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The Role of Trace Elements in Thyroid Cancers

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Abstract: Thyroid cancer is one of the most common endocrine cancers. It is known that excessive or insufficient intake of trace elements causes many diseases, including various types of cancer. This study evaluates the element concentration in thyroid tissue, nodule and serum of thyroid cancer patients. The study was conducted on 60 participants, 21 malignant and 39 benign. In thyroid tissue, nodule and serum samples obtained from malignant and benign individuals, copper (Cu), zinc (Zn), aluminum (Al), cobalt (Co), iron (Fe), nickel (Ni), silver (Ag), chromium (Cr), selenium (Se), cadmium (Cd), manganese (Mn), arsenic (As) and lead (Pb) were evaluated using ICP-MS. Nodule Pb level in the malignant group was found to be significantly higher than that of the nodule Pb in the benign group. In addition, as a result of the evaluation between nodule and tissue in the malignant and benign groups, Al and Mn were higher in the malignant group than in the nodule in the thyroid tissue; Ni, Cu and Se were found to be significantly lower. In addition, Al was higher in the benign group than the nodule in the thyroid tissue, while Ni was considerably lower ($p < 0.05$). All these results suggest that trace elements have profound roles in the etiology of thyroid cancer. © 2021 NTMS.

Keywords: Thyroid Cancer; Trace Element; Inductively Coupled Plasma-Mass Spectrometry.

1. Introduction

Although most of them are benign, thyroid gland carcinomas are the most common endocrine system malignancies. The malignancy rate in thyroid nodules is approximately 5% (1-3).

In recent years, trace element analysis has gained importance as the functions of trace elements in different fields have been found out. While the deficiency of essential trace elements causes various

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diseases, the presence of excessive amounts has a toxic effect. Again, the effects of trace elements on the human body and metabolism have determined of trace elements even more critical. For these reasons, trace element analyzes are carried out in many areas, and studies in this area continue.

Although trace elements are very low, they are directly or indirectly involved in many vital functions such as vitamin synthesis, hormone production, and cell respiration (4).

In biological systems, trace elements act as enzyme components or as catalysts in chemical reactions in cells. For this reason, it is known that excessive or insufficient intake of many elements causes many diseases, including various types of cancer. Among these metals, there are studies with the element iron (Fe) in terms of its biological functions in cancerous and normal cells in cancer biochemistry studies. The recent studies are related to the Fe element is carcinogenic due to its catalytic effect on hydroxyl radical formation, suppression of defense cells and triggering of cancer cell proliferation (5). Another study reported that blood selenium (Se) levels in some cancer patients were lower than in healthy individuals (6, 7).

Copper (Cu) and zinc (Zn) play an essential role in various biochemical reactions of the human organism. These metals are cofactors of the superoxide dismutase enzyme and significantly inhibit the initiation and progression of tumors through cell protection against substances that cause the formation of free radicals. In addition, copper takes place in this structure as a cofactor of DNA polymerase and RNA polymerase enzyme. Zinc and copper concentration ratios have been studied many times in different tumor tissues and various body fluids of different patients (8, 9).

All studies show us that element concentration should be evaluated in cancer patients. This study aimed to investigate serum, tissue, and nodule levels of elements such as Al, Cr, Mn, Fe, Co, Ni, Cu, Zn, As, Se, Ag, Cd, Pb in benign and malignant nodular thyroid diseases.

2. Material and Methods

Sixty patients who applied to Atatürk University Faculty of Medicine Research Hospital with the suspicion of thyroid cancer were included in this study. As a result of the pathological examinations of the patients participating in our study, 21 were found to be malignant and 39 to be benign. Approximately 3 mL of venous blood samples were taken from each patient and transferred to gel biochemistry tubes. The blood samples were waited for 30 minutes at the room temperature and then serum samples were separated by centrifugation at 3,500 rpm for 10 minutes. The thyroid tissues and serum samples taken from the same patients were stored in a deep freezer at -80 °C until the day of elemental analysis.

All tissue and serum samples were properly thawed on the study day. Element levels were pretreated to be measured with an ICP-MS device. The working principle of this device is that the samples in solution are sent to the ionization unit with argon (Ar) gas, and the atoms that ionized at high temperature are separated and detected in the mass spectrometer[10].

For this purpose, the samples were first grinded in the microwave oven (advanced microwave digestion system). For each sample; 0.1 ml of serum samples were taken and 2 ml of 65% HNO_3 was added. Then, 0.25 ml of 30% H_2O_2 was added. For tissue samples; After adding 2 ml of 65% HNO_3 and 0.5 ml of 30% H_2O_2 on 0.1 g tissue, it was waited for 15-20 minutes and then burned in a microwave oven at 180 ^{0}C for 20 minutes.

Standard solutions for the elements to be analyzed (Al, Cr, Mn, Fe, Co, Ni, Cu, Zn, As, Se, Ag, Cd, Pb) were prepared using 2% nitric acid solution at increasing concentrations. Calibration curves were drawn. Indium, Scandium, Germanium and Bismuth were used as internal standards to correct for deviations in the calibration curve during analysis. The milled samples diluted 1/10 times were subjected to elemental analysis in an Inductively Coupled Plasma Mass Spectrometer (ICP-MS, Agilent 7700).

2.1. Statistical analysis

Software SPSS version 21.0 (SPSS for Windows software; SPSS Inc., Chicago, IL, USA) package program was used for statistical analysis in the study. Kolmogorov-Smirnov test was applied to determine the homogeneity of the data. Mann Whitney-U test was performed because the data were not normal. Numerical variables were expressed as Median (Min - Max). The minimum criterion for statistical significance was $p<0.05$ for all comparisons.

3. Results

In table 1, nodule, tissue and serum element levels were compared in malignant and benign groups. According to the data in Table 1, it was observed that the level of nodule Pb in the malignant group was significantly higher than that of the nodule Pb in the benign group ($p<0.05$).

In table 2, the concentrations of all trace elements in the nodules and tissues of all patients were compared and it was determined that the Al element was significantly higher in the tissue compared to the nodule, and the Ni element was significantly lower in the tissue compared to the nodule ($p<0.05$).

Finally, based on the results of the evaluation of nodule and tissue element levels between the malignant and benign groups in Table 3 the Al and Mn element levels in the thyroid tissue in the malignant group were significantly higher than the nodule; Ni, Cu and Se element levels are observed to be significantly lower.

Table 1: Trace element levels of nodule, tissue and serum in malignant and benign groups.

Variables		Groups		
		MG	BG	P
		Median (Min-Max) (N:21)	Median (Min-Max) (N:39)	value
Al	Nodule(ug/g)	0.34 (0-2.07)	0.27 (0-2.05)	0.128
	Tissue(ug/g)	28.32 (0-96.47)	35.5 (0-92.45)	0.280
	Serum(ug/dL)	4.97 (1.18-7.66)	3.6 (1.48-7.8)	0.333
Cr	Nodule(ug/g)	8.3 (0.1-21.9)	8.3 (0.1-29.52)	0.805
	Tissue(ug/g)	7.1 (0.03-27.02)	7.8 (0.05-29.89)	0.595
	Serum(ug/dL)	0.82 (0.49-2.07)	0.98 (0.59-5.7)	0.056
Mn	Nodule(ug/g)	19.5 (0.05-118.22)	15.99 (0.24-1286.46)	0.467
	Tissue(ug/g)	22.22 (0-80.07)	30.74 (0.10-195.37)	0.140
	Serum(ug/dL)	0.07 (0-0.60)	0.15 (0-1.44)	0.062
Fe	Nodule(ug/g)	7824.26 (251-37188.72)	8345.65 (250-29725.12)	0.245
	Tissue(ug/g)	6269.43 (100.08-21467.45)	10360.03 (200.22-29523.42)	0.156
	Serum(ug/dL)	79.35 (7.98-201.28)	84.68 (17.37-301.95)	0.805
Co	Nodule(ug/g)	1.15 (0-8.4)	1.19 (0-5.68)	0.453
	Tissue(ug/g)	1.26 (0-3.09)	1.47 (0-6.27)	0.142
	Serum(ug/dL)	0 (0-0.33)	0.002 (0-0.112)	0.403
Ni	Nodule(ug/g)	10.73 (1.7-42.02)	10.60 (1.95-33.53)	0.793
	Tissue(ug/g)	7.55 (1.16-19.38)	7.22 (1.53-20.75)	0.934
	Serum(ug/dL)	0 (0-0)	0 (0-0)	1.000
Cu	Nodule(ug/g)	73.84 (0.21-304.03)	76.83 (0.13-259.18)	0.251
	Tissue(ug/g)	61.60 (1.28-222.45)	82.90 (1.49-354.93)	0.227
	Serum(ug/dL)	26.83 (15.32-38.23)	25.08 (11.22-37.86)	0.505
Zn	Nodule(ug/g)	2049.63 (60-15689)	2466.57 (59-13877.86)	0.725
	Tissue(ug/g)	1735.58 (500-6488.35)	2747.26 (353.26-16059.23)	0.096
	Serum(ug/dL)	52.78 (30.08-109.76)	53.25 (20-86.68)	0.680
As	Nodule(ug/g)	0.56 (0-3.54)	0.44 (0-1.34)	0.187
	Tissue(ug/g)	0.56 (0-1.86)	0.59 (0-2.15)	1.000
	Serum(ug/dL)	0.079 (0.056-0.142)	0.106 (0.056-0.128)	0.117
Se	Nodule(ug/g)	63.95 (0.36-453.7)	39.10 (0.29-293.18)	0.233
	Tissue(ug/g)	46.19 (0.27-166.74)	58.48 (5.47-483.95)	0.165
	Serum(ug/dL)	1.57 (0.83-2.42)	1.64 (0.78-2.42)	0.658
Ag	Nodule(ug/g)	0.33 (0.203-0.74)	0.28 (0.66-1.13)	0.258
	Tissue(ug/g)	0.268 (0-0.48)	0.29 (0.03-0.66)	0.680
	Serum(ug/dL)	0.135 (0.081-0.504)	0.129 (0.069-0.721)	0.505
Cd	Nodule(ug/g)	24.20 (0.004-197.34)	17.24 (0.008-161.98)	0.431
	Tissue(ug/g)	25.34 (0.01-107.88)	35.50 (0.08-196.79)	0.277
	Serum(ug/dL)	0.001 (0-0.035)	0.00 (0-0.038)	0.362
Pb	Nodule(ug/g)	5.4 (0-9.4)	4.3 (0-9.44)	0.036*
	Tissue(ug/g)	4.7 (0-7.8)	5.24 (0.02-33)	0.066
	Serum(ug/dL)	0.35 (0-2.81)	0.19 (0-3.76)	0.605

MG: Malign Group, BG: Benign Group. * $p<0.05$(statistically significant).

Table 2: Comparison of trace element levels in all nodules and tissues.

	Groups		
Variables	**Tissue(ug/g)** Median (Min-Max) (N:60)	**Nodule(ug/g)** Median (Min-Max) (N:60)	P value
Al	32.98 (0-96.47)	0.28 (0-2.07)	0.000*
Cr	7.63 (0.03-29.89)	8.39 (0.92-29.53)	0.694
Mn	23.82 (0-195.36)	17.63 (0.06-1286.47)	0.492
Fe	9490.25 (100.08-29523.42)	8047.67 (250-37188.72)	0.741
Co	1.31 (0-6.27)	1.17 (0-8.42)	0.721
Ni	7.54 (1.16-20.74)	10.67 (1.76-42.02)	0.000*
Cu	79.31 (1.28-354.93)	76.25 (0.13-304.03)	0.821
Zn	2068.95 (353.26-16059.23)	2339.82 (59-15689.01)	0.916
As	0.58 (0-2.15)	0.49 (0-3.54)	0.416
Se	48.19 (0.27-483.93)	46.67 (0.29-453.7)	0.777
Ag	0.28 (0-0.65)	0.31 (0.07-1.13)	0.287
Cd	27.29 (0.01-196.79)	19.63 (0.004-197.34)	0.817
Pb	4.98 (0-33)	4.99 (0-9.45)	0.960

* p<0.05 (statistically significant).

Table 3: The results of trace element evaluation of nodule and tissue in malignant and benign groups.

Variables		**Groups**			
		MG Median (Min-Max) (N:21)	P value	**BG** Median (Min-Max) (N:39)	P value
Al	Nodule(ug/g)	0.34 (0-2.07)		0.27 (0-2.05)	
	Tissue(ug/g)	28.32 (0-96.47)	0.00*	35.5 (0-92.45)	0.000*
Cr	Nodule(ug/g)	8.3 (0.1-21.9)		8.3 (0.1-29.52)	
	Tissue(ug/g)	7.1 (0.03-27.02)	0.720	7.8 (0.05-29.89)	0.738
Mn	Nodule(ug/g)	19.5 (0.05-118.22)		15.99 (0.24-1286.46)	
	Tissue(ug/g)	22.22 (0-80.07)	0.001*	30.74 (0.10-195.37)	0.137
Fe	Nodule(ug/g)	7824.26 (251-37188.72)		8345.65 (250-29725.12)	
	Tissue(ug/g)	6269.43 (100.08-21467.45)	0.128	10360.03 (200.22-29523.42)	0.601
Co	Nodule(ug/g)	1.15 (0-8.4)		1.19 (0-5.68)	
	Tissue(ug/g)	1.26 (0-3.09)	0.218	1.47 (0-6.27)	0.499
Ni	Nodule(ug/g)	10.73 (1.7-42.02)		10.60 (1.95-33.53)	
	Tissue(ug/g)	7.55 (1.16-19.38)	0.000*	7.22 (1.53-20.75)	0.008*
Cu	Nodule(ug/g)	73.84 (0.21-304.03)		76.83 (0.13-259.18)	
	Tissue(ug/g)	61.60 (1.28-222.45)	0.015*	82.90 (1.49-354.93)	0.175
Zn	Nodule(ug/g)	2049.63 (60-15689)		2466.57 (59-13877.86)	
	Tissue(ug/g)	1735.58 (500-6488.35)	0.059	2747.26 (353.26-16059.23)	0.171
As	Nodule(ug/g)	0.56 (0-3.54)		0.44 (0-1.34)	
	Tissue(ug/g)	0.56 (0-1.86)	0.177	0.59 (0-2.15)	0.967
Se	Nodule(ug/g)	63.95 (0.36-453.7)		39.10 (0.29-293.18)	
	Tissue(ug/g)	46.19 (0.27-166.74)	0.017*	58.48 (5.47-483.95)	0.171
Ag	Nodule(ug/g)	0.33 (0.203-0.74)		0.28 (0.66-1.13)	
	Tissue(ug/g)	0.268 (0-0.48)	0.165	0.29 (0.03-0.66)	0.801
Cd	Nodule(ug/g)	24.20 (0.004-197.34)		17.24 (0.008-161.98)	
	Tissue(ug/g)	25.34 (0.01-107.88)	0.491	35.50 (0.08-196.79)	0.765
Pb	Nodule(ug/g)	5.4 (0-9.4)		4.3 (0-9.44)	
	Tissue(ug/g)	4.7 (0-7.8)	0.662	55.24 (0.02-33)	0.760

MG: Malign Group, BG: Benign Group.* p<0.05 (statistically significant).

In the benign group, the tissue Al level was higher than the nodule, and the tissue Ni level was significantly lower ($p<0.05$). No significant difference was detected in other elements.

4. Discussion

In our study, the concentrations of elements such as Al, Cr, Mn, Fe, Co, Ni, Cu, Zn, As, Se, Ag, Cd, Pb in the serum, tissues and nodules of patients with thyroid cancer were determined and the relationships between malignant and benign tumors were investigated.

After understanding the various functions of trace elements in the organism, the deficiencies of these elements may be associated with cardiovascular system diseases, neurodegenerative diseases, carcinogenesis, and even the advisability of determining metals in the diagnosis of these pathological conditions has been confirmed in many studies in recent years (11).

The use of Pb in industry, the exploitation of natural resources and its use as a pesticide in agriculture cause environmental and food pollution. The hematopoietic system is the first to be affected by lead (12). Our study observed that Pb malign nodule levels increased significantly compared to benign nodule levels ($p<0.05$). Again, in the measurement we made in the serum samples of patients with malignant tumors, the Pb level was found to be higher than patients with benign tumors, although it was not statistically significant.

Copper is a trace element that plays a role in the biological oxidation and reduction reaction (13). Recent studies have shown that copper plays a role in both the etiology and growth of the tumor (14). In our study, Cu levels in the malignant patient group's tissues and nodules were lower than in the benign patient group. However, this decrease was not statistically significant ($p>0.05$).

In the studies carried out by Rink and Gabriel in 2000-2001, they stated that Zinc (Zn) is an essential element for normal immune system function and in the absence of Zn, function loss is seen in all immune cell types. Therefore, Zn deficiency has been shown to be effective in cancerization by causing immune dysfunction and increasing copper (Cu) absorption. In studies comparing malignant prostate tissue and normal prostate tissue, it was observed that the Zn level was 60-70% lower in malignant prostate tissue[15]. In our study, Zn levels in the serum, tissue and nodules of the malignant patient group were found to be lower than the benign patient group ($p>0.05$).

Cd activates genotoxic mechanisms such as single-strand DNA breakage and causes DNA repair inhibition (16, 17). In addition, Cd activates the protooncogene and inhibits apoptosis. Thus, it causes cancer (18). Studies on various types of cancer have shown significant relationships between cancer and Cd levels in a human who have been occupationally exposed to Cd (19). In the study of Yaman et al. on tissue samples, the Cd concentration was found to be high in malignant and benign prostate tissue, and no statistical difference and significance could be found between them (20). In our study, malignant Cd nodule was found higher than benign Cd. However, no statistical difference or significance was found between them ($p>0.05$).

The studies related to Se, relationships between cancer and Se were first identified, and it was suggested that high doses of Se are effective in the treatment of hematological tumors. However, in later studies, it was reported that high doses of Se caused cirrhosis and hepatocellular tumors in laboratory animals. The view that there is a relationship between cancer and Se was found to be significant when it was understood that Se protects macromolecules from oxidation stress and is a component of glutathione (21). In our study, Se was found to be higher in malignant nodules compared to benign nodules, but this elevation was not statistically significant. Nodule Se levels were found to be significantly higher than tissue Se levels in our malignant groups ($p<0.05$).

Msteo et al. reported that exposure to Ni might play a role in developing colon cancer by causing changes in the catalase enzyme system and antioxidant mechanisms (22). Our current study found nodule Ni levels to be significantly higher than tissue Ni levels in our malignant groups ($p<0.05$). Serum Ni levels could not be detected.

When the literature was examined, no study was found showing the trace element profile of patients with malignant and benign thyroid tumors. Finally, Al and Mn elements were significantly higher in malignant tissue than in malignant nodules; Ni, Cu and Se element levels are observed to be significantly lower in malignant tissue than in malignant nodules. The level of Al in benign tissue was higher than the benign nodule, and the level of Ni in benign tissue was found to be significantly lower than in the benign nodule.

5. Conclusions

The reported results may highlight the role of trace elements in the unexplained etiology of thyroid diseases. In addition, biochemical changes of trace elements on malignant and benign thyroid tumors can form a basis for diagnosis. We think that the trace elements will give more valuable results for the clinic by including control tissue groups from healthy individuals in the study.

Conflict of Interests

The authors approved that there is no conflict of interest.

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Author Contributions

Turkeri ON, Kurt N, Ozgeris FB and Bakan N contributed to the constructing the idea for research. Turkeri ON, Kurt N, Ozgeris FB and Bakan N

contributed to the planning the design of the work. Turkeri ON, Kurt N, Gul MA, Karadeniz E, and Akcay MN contributed to the execution of the experiments. Turkeri ON, Kurt N, Gul MA contributed to the analysis and interpretation of data. Yeni M, Karadeniz E, and Acay MN contributed to the biological materials. Turkeri ON, Kurt N, Gul MA contributed to the literature review. Turkeri ON, Kurt N, Yeni M, Ozgeris FB, Karadeniz E, and Akcay MN contributed to the critical review. Turkeri ON, Kurt N, Yeni M, Bakan N,, Karadeniz E and Akcay MN and contributed to the final approval of the version to be published.

Ethical Approval

This study was approved by the Atatürk University Faculty of Medicine Clinical Research Ethics Committee. (Dated 04.04.2016 and Number 3, Decision No. 02).

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References

1. Tan GH, Gharib H. Thyroid incidentalomas: management approaches to nonpalpable nodules discovered incidentally on thyroid imaging. *Ann Intern Med* **1997**; 126(3): 226-231.

2. Cibas ES, Ali SZ. The Bethesda System for Reporting Thyroid Cytopathology. *Thyroid* **2009**; 19(11): 1159-1165.

3. Crippa S, Mazzucchelli L, Cibas ES, Ali SZ. The Bethesda System for reporting thyroid fine-needle aspiration specimens. *Am J Clin Pathol* **2010**; 134(2): 343-344.

4. Kurt N. Türkiye' nin Doğusunda Yaşayan İntestinal Parazitli Çocuklarda Serum Çinko, Selenyum, Bakır, Magnezyum ve Demir Düzeyleri. Institute of Health Sciences, Department of Medical Biochemistry. Master Thesis. Erzurum: Ataturk University 2010.

5. Weinberg ED. The role of iron in cancer. *Eur J Cancer Prev* **1996**; 5: 19-36.

6. Z. Pawlowicz, B. A. Zachara, U. Trafikowska, et al., Blood selenium concentrations and glutathione peroxidase activities in patients with breast cancer and with advanced gastrointestinal cancer. *J Trace ElemElectol Health Dis* **1991**; 5: 275-277.

7. Kogata M, Kobayashi M, Yananura M et al., Selenium levels in malignant and normal tissues of gastroinestinal cancer patients. *J Clin Biochem Nutr* **1988**; 5: 93-101.

8. Chen MD, Song YM, Tsou CT et al., Leptin concentration and the Zn/Cu ration in plasma in women with thyroid disorder. *Biol Trace Element Res* **2000**; 75: 99-105.

9. Saner G, Baysal SV, Ünüvar E et al., Serum zinc, copper levels and copper/zinc ratios in infants with sepsis syndrome, J. Trace Elements Exp. Med. 2000; 13, 265-270.

10. Montaser A. Inductively Coupled Plasma Mass Spectrometry, 1rd ed., Wiley-VCH, USA, 1998: 1004p.

11. Golasik M, Przybyłowicz A, Woźniak A et al.. Essential metals profile of the hair and nails of patients with laryngeal cancer. *J Trace Elem Med Biol* **2015**; 31: 67-73.

12. Chiang LC, Chang JE, Wen TC. Indirect Oxidation Effect in Flectrochemical Oxidation of Landfill Leachate. *Water Research* **1995**; 29(2): 671-678.

13. Yücel, F. Arpaci, A. Özet, et al., Serum copper and zinc levels and copper/zinc ration in patients with breast cancer. *Biol Trace Elem Res* **1994**; 40: 31-38.

14. Goodman V, Brewer, G, Merajver S. Copper deficiency as an anti-cancer strategy. *Endocrinerelated Cancer* **2004**; 11(2): 255-263.

15. Costello LC, Franklin RB, TanM, Bagasra O. Zinc and prostate cancer: a critical scientific, medical, and public interest issue (United States). *Cancer Causes Control* **2005**; 16: 901-915.

16. McMurray CT, Tainer JA. Cancer, cadmium and genome integrity. *Nature Genetics* **2003**; 34: 239-241.

17. Waalkes MP. Cadmium carcinogenesis in review. *J Inorg Chem* **2000**; 79:241-244.

18. Shimada H, Shiao YH, Shibata M, Waalkes MP. Cadmium suppresses apoptosis induced by chromium. *J Toxicol Environ Health* **1998**; 54:159-168.

19. Platz EA, Helzlsouer KJ, Hoffman SC, Morris JS, Basket CK, Comstock GW. Prediagnostic toenail cadmium and zinc and subsequent prostate cancer risk. *Prostate* **2002**; 52: 288-296.

20. Celen I, Şenol F, Müezzinoğlu T. The effect of trace elements in prostate cancer. *Bull Urooncol* **2011**; 2: 27-32.

21. Koçak ÖF, Albayrak M, Özgeriş FB. Trace Elements Analysis in Cancer and Healthy Larynx Tissues by ICP-MS Method. *JIST* **2020**; 10(3): 1779-1785.

22. Msteo M, Martin B, Santos M et al. Catalase activity in erythrocytes from colon and gastric cancer patients. Influence of nickel, lead, mercury and cadmium. *Biol Trace Elem Res* **1997**; 57: 79-90.

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