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DETERMINATION OF LEAD AND CADMIUM IN THE SURFACE LAYERS OF IMPLANTS BASED ON α-Al_2O_3

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The content of lead and cadmium in the surface layers of intra-body implants based on α-Al_2O_3 and in their raw materials, was determined by extracting their aqueous solutions with 4% (v/v) acetic acid and Ringer's solution. The extracted metals in ionic form were determined electrochemically by differential pulse stripping voltammetry (DP ASV) at the hanging mercury drop electrode (HMDE). The method employed is used in optimizing the technology of preparation of impants and assessing their applicability in clinical practice.

Key words: calcium, implants, lead, surface, voltammetry

INTRODUCTION

Moders surgery utilizes a number of ceramic materials whose properties meet very well the exacting demands of modern medicine. Apart from the required mechanical properties, the products have to be chemically and biologically inactive and stable. The chemical and biological stabilities are closely related, because corrosion of the material in the medium of a live organism releases ionic and neutral components into the body system, and there is an extensive interaction between the implanted material and the organism.

The chemical and biological processes taking place "in vivo" are very poorly accessible to standard methods of analytical chemistry. The conditions of the living organism can be much more easily simulated "in vitro", and this is also the basis of the methods used so far in assessing the chemical and mechanical properties of these modern materials and products.

The evaluation of material properties of ceramic products for surgery is covered by a number of foreign standard specifications [1–8]. However, none of those is concerned with the releasing of toxic metals, such as lead and cadmium, from the surface in the medium of the living organism. The issue in question is to determine lead and cadmium in the liquid medium which is in a dynamic equilibrium with the solid phase of the ceramic implant. The problem defined in this way can be resolved under laboratory conditions by creating the system ceramic implant – aqueous extracting solution. Determination of lead and cadmium content in the surface layers of raw materials used in the manufacture of implants from sintered corundum, and in the products proper, is indispensable also from the standpoint of selecting suitable initial materials and manufacturing technology.

The Annual Book of ASTM Standards of 1991 specifies a number of extraction methods used in the evaluation of materials used in medicine: One is concerned with a procedure for preparing the certificate on analysis of metallic orthopedic endoprostheses retrieved from the bodies of patients [2], another with a procedure for a non/specific acute test of toxicity used in determining the biocompatibility of medical instruments on rabbits [3], another used in extracting plastics in media simulating the medium of the human body [4], i.e. a 0.85% to 0.95% solution of NaCl, vegetable oils (sesame and cotton) and water for injections, at temperatures of 37 ± 1°C (120 hours), 50 ± 2°C (24 hours) and 121 ± 2°C (2 hours) respectively. The sample size for this test is chosen with respect to its area, i.e. at a thickness of $\leq$ 0.5 mm, a minimum of 120 cm^2, at a thickenss of $\geq$ 0.5 mm and $\leq$ 0.1 mm, a minimum of 60 cm^2, and at a thickness of $\geq$ 1 mm, a minimum weight of 4 g. This standard and its stipulations may also be used in assessing the respective raw materials, intermediates and final products. It is employed as a reference method in the testing of plastics used in the health service.

The last extraction method listed in the Annual Book of ASTM is a non-specific test [5] for the detection of extractable substances in materials used in medicine. It consists of intravenous application to mice of extracts from the materials being tested, in an NaCl aqeous solution.

The same Annual Book likewise specifies the requirements for sintered alumina used for surgery implants, namely the minimum content of Al_2O_3 of 99.5%, and the maximum admissible content of SiO_2 of 0.1% [6]. The procedure for determining the biocompatibility of non-porous implants with respect to muscle and bone tissues is carried out "in vivo" on rabbits, rats and dogs [7]. And finally, there is the method for specifying the composition of hydroxylapatite [8] used as ceramic surgery implants, which stipulates the maximum concentration of trace elements in the initial material, i.e. hydroxylapatite.

Table I

Applicability scope of current analytical methods

Method	Concentration range (mole dm^3)
Atomic absorption spectrometry	10^{-6} to 10^{-7}
Atomic fluorescence spectrometry	10^{-7} to 10^{-8}
Neutron activation analysis	10^{-7} to 10^{-10}
Classical polarography	10^{-1} to 10^{-6}
Anodic dissolution voltammetry with hanging mercury drop electrode	10^{-7} to 10^{-9}
Anodic dissolution voltammetry with solid electrodes or surface-filter electrodes	10^{-9} to 10^{-10}

Namely, the maximum admissible contents are 3 ppm for arsenic, 5 ppm for cadmium, 5 ppm for mercury, 30 ppm for lead, and 50 ppm for the total of heavy metals.

Among the methods used in connection with medicine there is none that would specifically stipulate determination of lead and cadmium in extracts from surface layers of ceramic materials. In this connection, use can be made of the already standard method of testing the extractability of glass and ceramic vessels intended for preserving foodstuffs [9–11], as well as of the method for determining the resistance to corrosion of these materials [1]. In both instances, the methods simulate the "in vivo" conditions, where the body tissues and liquids are substituted by aqueous solutions of various electrolytes.

Another possibility was to use clinical tests with implants whose surfaces had been doped with cadmium and lead atoms. Following exposure in a living organism, the implants would be removed and the content of both metals in the surface layer established by the tracing method as ^{109}Cd (soft gamma emitter) and ^{210}Pb (soft beta emitter).

The use of extraction methods in controlling the content of these toxic compounds requires analytical methods exhibiting a large enriching factor, accuracy, precision, a very low determination limit and relative simplicity. Anodic stripping voltammetry (ASV) [16] is one of the methods meeting these requirements. A survey of the most frequently employed methods of trace analysis is given in Table I.

EXPERIMENTAL

Material of the samples

The analyses were made on two types of materials, i.e. the initial raw material, powdered α-Al_2O_3 (Sumitomo Chemical Co., Ltd., Japan), and sintered corundum products intended for clinical applications, or their parts. The initial raw material was a powder with particles 0.6 to 0.8 μm in size, free of agglomerates, with a specific surface area of 3 m^2g^{-1}, chemically 99.99% α-Al_2O_3, sintering temperature 1550–1600°C. The oval shape of the particles free of agglomerates is well discernible in Fig. 1.

The character of the sintered material is shown in Fig. 2. The mean particle size is 2.5 μm (80%), with a maximum particle diameter of 4 μm. The grain boundaries are free of any glassy phase and defects – cf. Fig. 3).

Extraction

The surface layers of the specimens were extracted with two agents to ISO 7086/1-2 [9, 10] and ČSN 72 5520 [11], using 4% (v/v) aqueous solution of acetic acid (Suprapur, Merck) in high-purity water purified by sub-boiling distillation [12]. The time of extraction was 30 days at 37 ± 2°C [4].

Table II

Composition of Ringer's solution [1]

Component (aqueous solution)	Parts by vol.
0.9% NaCl	94
1.14% KCl	4
1.22% $CaCl_2$	3
2.11% KH_2PO_4	1
3.82% $MgSO_4$	1
1.3% $NaHCO_3$	14
1 mole dm^{-3} Na_2HPO_4	13

Table III

Absorption of Pb and Cd ions in vessel walls

Value of signal after			1	5	14
			days		
Pb	$I_p (A \times 10^{-8})$	Glass	0.415	0.391	0.386
		PE	0.433	0.422	0.419
Cd		Glass	0.327	0.313	0.305
		PE	0.307	0.295	0.290

The second extraction agent was Ringer's solution [1] used in assessing the corrosion resistance of ceramic implants based on Al_2O_3. The total time of exposure to Ringer's solution was 3 months [1]. The composition of the solution having pH 7–7.4 is given in Table II.

The material to be extracted was available either in powedered form or in that of sintered products of various shapes. In both instances, it was first carefully washed with high-purity water and left in the water overnight to release surface contamination. After rinsing, the specimens were dried at 105°C to constant weight. The extraction was carried out with a volume of 20 to 60 ml of extractive agent in a thermostat against a blank experiment.

Preparation and cleaning of vessels

All of the vessels employed, including the voltammetric cells, the electrode system and the metering devices were cleaned by extraction with dilute HNO_3 (0.3 mole dm^{-3}) and with high-purity water.

In view of the literary data [13] according to which after 5 days and at pH = 5 the walls of glass vessels are virtually saturated with lead ions and after that the lead concentration is practically constant, the contents of both metals in glass and polythene vessels were monitored so as to eliminate the effect of absorption of ions in the vessel walls. As shown by the results listed in Table III, in the trace region the absorption of lead and cadmium in the walls of glass (SIMAX ČSN 70 4106) or polythene vessels is not subject to any time limit. In view of the better results obtained with high-density polythene vessels, only these were used in the extracting. The inner surface of the extraction vessels was kept in contact with high-purity water for at least 30 weeks before use.

Analysis

In determining the lead and cadmium content in the extracts obtained by differential pulse anodic stripping voltammetry (DP ASV), use was wade of the hanging mercury drop electrode (HMDE) connected to the ECM 700 electrochemical system (ZWG, Berlin). The basic electrolyte was composed of acetate buffer with a pH of 4 to 4.7.

The standard solutions of lower concentrations were prepared from stock solutions shortly before use. Thanks to the several years of use of the vessels, a steady state between the standard solutions and the internal surface of the vessels in the exchange of Pb and Cd ions was established [13].

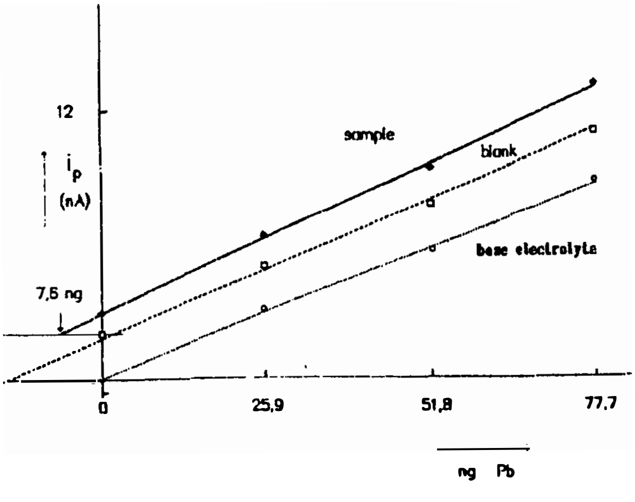

Fig. 4. Procedure of evaluating the Pb content in the measuring cell by the standard addition method.

Table IV

Lead and cadmium content in reference materials
BCR No. 176 and SRSO14-50
BCR No. 176 – City waste incineration ash

	Found) (ppm)	Relative stand. deviation (%)	Declared (ppm)	95% confidence interval
Pb	8960	19.4	10.870	+170
Cd	562	15.2	470	+9

srs014-50 – Bag house dust

	Found) (ppm)	Relative stand. deviation (%)	Declared (ppm)	95% confidence interval
Pb	1480	18.7	1914.2	21.5
Cd	411	14.5	510	9.. 3

Table V

Detection and determination limits of Pb and Cd in extractive agents

4% (v/v) acetic acid

Characterictics			Pb	Cd
Number of measurements	n		6	6
Peak current	i_p	(nA)	0.201	0.092
Standard deviation	s	(nA)	0.0466	0.0066
relative	s_r	(%)	23.2	7.2
Detection limit	$3 \times s_r$	(nA)	0.140	0.0198
Determination limit	$10 \times s_r$	(nA)	0.466	0.066
(ng of metal per 60 ml of extractive solution)			445	188

Ringer's solution

Number of measurements	n		6	6
Peak current	i_p	(nA)	0.795	0.308
Standard deviation	s	(nA)	0.0891	0.0195
relative	s_r	(%)	11.2	6.3
Detection limit	$3 \times s_r$	(nA)	0.267	0.058
Determination limit	$10 \times s_r$	(nA)	0.891	0.195
(ng of metal per 60 ml of extractive solution)			850	197

Table VI

The results of determining Pb and Cd in acetic acid extract [9–11], 4% (v/v), for $n = 6$ by the DP ASV method

Sample	Weight (g)	Volume of agent (ml)	Time of extraction (days)	Temperature (°C)
2	14.4882	60	90	37 + 2
	Pb below determination limit (i.e. 455 ng in 60 ml of extract above detection limit)		Cd below determination limit (i.e. 188 ng in 60 ml of extract above detection limit)	

Table VII

The results of determining Pg and Cd in Ringer's solution extract [1] for n = 6 by the DP ASV method

Sample	Weight (g)	Volume of agent (ml)	Time of extraction (days)	Temperature (°C)
1	19.6626	60	90	37 + 2
	Pb below determination limit (i.e. 850 ng in 60 ml of extract above the detection limit)		Cd below determination limit (i.e. 197 ng in 60 ml of extract above the detection limit)	

Blanks, precision and accuracy

The metals were quantified by using the standard addition method. The F-test [14] and the Q-test [15] were employed to optimize the parameters and evaluate the results. A diagram of the standard addition method is shown in Fig. 4 for both basic electrolytes.

The accuracy of the metal contents determination was examined by comparison with the results obtained for the BCR reference materials BCR No. 176 (City Waste Incineration Ash, Community Bureau of Reference, Brussels) and SRSO 14-50 (Bag House Dust, Fisher Scientific). The contents of the two metals as determined for n = 6 to 12, compared to the certified values, are listed in Table IV

THE RESULTS AND DISCUSSION

Standard deviation, detection limits and determination limits

A series of blank experiments were carried out to establish the standard deviation, the detection limits and determination limit. Both extractive solutions were placed in identically treated extraction vessels at 37 ± 2°C, and their content analyzed after 90 days. The results are listed in Table V.

The results indicate that both methods yield comparable values of standard deviation, not exceeding 23%. The values of the determination limit are lower and therefore more advantageous when using dilute ecetic acid as the extractive agent.

Comparison of yields of extractive agents

Both extractive solutions employed were applied to samples of sintered α-corundum of identical composition from a single manufacturing batch. The results are listed in Tables VI and VII.

The results given in Tables VI and VII do not allow to assess which of the two agents is more suitable for extraction. In view of the lower values of the determination limits, which for the given samples amounted to about 31 ng lead and 132 ng cadmium per 1 g of

Table VIII

The results obtained for the materials at various stages of technological processing

Powdered α-corundum		– 4% (v/v) acetic acid	
Weight (g)	Volume of agent (ml)	Amount of metals released by extraction* Pb (ng)	Cd (ng)
1.7680	20	below determination limit, i.e. (64)	(64)
0.1768	20	below determination limit, i.e. (640)	(206)
Dish (α-corundum)		– 4% (v/v) acetic acid	
16.4191	100	658	20
Prim (α-corundum)		– 4% (v/v) acetic acid	
1.9515	20	77	< 20

*The given values relate to 1g of extracted solid material.
The time of extraction was 30 days.

sample, dilute acetic acid appears to be more convenient. In the case of Ringer's solution, the corresponding values were 43 ng Pb and 10 ng Cd.

The results of analyses used to optimize the preparation technology

A series of analyses were carried out with the aim to contribute to the attainment of the most suitable procedures for the preparation and manufacture of surgery implants based on α-corundum. The set of results is presented in Table VIII.

The surface of the respective dish contained considerable amount of lead. Subsequent investigations showed that the specimen was fired in a furnace originally used for other purposes, among others in a study of lead crystal. It should be pointed out that the firing temperature of the corundum dish exceeded substantially the melting point of PbO, i.e. 886°C.

However, the occurrence of the unusually high lead content in the surface layer of the material allowed the two extractive solutions to be compared. The results of extracting two samples of approximately identical surface area and weight are given in Table IX.

CONCLUSION

The results given in Tables V through IX show that dilute acetic acid and Ringer's solution provide comparable results as to the yields of lead and cadmium in the surface layer of sintered powdered α-Al$_2$O$_3$. The simplest extraction system, i.e. 4% (v/v) acetic acid, exhibits a lower determination limit, easier preparation, a lower value of the standard deviation and a generally lower background. Ringer's solution, intended for determining the corrosion stability of ceramics based on Al$_2$O$_3$, attacks more their surface, thus bringing about higher yields of the two metals on extraction.

Differential pulse anodic stripping voltammetry (DP ASV) at the hanging mercury drop electrode (HMDE) is a highly sensitive method permitting, in limit cases, the determination limit of down to 7 ng Pb and 4 ng Cd per 1 ml of the extractive solution to be achieved.

Table IX

Extraction of a surface layer with a high lead content.
Time of extraction: 30 days; n = 4.

Weight (g)	Volume of agent (ml)	Total conc. of Pb in sample (ng)	Released proportion (ng Pb g^{-1})
4% (v/v) acetic acid			
1.8372	20	588	<20
1.9231	20	603	<20
2.1227	20	654	<20
2.5413	20	613	<20
Mean values (ng)^b		296	-
Rel. standard deviation^b		12.1	--
Ringer's solution			
1.7139	20	854	<20
1.8288	20	773	<20
2.0127	20	666	<20
2.4321	20	813	<20
Mean values (ng)^b		396	
Relative standard deviation^b		20.2	

[*] The given values relate to 1 g of extracted solid material.

In none of the instances did the amounts of lead and cadmium transferred into the extractive solutions by extraction exceed the limits stipulated for container glass intended for the preservation of foodstuffs [10], that is 2.5 mg Pb and 0.25 mg Cd per 1 litre of extracting agents employed.

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STANOVENÍ OLOVA A KADMIA V POVRCHOVÝCH VRSTVÁCH IMPLANTÁTŮ NA BÁZI α-Al_2O_3

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Ke stanovení obsahu olova a kadmia v povrchové vrstvě nitrotělních implantátů na bízi α-Al_2O_3 a surovin pro jejich výrobu bylo použito v souladu s postupem pro ověření korozní stability keramických implantátů na bízi Al_2O_3 [1] Ringerova roztoku o pH 7 ÷ 7,4 ISO. Celková doba působení Ringerova roztoku na zkoumaný vzorek byla 3 měsíce. Druhým extrakčním činidlem byl vodný roztok 4% (V/V) kyseliny octové podle ISO 7086/1-2 [9, 10] a ČSN 72 5520 [11]. Doba extrakce činila při teplotě 37 ± 2 °C 30 dnů.

Z výsledků uvedených v Tab. V až IX vyplývá, že zředěná kyselina octová i Ringerův roztok poskytují srovnatelné výsledky co do výtěžnosti olova a kadmia v povrchové vrstvě slinutého i práškového α-Al_2O_3. Jednodušší extrakční systém, t.j. 4% (V/V) kyselina octová, se vyznačuje nižší mezí stanovitelnosti, snazší přípravou, nižší hodnotou směrodatné odchylky, celkově nižším pozadím a nižší výtěžností extrakce oproti Ringerovu roztoku.

Diferenční pulzní anodická stripping voltametrie (DP ASV) na statické rtuťové kapkové elektrodě (HMDE) je velice citlivou metodou umožňující v limitních případech dosažení meze stanovitelnosti až 7 ng Pb a 4 ng Cd v 1 ml extrakčního roztoku.

Množství olova a kadmia převedené při extrakci do použitých extrakčních roztoků v žádném ze zkoumaných případů nepřekročilo limity uváděné pro duté sklo určené pro přechovávání potravin [10], t.j. 2,5 mg Pb a 0,25 mg Cd na 1 l použitých extrakčních činidel.

Obr. 1. Oválný tvar částic bez aglomerátů. Práškový α-Al_2O_3 (Sumitomo Chemical Co., Ltd., Japonsko). V měřítku 1 cm = 5 μm.

Obr. 2. Hranice zrn vypáleného vzorku bez skelné fáze a poruch.

Obr. 3. Průměrná velikost zrn ve vypáleném vzorku. Frakce velikosti 2,5 μm 80%. Maximální velikost zrna 4,0 μm.

Obr. 4. Postup při vyhodnocení obsahu Pb v měrné cele metodou standardních přídavků.

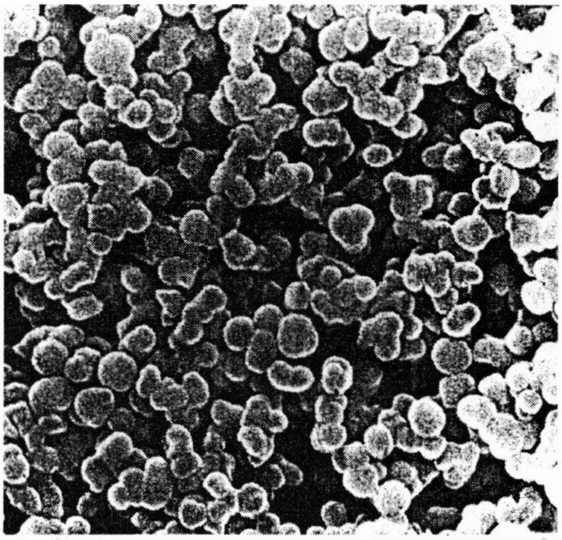

Fig. 1. Oval shape of the particles free of agglomerates. Powdered α-Al_2O_3 (Sumitomo Chemical Co. Ltd., Japan). Scale: 1 cm = 4 μm.

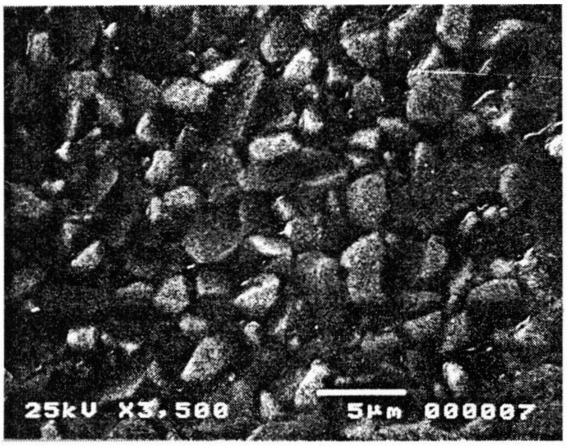

Fig. 2. Grain boundary of fired sample, free of glassy phase and defects.

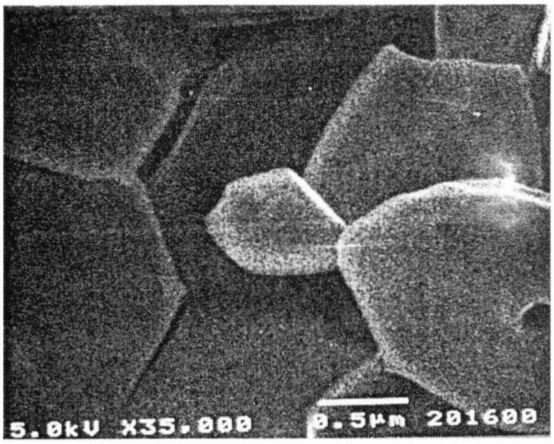

Fig. 3. The mean grain size in fired sample. 80% of fraction size 2.5 μm. Maximum grain size 4.9 μm.