of the prostate gland is the production of prostatic fluid [46]. It contains a high concentration of Rb, Zn and some other TEs, in comparison with levels in blood serum and other human body fluids. The first finding of remarkably high levels of Zn in human Expressed Prostatic Fluid (EPF) was reported in the early 1960s [47]. After analyzing EPF expressed from the prostates of 8 apparently healthy men, aged 25-55 years, it was found that Zn concentrations varied from 300 to 730 mg/L. After this finding several investigators suggested that the measurement of Zn levels in EPF may be useful as a marker of abnormal prostate secretory function [48,49]. This suggestion promoted more detailed studies of the TEs concentrations in the EPF of healthy subjects and in those with different prostatic diseases, including prostate cancer [49-70].

TEs are vital for the normal functioning of the human body [71]. For example, Zn is an essential nutritional TE, especially in terms of proteins and nucleic acids metabolism. It is required for the catalytic activity of at least 300 enzymes, and is involved in the human immune system, in tissue repair, and in DNA syntheses. There are a lot of data on the subject. However, the exact role of Zn and other TEs in normal and pathophysiology of the prostate is until now unknown. Several studies have reported the TEs contents in EPF of normal and affected gland [47-56,72-85]. However, further investigation has been considered necessary to provide clearer hypothesis about the role of TEs in etiology and pathogenesis of prostate disorders, because the findings of various studies indicate some discrepancies.

The present study addresses the significance of prostatic fluid TEs levels as biomarker. Therefore, we systematically reviewed the available literature and performed a statistical analysis of TEs concentrations in EPF of normal gland, which may shed valuable insight into the etiology and diagnosis of prostate disorders.

Results

Table 1: Reference data of trace element concentrations in human prostatic fluid (mg/L).

Element	Reference	Meth.	n	Age	M±SD	Range*
Br	Zaichick et al. (2016) [52]	EDXRF	51	18-82	3.58±3.31	0.16-10.0
	Zaichick Zaichick (2018) [53]	EDXRF	13	18-40	6.35	-
			38	41-82	2.86	-
	Zaichick Zaichick (2018) [54]	EDXRF	42	31-75	2.81±2.88	0.490-8.53
	Zaichick Zaichick (2018) [55]	EDXRF	38	41-82	2.86±2.93	0.490-8.53
Zaichick Zaichick (2018) [56]	EDXRF	38	41-82	2.86±2.93	0.490-8.53	
Cd	Mo et al. (2000) [83]	ICP-AES	25	57.4±6.8	0.146	0.120-0.176
Cu	Mo et al. (2000) [83]	ICP-AES	25	57.4±6.8	0.416	0.354-0.473

Materials and Methods

Data sources and search strategy

Aiming at finding the most relevant articles for this review, a thorough comprehensive web search was conducted from Scopus, PubMed, MEDLINE, ELSEVIER-EMBASE, Cochrane Library, and the Web of Science databases between 1942 to November 2019, using the key words: trace element concentration, expressed prostatic fluid, and their combination. For example, the search terms for such TE concentration as Zn were: 'zinc concentration', 'Zn concentration', 'zinc content', 'Zn content', 'zinc level', 'Zn level', 'prostatic fluid zinc', 'prostatic fluid Zn', 'zinc of expressed prostatic fluid', and 'Zn of expressed prostatic fluid'. The language was not restricted. The titles from the search results were evaluated closely and determined to be acceptable for potential inclusion criteria. Also, references from the selected articles were examined as further search tools. Relevant studies noted in the reference lists of each selected article were also evaluated for inclusion.

Eligibility criteria

Studies were included if the control groups were healthy human males with no history or evidence of andrologia or urologic disease and TEs were detected in samples of EPF. Studies were excluded if they were case reports or reviews. Studies involving subjects that were using Zn and other TEs supplementation were also excluded.

Data extraction

A standard extraction of data was applied, and the following available variables were extracted from each paper: method of TEs determination, number and age of health persons, samples preparing, mean and median of TEs concentrations, standard deviations of mean, and range of TEs concentrations.

Statistical analysis

Studies were combined based on means of TEs concentrations in EPF. The articles were analyzed and "Median of Means" and "Range of Means" were used to examine heterogeneity of TEs concentrations. The objective analysis was performed on data from the 29 studies, with about 900 healthy subjects.

Fe	Zaichick et al. (2016) [52]	EDXRF	51	18-82	9.04±7.28	1.27-39.8
	Zaichick Zaichick (2018) [53]	EDXRF	13	18-40	12.1	-
			38	41-82	8.29	-
	Zaichick Zaichick (2018) [54]	EDXRF	42	31-75	8.29±7.49	1.27-39.8
	Zaichick Zaichick (2018) [55]	EDXRF	38	41-82	8.30±7.62	1.27-39.8
Zaichick Zaichick (2018) [56]	EDXRF	38	41-82	8.30±7.62	1.27-39.8	
Rb	Zaichick et al. (1981) [49]	EDXRF	15	-	1.11±0.57	-
	Zaichick et al. (2016) [52]	EDXRF	51	18-82	1.10±0.51	0.38-2.45
	Zaichick Zaichick (2018) [53]	EDXRF	13	18-40	0.91	-
			38	41-82	1.16	-
	Zaichick Zaichick (2018) [54]	EDXRF	42	31-75	1.15±0.51	0.376-2.45
	Zaichick Zaichick (2018) [55]	EDXRF	38	41-82	1.16±0.52	0.376-2.45
Zaichick Zaichick (2018) [56]	EDXRF	38	41-82	1.16±0.52	0.376-2.45	
Sr	Zaichick et al. (2016) [52]	EDXRF	51	18-82	≤0.76	-
	Zaichick Zaichick (2018) [53]	EDXRF	13	18-40	0.87	-
			38	41-82	1.27	-
	Zaichick Zaichick (2018) [54]	EDXRF	42	31-75	1.17±0.83	040-3.44
	Zaichick Zaichick (2018) [55]	EDXRF	38	41-82	1.27±0.84	040-3.44
Zaichick Zaichick (2018) [56]	EDXRF	38	41-82	1.27±0.84	040-3.44	
Zn	Birnbaum et al. (1961) [72]	XRF	-	-	490	-
	Mackenzie et al. (1962) [47]	XRF	8	37(25-55)	490±130	265-666
	Burgos (1974) [73]	-	-	-	47.1	-
	Marmar et al. (1975) [74]	AAS	33	-	451±215	-
	Anderson Fair (1976) [75]	AAS	15	50(30-74)	352±190	-
	Fair et al. (1976) [76]	AAS	49	52(24-76)	455±208	150-1000
	Paz et al. (1977) [77]	AAS	53	-	299±202	-
	Fair Cordonnier (1978) [78]	AAS	63	52(24-76)	455±208	-
	Homonnai et al. (1978) [79]	AAS	12	-	335±45	-
	Marmar et al. (1980) [48]	AAS	33	-	451±215	-
	Zaichick et al. (1981) [49]	EDXRF	15	-	580±183	-
	Zaneveld Tauber (1981) [80]	-	-	-	50.3	-
	Kavanagh et al. (1982) [81]	AAS	35	49.2	580	-
	Kavanagh (1983) [82]	AAS	152	-	595±222	52-1308
	Zaichick et al. (1996) [50]	EDXRF	22	49(22-75)	590±210	291-1118
	Mo et al. (2000) [83]	ICPAES	25	57.4±6.8	305	243-379
	Cai et al. (2002) [84]	AAS	22	-	220±85	-
	Gómez et al. (2007) [85]	AAS	10	44(40-62)	519±374	131-1242
	Costello Franklin (2009) [51]	EDXRF	24	-	588	-
	Zhuang et al. (2009) * [84]	AAS	20	-	802±39	-
	He et al. (2013)* [84]	AAS	40	-	825±71	-
	Zaichick et al. (2016) [52]	EDXRF	51	18-82	573±202	253-048
Zaichick Zaichick (2018) [53]	EDXRF	13	28(18-40)	501±47	-	
		38	59(41-82)	598±34	-	
Zaichick Zaichick (2018) [54]	EDXRF	42	31-75	559±204	253-948	
Zaichick Zaichick (2018) [55]	EDXRF	38	41-82	598±207	253-948	
Zaichick Zaichick (2018) [56]	EDXRF	38	41-82	598±207	253-948	

Note: M-Arithmetic Mean, SD-Standard Deviation of Mean, EDXRF-Energy Dispersive X-Ray Fluorescence, ICPAES - Inductively Coupled Plasma Atomic Emission Spectrometry, XRF-X-Ray Fluorescence, AAS-Atomic Absorption Spectrophotometry.*Data of Chinese researches taken from the review Cui, et al. (2015) [84].

A total of 1885 unduplicated studies were identified. Among them 26 studies were ultimately selected according to eligibility criteria, that investigated Bromine (Br), Cadmium (Cd), Copper (Cu), Iron (Fe), Rb, Strontium (Sr), and Zn concentrations in EPF of normal prostate (Table 1). Table 1 summarizes general data from the 26 studies. The retrieved studies involved about 900 apparently healthy subjects. The ages of subjects were available for 12 studies and ranged from 18-82 years. The information about analytical method was available for 24 studies.

Fife studies determined Br, Fe, and Sr concentration in EPF using energy dispersive X-ray fluorescence analysis (EDXRF) [52-56]. One study investigated Cd and Cu levels in EPF by inductively coupled plasma atomic emission spectrometry (ICP-AES) [83]. Method EDXRF was used in six studies for the measurement of prostatic fluid Rb contents [49,52-56]. Concentration of Zn in EPF

was determined in all 26 selected studies [47-56,72-85]. Fourteen studies determined Zn concentration by the destructive analytical methods: thirteen using Atomic Absorption Spectrophotometry (AAS) and one using ICPAES. Ten studies detected Zn concentration in EPF by the nondestructive analytical methods, such as X-ray Fluorescence Analysis (XRF, 2 studies) and EDXRF (8 studies).

Table 2 depicts the median and range of means of the Br, Cd, Cu, Fe, Rb, Sr, and Zn concentrations in normal human prostatic fluid founded in our review. Table 3 & 4 present data of Zn concentration in EPF of normal human prostates obtained by the destructive (AAS and ICP-AES) and nondestructive (XRF and EDXRF) analytical methods, respectively. Table 5 presents the differences between the mean of Br, Cd, Cu, Fe, Rb, Sr, and Zn concentration in the prostatic fluid obtained by our review and the mean of these elements in blood serum, urine, breast milk, and mixed saliva of Reference Man

Table 2: Median and range of means of trace element concentrations in human prostatic fluid.

Element	Number of References	Median of means mg/L	Range of means ($M_{min} - M_{max}$), mg/L	Ratio M_{max}/M_{min}
Br	5	2.86	2.81-6.35	2.26
Cd	1	0.146	-	-
Cu	1	0.416	-	-
Fe	5	8.3	8.29-12.1	1.44
Rb	6	1.13	0.91-1.16	1.27
Sr	5	1.22	$\leq 0.76-1.27$	>1.67
Zn	25	501	47.1 - 825	17.5

Table 3: Reference data of Zn concentration in normal prostatic fluid investigated by destructive AAS and ICP-AES methods.

Reference	Method	n	Age, years M(Range)	Zn, mg/L $M \pm SD$
Marmar, et al. (1975) [74]	AAS	33	-	451 \pm 215
Anderson, Fair (1976) [75]	AAS	15	50(30-74)	352 \pm 190
Fair, et al. (1976) [76]	AAS	49	52(24-76)	455 \pm 208
Paz, et al. (1977) [77]	AAS	53	-	299 \pm 202
Fair, Cordonnier (1978) [78]	AAS	63	52(24-76)	455 \pm 208
Homonnai, et al. (1978) [79]	AAS	12	-	335 \pm 45
Marmar, et al. (1980) [48]	AAS	33	-	451 \pm 215
Kavanagh, et al. (1982) [81]	AAS	35	49.2	580
Kavanagh (1983) [82]	AAS	152	-	595 \pm 222
Mo, et al. (2000) [83]	ICPAES	25	57.4 \pm 6.8	305
Cai, et al. (2002) [84]	AAS	22	-	220 \pm 85
Gómez, et al. (2007) [85]	AAS	10	44(40-62)	519 \pm 374
Zhuang, et al. (2009) * [84]	AAS	20	-	802 \pm 39
He, et al. (2013) * [84]	AAS	40	-	825 \pm 71
Median of means, mg/L			453	
Range of means ($M_{min} - M_{max}$), mg/L			220 - 825	
Ratio M_{max}/M_{min}			(825/220) = 3.75	

Note: M-Arithmetic Mean, SD-Standard Deviation of Mean, AAS-Atomic Absorption Spectrophotometry, ICPAES- Inductively Coupled Plasma Atomic Emission Spectrometry.

*Data of Chinese researches taken from the review Cui, et al. (2015) [84].

Table 4: Reference data of Zn concentration in normal prostatic fluid investigated by nondestructive XRF and EDXRF methods.

Reference	Method	n	Age, years M(Range)	Zn, mg/L M±SD
Birnbaum, et al. (1961) [72]	XRF	-	-	490
Mackenzie, et al. (1962) [47]	XRF	8	37(25-55)	490±130
Zaichick, et al. (1981) [49]	EDXRF	15	-	580±183
Zaichick, et al. (1996) [50]	EDXRF	22	49(22-75)	590±210
Costello, Franklin (2009) [86]	EDXRF	24	-	588
Zaichick, et al. (2016) [52]	EDXRF	51	18-82	573±202
Zaichick, Zaichick (2018) [53]	EDXRF	13	28(18-40)	501±47
		38	59(41-82)	598±34
Zaichick, Zaichick (2018) [54]	EDXRF	42	31-75	559±204
Zaichick, Zaichick (2018) [55]	EDXRF	38	41-82	598±207
Zaichick, Zaichick (2018) [56]	EDXRF	38	41-82	598±207
Median of means, mg/L			584	
Range of means ($M_{min} - M_{max}$), mg/L			490 - 598	
Ratio M_{max}/M_{min}			(598/490) = 1.22	

Note: M-Arithmetic Mean, SD-Standard Deviation of Mean, XRF-X-Ray Fluorescence, EDXRF-Energy Dispersive X-Ray Fluorescence.

Table 5: The differences between the mean of Br, Cd, Cu, Fe, Rb, Sr, and Zn concentration in the prostatic fluid and in blood serum, urine, breast milk, and mixed saliva of Reference Man (mg/L).

Element	This work	Reference Man [90-92]					Ratios			
	Prostatic fluid	Blood serum	Urine	Breast milk	Mixed saliva	1/2	1/3	1/4	1/5	
	1	2	3	4	5					
Br	2.86	4.5	6	2.5	1.5	0.64	0.48	1.14	1.91	
Cd	0.146	0.0002	0.003	<0.001	-	730	48.7	>146	-	
Cu	0.416	0.95	0.045	0.3	0.08	0.44	9.24	1.39	5.2	
Fe	8.3	1	0.15	0.45	0.61	8.3	55.3	18.4	13.6	
Rb	1.13	0.15	2.5	0.75	0.69	7.53	0.45	1.51	1.64	
Sr	1.22	0.02	0.17	0.02	0.18	61	7.18	61	6.78	
Zn	584	0.95	0.25	1.5	0.47	615	2336	389	1243	

Discussion

Samples of EPF are much more available for study than prostate tissue and can be obtained without damaging the prostate gland. Information about TEs concentrations in prostatic fluid in different prostatic diseases is of obvious interest, not only to more profoundly understand the etiology and pathogenesis of prostatic diseases, but also for their diagnosis, particularly for prostate cancer diagnostics. Thus, it dictates a need in reliable values for the TEs concentrations in the EPF of apparently healthy subjects ranging from young adult males to elderly persons. The range of means of Br concentration reported in the literature for normal EPF varies from 2.81mg/L [54] to 6.15mg/L [53] with median of means 2.81mg/L (Table 1&2).

Because the Cd and Cu levels in EPF were investigated only in one study [83] it was impossible to calculate the median and range of means for these TEs. The means presented in this study for the Ca and Cu concentrations were 0.146mg/L and 0.416mg/L, respectively. The range of means of Fe concentration reported

in the literature for normal EPF varies from 8.29mg/L [54] to 12.1mg/L [53] with median of means 8.30mg/L (Table 1&2). The range of means of Rb concentration reported in the literature for normal EPF varies from 0.91mg/L [53] to 1.16mg/L [55] with median of means 1.13mg/L (Table 1&2). The range of means of Sr concentration reported in the literature for normal EPF varies from ≤0.76mg/L [52] to 1.27mg/L [56] with median of means 1.22mg/L (Table 1&2).

The narrow ranges of means of Br, Fe, Rb, and Sr were demonstrated in the present review because all these elements were investigated only one group of researches. The other situation with the range of means was found for Zn concentration in EPF which was determined in 26 studies by different groups of researches. The range of means of Zn concentration reported in the literature for normal EPF varies widely from 47.1mg/L [73] to 825mg/L [84] with median of means 501mg/L (Table 1&2). Other words maximal value of cited means of Zn concentrations 17.5 times higher

minimal value of cited means (Table 2). As indicated above, the range of means of Zn concentration reported in the literature for normal EPF varies widely. This can be explained by a dependence of Zn content on many factors, including age, ethnicity, mass of the gland, and others. Not all these factors were strictly controlled in cited studies. However, published data allowed us to estimate the effect of age on Zn concentration in EPF of normal prostate.

In one study a significant increase in Zn concentration with increasing of age was shown by the Pearson's coefficient of correlation between age and Zn concentration in EPF [53]. According this study Zn concentration in EPF of apparently healthy men aged 41-82 years was about 20% higher than in age from 18 to 40 years. But this finding does not agree with other published data. For example, in the first quantitative XRF analysis of Zn concentration in EPF of 8 apparently healthy men aged 25-55 years no significant variation with age was recognized, despite no statistical treatment of results was done in this investigation [47]. Fair and Cordonnier [78] did not find any changes in metal level with age using AAS for Zn measurement in EPF specimens obtained from 63 normal male subjects in age from 24 to 76 years. The conclusion was followed from the level of differences between the mean Zn results for three age groups evaluated by parametric Student's t-test.

Additionally, Zn, concentration in prostatic fluid showed no age relationship in the study of Kavanagh et al. [81] when 35 specimens obtained from normal male subjects in age from 15 to 85 years were measured by AAS and the Pearson correlation between age and Zn concentration was used. It is, therefore, reasonable to assume that Zn level in EPF do not change with age or, at least, slightly increase in age above 40 years. Another and, in our opinion, leading cause of inter-observer variability was insufficient quality control of results in these studies. In many reported papers such destructive analytical methods as AAS and ICP-AES were used. These methods need in sample acid digestion under high temperature. There is evidence that by use of this treatment some quantities of TEs, including Zn, are lost [86-88].

On the other hand, TEs of chemicals used for acid digestion can contaminate the EPF samples. Thus, when using destructive analytical methods, it is necessary to control for the losses of TEs, for complete acid digestion of the sample, and for the contaminations by TEs during sample decomposition, which needs adding some chemicals. It is possible to avoid these not easy procedures using non-destructive methods. Such method as XRF and, particularly, EDXRF is a fully instrumental and nondestructive analytical tool because a drop of EPF or other biological fluid is investigated without requiring any sample pretreatment or its consumption [52,89-91]. In present study, in 14 articles Zn concentration in EPF samples was determined by the destructive analytical methods (13 articles-AAS and 1 article-ICP-AES) and in 10 articles nondestructive analytical methods were used for this purpose (2 articles-XRF and 8 articles-EDXRF).

Thus, published data allowed us to estimate the effect of acid digestion at the results of Zn determination in EPF on normal prostates (Table 3&4). In articles with destructive analytical methods the range of means for Zn concentration in EPF of normal prostates varied from 220mg/L to 825mg/L (ratio $M_{max}/M_{min}=3.75$), with median of means 453 mg/L (Table 3). The articles with nondestructive analytical methods have the rather narrow range of means for Zn concentration in EPF of normal prostates from 490mg/L to 598mg/L (ratio $M_{max}/M_{min}=1.22$), with median of means 584mg/L. Thus, median of means for Zn concentration in EPF of normal prostates obtained by destructive analytical methods is 22% lower than that obtained by nondestructive methods. It is, therefore, reasonable to conclude that the choice of analytical method and quality control of results are very important factors for using the Zn and other TEs concentration in EPF as biomarker.

The obtained median of means for Cd concentrations in EPF of normal gland was two orders of magnitude higher than mean values of the metal content in blood serum and breast milk, and about 50 times higher than in urine. The median of means for Fe concentrations in normal human prostatic fluid was at least one order of magnitude higher than mean values of the metal content in urine, breast milk, and mixed saliva, and 8 times higher than in blood serum. The median of means for Sr concentrations in normal human prostatic fluid was 60 times higher than mean values of the metal content in blood serum and breast milk, and 7.2 and 6.8 times higher than in urine and mixed saliva, respectively. The median of means for Zn concentrations in normal human prostatic fluid was at least three orders of magnitude higher than mean values of the metal content in urine and mixed saliva, and two orders of magnitude higher than in blood serum and breast milk.

Thus, the comparison of obtained data with TEs concentrations in some fluids of Reference Man demonstrated that the human prostatic secretion is a target fluid of human body for Cd, Fe, Sr, and Zn. There is some limitation in our study, which need to be taken into consideration when interpreting the results of this review. The concentrations of only seven TEs including Br, Cd, Cl, Fe, Rb, Sr, and Zn were measured in EPF. The sample size of each study was relatively small, and a total of about 900 normal controls were investigated from all 26 studies. As such, it is hard to make definitive conclusions about the clinical value of the TEs concentration in EPF as biomarker.

Conclusion

The present study is a comprehensive study regarding the determination of Br, Cd, Cl, Fe, Rb, Sr, and Zn concentration in EPF as a biomarker for the diagnostics of prostate disorders. The study has demonstrated that the human prostatic secretion is a target fluid of human body for Cd, Fe, Sr, and Zn. Because of small sample size and high heterogeneity of data for Zn, we recommend other primary studies.

Compliance with Ethical Standards

Conflicts of Interest

The authors declare that they have no financial conflicts of interest.

Ethical Statement

There have been no human or animal experiments carried out for this article.

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