

Heavy Metals in Uroliths

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Abstract

Urine concrements were studied in patients from the Donetsk region and piedmonts of the Carpathians Region. The mineral composition of concrements was studied with the help of X-ray and IR spectroscopy methods. A semiquantitative estimation of chemical trace element content of uroliths was carried out by X-ray spectral microprobe technique on a raster electron analysing microscope DS-130 C (Akashi, Japan) and a microanalyser Camebax (France). The results obtained witness to the fact that the main carriers of heavy metals in the concrements are oxalates, phosphates and amorphous organic substance. The distribution of trace elements between concrement components has a complicated pattern. The main carriers of copper, zinc, and manganese are oxalates, however, under certain conditions they may be components of phosphates. Characteristic of lead and iron is isomorphic inclusion into phosphates (apatite). To a smaller degree, they are associated with oxalates. Mercury, and partly lead, zinc, iron and manganese seem to be able to form micrograins in the form of independent phases – calomel, cerussite, hopeite, humboldtine and manganese carbonate. Partially, all heavy metals may be contained in amorphous organic substance.

INTRODUCTION

It is known that soft and hard human tissues and blood contain certain amounts of trace elements, including heavy metals which play an important role in the functioning of the organism [1, 2]. However, an excess of trace elements in the human organism over the necessary standard presents a real hazard even at the population level. It may be caused both by natural factors and by technogenous pollution of the environment which has lately reached a considerable degree and contributes to the growth of occurrence of diseases [3–7]. The increase of toxic compound content of the environment is directly associated with the increasing amount of technogenous wastes. For example, on 01.01.1996, their mass in the Russian Federation amounted to 85–90 billion, and in Ukraine, to 28 billion tons, of which no more than 12–20 % are utilized [8]. According to [8], «in separate regions of the countries in question, there are the following amounts (thousand tons) of industrial wastes per capita: in the Urals 1.9, in the Krivoy Rog Basin 4.4,

in the Donets Coal Basin 2.6, in Kazakhstan (in coal mining and metallurgical regions) 3.3–3.7. The level of technogenous load per one square kilometer in these regions (thousand tons) amounts to 43 in the Ural, 190 in the Donbas and 1300 in the Krivoy Rog Basin» (p. 66).

It is quite probable that one of the causes contributing to urolithiasis is the general environment pollution manifested in a qualitative and quantitative change of trace element content of uroliths [9]. At present, there is rather vast information about semiquantitative trace element content of concrements which are estimated with the help of spectral analysis, both taking into account, or ignoring, the mineral composition. However, the data on the trace element content obtained by means of X-ray spectral analysis in micrograins and microlayers of concrements [10–13] are rather scarce, *i. e.* the question of the form in which the trace elements exist in uroliths is still open. Besides, such analytical data can shed some light not only on the relation between the environment pollution and the concrement formation, but also on separate aspects of their genesis. For

example, according to [14], zinc, manganese, copper and other heavy metals can either contribute to formation of weddellite, or destabilize its development. Other researchers assert that zinc, copper and especially mercury contribute to dissolution of oxalates in urine [15].

OBJECTS AND METHODS

We studied concrements consisting of phosphates and oxalates (14 specimens), as well as 1 brushite, 8 urate, and 1 cystine, concrements. Three phosphate and oxalate, 4 urate, and the brushite and cystine specimens belonged to patients from the piedmonts of the Carpathians, the rest of the concrements having been surgically removed from patients from the Donetsk Region. In the piedmonts of the Carpathians, a transtechnogenous contamination by elements of the 4th toxicity group (Mn, Ba, V, Sr, Zr) is observed, while in the Donetsk Region, pollution by elements of the first three toxicity groups (1 – Pb, Zn, Be, P, Hg; 2 – Pb, Zn, Be, P; 3 – Cu, Co, Ni, Mo, Sn, Cr) takes place. However, it is noteworthy that the cities in the piedmonts of the Carpathians, as it can be seen on the example of L'vov [5], seem to be characterized by a considerable contamination of their territory by heavy metals Pb, Zn, Cu, Mn, etc.

The mineral composition of concrements was studied with the help of X-ray and IR spectroscopy. Semiquantitative assay of urolith trace element content was carried out by means of X-ray spectral microprobe technique on a raster electron analysing microscope DS-130C Akashi (Japan) and a microanalyser Camebax (France). Analyzed were polished cross-sections of uroliths for the presence of trace elements with ordinal numbers $Z > 10$ by K-, L-, and M-bands of X-ray spectra. The probe diameter was 0.12–0.5 μm .

RESULTS AND DISCUSSION

We assayed the content of heavy metals – Cu, Pb, Zn, Hg, Fe and Mn – in the uroliths studied depending on their mineral composition L and compared the results obtained with the published data on the presence of these

trace elements in uroliths of patients from various regions of Europe and Asia.

Copper

We have come across information where the authors consider the trace element content taking into account, or ignoring, the mineral composition of uroliths and of their incinerated residues. In the former case, according to the data by I. A. Flerovskiy [17], the content of this trace element in concrements from patients from the Khabarovsk Region varied from 0.0001 to 0.003 %, whereas in patients from the Novosibirsk Region [18] and Kazakhstan [19] the range of copper content is much wider and amounts to 0.0001–0.007 and 0.0001–0.003 %, respectively (Table 1). In concrements of patients from the Chelyabinsk Region, the average copper content is $(0.0039 \pm 0.0004) \%$ [9], *i. e.* the highest. Copper content of urinary bladder concrements, as one can see in Table 1, is approximately at the level of uroliths in kidneys of patients from the Novosibirsk Region and Kazakhstan, and amounts to 0.0001–0.007 and 0.0002–0.003 %, respectively [20, 21].

The occurrence of copper in uroliths is mostly high (78.0–98.04 %, see Table 1) [17, 18], however in separate cases, *e. g.* in uroliths of patients from Kazakhstan and the Magadan Region [21, 22], it is much lower and amounts to 14.8 and 44.3 %, respectively. It is noteworthy that the occurrence frequency depends on the level of the trace element content, which can be followed up on the example of analysis of uroliths of patients from Uzbekistan and Dagestan [23, 24]. In the former case there are only traces of copper, 0.001 and 0.01 %, which corresponds to occurrence of 50.0, 39.13 and 8.70 %, respectively. An approximately the same picture is observed when analyzing the concrements of patients from Dagestan where intervals of copper content of 0.001–0.003 and 0.03–0.1 % correspond to occurrence of 83.34 and 8.33 % [24].

Some authors have assayed copper content of uroliths taking into account the mineral composition. For example, according to [25], in oxalate uroliths this element has been found in four intervals of 0.0001–0.00045 and up to 0.01–0.05 %, the maximal occurrence being in the

TABLE
Trace element content of uroliths (A) assayed by a semiquantitative spectral analysis, and their occurrence (B), %

No.	Number of studied stones	Cu		Pb		Zn		Fe		Mn	
		A	B	A	B	A	B	A	B	A	B
1	20	0.0039±0.0004		0.0022±0.0003		0.0435±0.0041		0.017±0.0007		-	
2	102	0.0001-0.007	98.04	0.001-0.005	98.04	0.001-0.07	60.0	0.001-0.01	100.0	0.001-0.005	-
3	61	0.001-0.002	44.3	0.001-0.01	93.4	0.01-0.1	49.2	0.001-0.1	82.0	0.001-0.01	14.8
4	200	0.001-0.003	78.0	0.001-0.2	82.5	0.01-0.1	54.0	0.01-1.0	90.5	0.001-0.01	45.0
5	52	0.0001-0.002	94.2	0.001-1.0	88.5	0.005-0.1	26.9	-	-	0.0001-0.07	84.6
6	275	0.0001-0.003	99.3	0.0003-0.03	100.0	0.003-1.0	72.7	0.0003-0.3	98.9	0.0001-0.003	61.8
7	81	0.001-0.003	14.8	0.001-0.031	58.0	0.005-0.03	53.1	Traces	100.0	-	-
8	55	0.0002-0.003	81.8	0.000-0.03	90.9	0.003-0.3	65.5	-	-	0.0001-0.003	50.9
9	90	0.0001-0.007	81.1	Traces-0.009	12.2	0.1-0.07	31.1	Traces-0.04	91.1	0.0001-0.0003	8.9

Note. 1 — Chelyabinsk Region [9], 2 — Novosibirsk Region [18], 3 — Magadan Region [22], 4 — Khabarovsk Region [17], 5 — Tomsk [39], 6-8 — Kazakhstan [19, 21, 46], 9 — Moscow Region [20]. 1-6 — mainly kidney stones, 7 — stones of urether, 8, 9 — urine bladder stones, 1 — assayed by atomic absorption and atomic emission spectral analysis.

former, *i. e.* at the lowest content. In phosphate and urate concrements, copper has been detected at the levels of 0.0001-0.001 and 0.001-0.01 %, with respective occurrence of 90.9 and 33.3 %. Its relatively high content (0.02 %) was found in a phosphate-oxalate concrement, whereas in a phosphate one it was much lower (0.0005 %) [1]. According to [19], the proportion of copper in oxalates is somewhat higher than in phosphates — 0.0015 *versus* 0.0009 and 0.00012 %, and in urates it is 0.0007 %. It is noteworthy that the absence of information about calcium, phosphorus and magnesium content in [19] makes it impossible to specify the mineral composition of stones, in particular, urates. According to [26], copper may occur in struvite, where it substitutes magnesium. Even due to these scarce data, one may hypothesize that copper most probably is contained in oxalates and phosphates.

There is also information about this trace element content of incinerated residue of stones. For example, according to [27], the proportion of copper in the ash of concrements of patients from Kyrgyzstan varies from trace amounts to 0.05 %, whereas in similar residues of concrements of patients from Kemerovo Region and Turkmenistan, it is equal respectively to 0.001-0.05 and (0.0003 ± 0.00001) % [28, 29]. The relatively low content of this trace element in the ash of concrements from patients from Turkmenistan is probably accounted for by the fact that here prevalent are cases of disease of patients from rural localities where the environment is less contaminated by heavy metals than in industrial regions. Such a situation is reported also by I. A. Flerovsky [17].

Publications are known where the authors have made an attempt to assay the copper content of ash of concrements taking into account their mineral composition [30, 31]. According to the data of N. I. Tarasov [30], the highest copper level of struvite ash is (0.0006 ± 0.0001) %. However, taking into account the high calcium content of these stones, one may suppose that in them copper is included isomorphically in the composition of oxalates or apatite. In wevellite and urate ash, the copper content is (0.00026 ± 0.00006) and (0.0003 ± 0.0001) %, respectively. In the latter case, this is determined by the presence of phosphates

and oxalates in urates, which is confirmed by the presence of considerable amounts of Ca and P [31]. According to [31], in the ash of uroliths of patients from Germany, where the material is selected more thoroughly in the mineral aspect than in the works of previous authors, there is a clear-cut diminution of copper content (0.00438 – 0.0033 – 0.00157 %) in the series of oxalates – phosphates – urates. It is noteworthy that at a low copper content of concrement ash, this rule may be not always observed, taking into account the capacity of spectral analysis, which can be seen on the example of incinerated residues of all the mineral groups of concrements of patients from Hungary, where the copper content amounts to 0.0001–0.001 %, being the lowest among all heavy metals [32]. The low content seems to be accounted for by the same causes as in Turkmenistan.

We have assayed copper in stones of various mineral compositions. In oxalate-phosphate uroliths, it is fixed in micrograins and microlayers of 5 specimens out of 17. A relatively high content of this trace element was found in fragments of white, more seldom gray, color in specimens No. 724, 884 and 872, where it was equal to 0.2, 0.3–0.6 and 0.1–0.3 % (Table 2). In specimens No. 869 and 810, the proportion of copper was only <0.1 and traces – 0.01 %. In specimens No. 872, 724 and 884, the distribution of the trace element reflexes was close to that of calcium, whereas with phosphorus reflexes it coincided only within the limits of separate sites of the surface analyzed. Taking into account the fact that the calcium content of grains and microlayers of uroliths is higher than that of phosphorus, and the distribution of copper reflexes is closer to that of calcium, one may suppose that copper is included in the structure of oxalates. Nevertheless, its partial isomorphous presence also in apatite is not ruled out, either. It is noteworthy that the hypothesis of Cu being included in oxalates is confirmed also by the fact that in specimen No. 884, phosphorus reflexes are attached to only one edge of the microlayer analyzed, while copper reflexes are found all along the surface under study (Fig. 1). In specimen No. 869 where the spherical formations of white color consist mainly of apatite, as it can

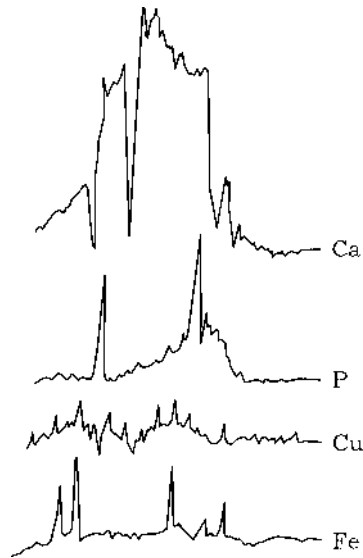


Fig. 1. Reflexes of Ca, P, Cu and Fe in a separate site of the microlayer of specimen No. 884.

be judged by Ca and P reflexes, the copper seems to be included isomorphically in its composition (see Table 2). Finally, in gray micrograins of specimen No. 810 where an insignificant Ca content has been found, copper is possibly contained either in oxalate residues or in amorphous organic substance. No copper has been found in the brushite stone.

In urate stones, the trace element was found in three specimens – No. 807₁, 817, 883 – out of eight studied (see Table 2). Its proportion in microlayers and micrograins varies from a vestigial content to 0.01 and 0.05–0.1 % (see Table 2). In specimen No. 807₁, copper reflexes are scattered all along the surface under study within the limits of the grain investigated and coincide with those of calcium, *i. e.* it is a component of oxalate, while in specimen No. 817 its reflexes coincide with those of Ca and P whose amounts are approximately equal, and the trace element is most probably present in the apatite. In specimen No. 883, the heavy metal is also scattered all along the surface studied of the microlayer of light-gray color where its reflexes coincide with those of calcium and phosphorus; however, since the content of the latter does not exceed 1.0 %, one may suppose that copper is contained in oxalates.

Our hypothesis of copper being contained in oxalates and phosphates (apatite) is confirmed by the studies carried out by L. I. Fomichev

TABLE 2

Trace element content of micrograins and microlayers of uroliths, %

No.	Peculiarities of microobjects of specimen	Ca	P	Cu	Pb	Zn	Hg	Mn	Fe
<i>Oxalate-phosphate</i>									
724	Grains of white color	10.0-40.0	1.0-3.5	0.2	0.15	-	-	Traces-0.01	Traces-0.01
824	The same	2.5	2.0	-	0.5	1.0	0.5	0.3	0.3
810	Grains of dark color	1.5	-	Traces-0.01	-	-	Traces-0.01	0.01	0.5
891	Microlayers of light and gray color	2.0-50.0	2.0-12.0	-	0.4	0.1-0.5	0.5	0.5-2.0	0.5
887	Microlayers of various shades	6.0-25.0	4.0-10.0	-	0.2-0.5	0.2-0.5	0.5-0.85	1.0-1.5	0.1-0.2
861	Grains of white color	25.0-30.0	20.0	-	0.5-0.75	-	0.5-0.7	Traces-0.01	0.25-0.5
869	Spherical formations of white color	50.0-55.0	10.0-15.0	<0.1	0.2-0.5	-	-	-	Traces-0.05
766	Microlayers of white color	10.0-15.0	1.5-2.0	-	Traces-0.01	0.01-0.5	-	-	-
877	Single gray sites	23.0-36.0	2.0-9.0	-	0.2-0.5	0.5-0.75	0.15-0.5	0.5-1.5	0.3
881	Microlayer of white color	25.0	6.0-17.0	-	0.3-0.5	-	-	>0.1	0.1
870	Microlayers of white and light brown color	10.0-15.0	0.5-2.0	-	0.1-0.5	-	-	0.1-0.15	0.2; 0.1
872	Grains of white and gray color	30.0-35.0	10.0-15.0	0.1-0.3	0.1-0.5	-	-	0.1	0.5; 0.2
772	Grains of white color	5.0-50.0	0.5-1.5	-	0.1	0.2; 0.1	>0.5	0.2	-
884	Microlayers of gray and light gray color	5.0-36.0	5.5-7.0	0.3-0.6	0.5	-	-	1.0-1.5	0.5-1.2
<i>Brushite</i>									
822	Single grains of dark color	45.0-50.0	40.0-45.0		Traces-0.01	Traces-0.01	Traces-0.01	-	Traces-0.01
<i>Urate</i>									
807 ₁	Interlayers of white color	0.1-15.0	-	Traces-0.01*	0.15	-	-	0.25	Traces-0.01
807 ₂	Grains of white color	2.5	1.0	-	-	-	0.1-0.3	1.0-1.5	0.5
885	Micrograins of white color	0.5-10.7	0.04-0.07	-	0.1-0.15	0.05-0.2	0.1	-	0.1
879	Microlayers of dark-gray color	0.1-14.0	0.05-5.0	-	0.2-0.3	0.1-0.35	0.2	0.3-1.0	0.1-0.15
813	Small grains of dark color	-	-	-	-	-	-	0.5	Traces->0.01
890	Microlayers of white color	1.5-30.0	0.8-20.0	-	0.1-0.5	-	-	0.1	0.2
817	Grains of white color	0.2	0.2	Traces-0.01	0.2	0.2	0.1-0.5	-	Traces-0.01
883	Microlayers of light gray color	8.0-30.0	1.0	0.05-0.1	1.0-1.5	0.115	0.1	0.5-0.9	-
<i>Cystine</i>									
827	Microlayers of organic substance	-	Traces-0.01	Traces-0.01	Traces-0.01	-	-	Traces-0.01	Traces-0.01

[33]. According to this author, its content is correlated with the incombustible stone residue, the coefficient of correlation being equal to 0.68 ± 0.21 . In this case, it is possible to hypothesize that the trace element is contained in the apatite structure. However, one has to note that oxalates are not decomposed when stones are incinerated, but are transformed at the temperature of $450\text{ }^{\circ}\text{C}$, according to thermal studies, into a solid carbonate phase [34, 35], *i. e.* the copper contained in them will go into the ash. In this connection, we are inclined to the conclusion that the high coefficient of correlation confirms the presence of the trace element in the structure of both oxalates and apatite (phosphates). Besides, the presence of copper in biogenic apatites is confirmed by [36–38].

In the cysteine stone, reflexes of copper are attached to organic substance where it is found, most probably, in a scattered state.

Lead

A wide range of this trace element content (0.0001–1.0 %) has been found in uroliths of patients from Tomsk [39], a smaller one is characteristic of uroliths from patients from the Khabarovsk Region (0.001–0.2 %) [17]. In concrements of patients from Kazakhstan, as compared with those from the Khabarovsk Region, the lead content is by an order lower (0.0003–0.03 %) [19]. In uroliths of patients from the Novosibirsk Region, the proportion of this trace element, as it can be seen in Table 1, has an intermediate value varying from 0.001 to 0.005 % [18]. Within the limits of (0.0022 \pm 0.00003) %, lead has been found in concrements of patients from the Chelyabinsk Region [9].

According to Table 1, the occurrence frequency of this trace element in concrements varies within a wide range, being sometimes as high as 100 % [19], while in urine bladder uroliths it may be as low as 12.2 % [20]. The occurrence of lead, like that of copper, may depend on its content in uroliths. For example, in concrements of patients from Uzbekistan its proportion amounts to 0.001 and 0.01 %, at the occurrence of 73.91 and 17.39 % [23]. Sometimes, such a rule may be not manifested,

which can be seen on the example of Daghستان where the content of this trace element in stones has been found in ranges of 0.001–0.003 and 0.003–0.01 % at a not high occurrence of 8.33 and 16.67 %, respectively [24].

Attempts are known to estimate the lead content taking into account the peculiarities of the mineral composition of stones. For example, according to [25], this trace element has not been found in oxalate and urate concrements, while in phosphates its content amounts to 0.001–0.001 % at the occurrence of 63.6 %. According to [1], the maximal proportion of this trace element (0.02 %) has been found in a carbonate stone; probably, this was an aragonite, since, according to [40], lead may be an isomorphic admixture only in this mineral. In one stone consisting of various minerals, including oxalates and phosphates, this heavy metal was also found, and its proportion was 0.005 % [1]. Judging by the above data, lead is most probably contained in apatite as an isomorphic admixture. According to Yu. G. Kozlovsky [19] who studied lead content of uroliths with various composition in patients from Kazakhstan, there is a rather clear-cut tendency to diminution of lead content in the series of phosphate formations (0.017 and 0.013 %) – oxalate formations (0.0025 %) and, finally, struvite and uric acid (0.00047 and 0.0005 %). However, one has to note that in struvite its proportion may be considerably higher (<0.05%), which is evidenced by [41].

Lead, like copper, has been assayed in concrement ash. For example, according to V. F. Khomenko [28], the ash of stones of patients from the Novosibirsk Region contains 0.001–0.2 % of this metal. Its relatively low content (0.002 \pm 0.0003 %) is characteristic of ash of uroliths from patients from Turkmenistan living mostly in rural localities [29]. The same tendency was pointed out by I. A. Flerovsky [17]. According to N. I. Tarasov [30], the highest lead content was found in the ash of struvite (0.0025 \pm 0.001 %) which was followed by wavellite (0.002 \pm 0.0004 %) and, finally, by uric acid (0.0015 \pm 0.0004 %). Therein, it is noteworthy that the ash studied contained a considerable amount of Ca and P, *i. e.* the initial mineral formations contained apatite which probably is not a lead carrier.

In the uroliths of oxalate-phosphate composition studied by us, lead was detected in 13 out of 14 specimens (see Table 2) where it was found in white, more seldom in gray, grains, and in microlayers. Its content varied mainly from 0.1 to 0.5 %. In white grains of specimen No. 861, the trace element content was the highest, and reached the value of 0.5–0.75 and 0.2–0.5 %, respectively. The lowest level – from vestigial to 0.01 % – was found in white microlayers of specimen No. 766. In concrement 881, on the general background of 0.15 %, single micrograins with a lead content of 0.3–0.5 % were found.

The distribution of lead reflexes along the whole surface analyzed shows that, *e. g.*, in microlayers of specimen No. 766, they coincide with those of phosphorus and calcium, *i. e.* the trace element is a component of phosphates, more exactly apatite (Fig. 2). The same picture is observed in another 4 specimens. In the remaining 8 stones examined, the lead reflexes along the whole surface analyzed partially coincide with reflexes of phosphorus and calcium, and partially only with those of calcium, which is seen in Fig. 3 on the example of concrement 877. One may hypothesize that in those sites of micrograins and microlayers where lead reflexes coincide with those of only calcium, and where those of phosphorus are absent, it is included in oxalates where it substitutes calcium. This is confirmed by the data of spectral analysis of oxalate stones [30, 32, 42]. The author of [40] admits such a substitu-

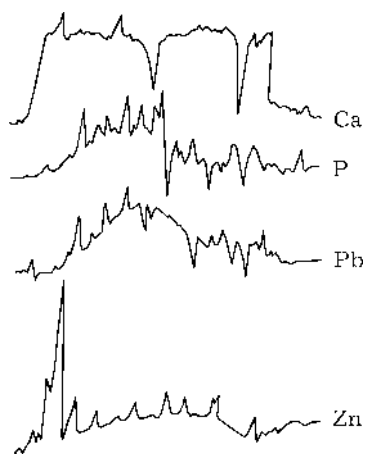


Fig. 2. Reflexes of Ca, P, Pb, and Zn in a separate site of microlayer of specimen No. 766.

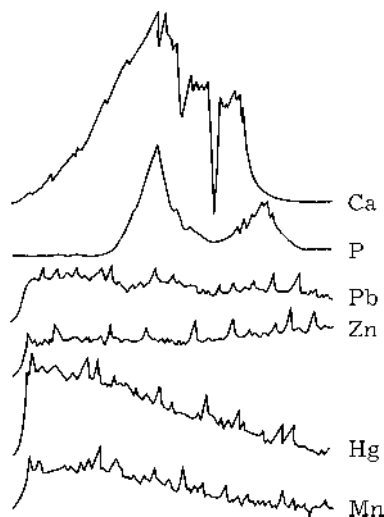


Fig. 3. Reflexes of Ca, P, Pb, Zn, Mn and Hg in a separate site of white microlayer of specimen No. 877.

tion in minerals – betaphite, vanadinite and wolfenite. These hypotheses are confirmed by the data of laser spectral analysis in separate points of a wavellite stone where a low lead concentration was found [43]. However, it is not ruled out that lead is contained at a sub-microscopic level either in carbonate (cerussite) nanograins scattered among wavellite needles, or in concomitant admixtures of organic substance. For example, the author of [33] admits the existence of Pb-containing mucopolysaccharides. In geological objects, *e. g.* in phosphorites, lead, according to V. N. Kholodov's and D. A. Mineev's [44] opinion, is also contained in the organic substance. In the amorphous organic substance of uroliths, this trace element can be concentrated, probably, due to life activity of microorganisms which take an active part in concrement formation [45]. Such a possibility has been pointed out also by V. I. Katkova [25].

In the brushite stone, the lead is present both in single dark grains and in the organic substance along the whole surface analyzed where its proportion varies from vestigial to 0.01 %. This may be accounted for by the fact that the trace element is in the organic substance in a scattered state.

Out of the 8 urate stones studied, lead was detected in 6 specimens. It was found in white or gray microlayers and micrograins of concrements. Its content of four specimens

(No. 807₁, 885, 879 and 817) was within the range of 0.1–0.3 %, while that of microlayers of specimen No. 890 reached 0.1–0.4 %, and that of specimen No. 883, 1.0–1.5 %. Analyzing the X-ray spectral data and bearing in mind that in specimens No. 879, 890 and 883 the lead reflexes along the whole surface under study coincide with those of phosphorus, we came to the conclusion that it is isomorphically included in the apatite structure. In specimen No. 807₁, in the absence of phosphorus reflexes, the lead is probably in a scattered state in the amorphous organic substance. In microlayers of light gray color of specimen No. 803, this heavy metal, judging by the distribution of phosphorus reflexes, is probably included partially in apatite, and partially in the amorphous organic substance.

In the cystine stone, lead has been found along the whole surface studied in an insignificant amount (vestigial to 0.01 %) and associated with the amorphous organic substance. In this way, this trace element is included first of all in apatite, then in oxalates, and finally in the amorphous organic substance.

Zinc

The highest level of zinc (0.003 to 1.0 %) has been detected in concrements from patients from Kazakhstan [19]. Its content is somewhat lower (0.01–0.1%) in concrements from patients from the Khabarovsk and Magadan regions [17, 22], and approximately the same in uroliths from patients from Tomsk [39]. In stones of patients from the Chelyabinsk Region, the zinc level is $(0.0435 \pm 0.0041) \%$ [9], *i. e.* within the above indicated range. In urine bladder stones, according to [46], the proportion of this trace element amounts to 0.003–0.3 % (see Table 1).

The occurrence of Zn in concrements is lower than that of lead and is within the limits of 26.9–72.7 % (see Table 1). It is noteworthy that it depends on the level of the trace element content. This can be seen on the example of concrements from patients from Uzbekistan where the proportion of Zn is 0.001, 0.01 and 0.1 % corresponds to the occurrence of 4.35, 32.61 and 8.70 %, respectively [23], *i. e.* a relatively low and a high content is found in insignificant numbers of stones. One has to note

that in uroliths from patients from Dagestan, according to [24], Zn has been detected only within the range of 0.03–0.1 %, which corresponds to the third (high) level of concrements from patients from Uzbekistan, their occurrence frequencies being almost the same – 8.33 and 8.70 %.

Like in the case of Cu and Pb, the published works contain data on Zn content, taking into account the mineral composition of stones. Thus, interesting results are presented by V. I. Katkova [25] who has estimated this trace element content of oxalate stones and found it to be 0.01–0.05 % at the occurrence frequency of 38.5 %, while in phosphate stones its proportion is 0.01–1.0 % at the occurrence of 18.2 %. It is also noted that in urate stones Zn is contained at the level of 0.001–0.01 %, which is lower than that in phosphates. The occurrence in urate stones is as high as 33.3 %, *i. e.* higher than in phosphate stones. Hence it follows that the lower the content, the higher the occurrence of the trace element of uroliths is. According to [1], the proportion of zinc in the carbonate stone was 0.05 %, while in a concrement from the mixture of minerals, including probably oxalates and phosphates, its content increased and amounted to 0.2 %. In the phosphate-oxalate and phosphate stones, this trace element, according to [1], was not detected. According to [19], in stones from patients from Kazakhstan, the highest zinc content (0.57 %) was found in apatite, a somewhat lower one (0.21 %) in apatite with oxalates, a relatively low one (0.017 and 0.08 % in oxalate and struvite, respectively, and, finally, the lowest one (0.002 %) in uric acid. It is noteworthy that the lower zinc content of struvite (<0.05 %) was found by the authors of [41]. According to [13], in wavellite the proportion of zinc is $(0.02 \pm 0.002) \%$, which almost coincides with the data of [19], whereas in wadellite its level is twice higher than in oxalate monohydrate $(0.043 \pm 0.004 \%)$. In [13], data are presented on the occurrence of zinc depending on its content in oxalates. For example, its occurrence in wavellite, at the content of 0.008–0.02 %, is 55.2 %, while as the proportion of the trace element increases to 0.032–0.05 %, it decreases to 13.8 %. The minimal zinc content (0.001–0.03 %) in wadellite corre-

sponds to the occurrence of 29.4 %, the content of 0.03–0.06 % is characterized by maximal occurrence (55.9 %), and, finally, the highest content (0.06–0.09 %) corresponds to minimal occurrence (14.7 %). In this way, the most frequently found in oxalates from patients from Hungary is an intermediate zinc content, which is in accordance with the data on Uzbekistan.

Let us consider the trace element content of incinerated residues of stones. For example, in the ash of stones from patients from Kyrgyzstan, zinc is contained at the level between vestigial and 0.3 %, at the occurrence of 23.3 % [27]. An almost the same proportion of it is in the incinerated residue of uroliths of patients from Turkmenistan, which makes up (0.3 ± 0.02) % [29], while in the residues of stones from patients from Hungary it is much lower and varies from 0.01 to 0.1 % [30]. In [47], intervals of zinc content of the incinerated residue of stones from patients from Germany were established which amount to <0.004, 0.004–0.01 and 0.01–0.02 at the occurrence of 51.0, 45.0 and 4.0 % [48], *i. e.* as the content increases, the occurrence diminishes.

Data are known on the amount of zinc in the ash of concrements from patients from Turkmenistan, taking into account their mineral composition [30]. For example, the highest zinc content (0.4 ± 0.02 %) is characteristic of struvite ash, a somewhat lower one (0.3 ± 0.07 %), of wavellite ash, and a still lower one (0.2 ± 0.03 %) is characteristic of ash of uric acid. Besides, in [31] it has been established that in the ash of stones from patients from Germany, the phosphate residue contains 0.081 % of zinc, the mixture of oxalates and phosphates 0.0613 %, pure oxalates 0.0355 %, and urates 0.006 %. These data witness to the fact that zinc most probably is first included in the composition of apatite, and then in that of oxalates. Interesting results were obtained by the author of [47] who, when estimating the Zn content, noticed that as the ash mass increased from 0–0.5 to >85.0 %, the content of this trace element increased considerably from 0.0047 to 0.073 %. These data witness to Zn being contained in phosphates, since the latter give the maximal amount of ash.

Our studies of oxalate-phosphate stones have demonstrated that zinc is contained in

microlayers and micrograins of six uroliths out of fourteen. For example, in specimen No. 772, its proportion is 0.2 %, and in specimens No. 891, 887, 766 it is as large as 0.5 %. In microfragments of concrement No. 877, the level of this trace element is still higher and varies from 0.5 to 0.75 %, and, finally, in concrement No. 824 it reaches the value of 1.0 % (see Table 2).

The most clearly zinc reflexes were observed in white grains of specimen No. 824, where they clearly correlate, along the whole surface analyzed, only with those of calcium, which witnesses to its being included in the structure of oxalates. On the example of specimen No. 766, one can see that in one site zinc reflexes coincide with those of calcium, and in another one, with those of calcium and phosphorus, *i. e.* the trace element probably participates in the structure of oxalates and phosphates (see Fig. 2). It is noteworthy that the presence of oxalates is confirmed not only by the fixation of reflexes of only calcium, but also by its considerable excess over the content of phosphorus. In specimens No. 877 and 887 (see Fig. 3), the distribution of zinc reflexes coincides with those of calcium and partly in combination of phosphorus with calcium, *i. e.* has the same pattern as in specimen No. 766. In specimens No. 772 and 891, the distribution of zinc along the whole surface analyzed coincides with that of calcium and phosphorus; however, the considerable prevalence of calcium gives reasons to hypothesize the presence of oxalate, *i. e.* zinc may be included in the structure of both oxalates and apatite. One has to underline that the presence of zinc in the apatite is confirmed by numerous studies, including experimental ones [37, 38, 49–51].

In the brushite stone (specimen No. 822), zinc was detected both in dark grains containing a considerable amount of organic substance and directly in the amorphous organic substance, in equal intervals – from vestigial to 0.01 %. One may suppose that this trace element in the objects studied is in a scattered state. It is noteworthy that the presence of zinc in the organic substance of phosphorites is confirmed by [44]. It is not ruled out that a considerable role in zinc accumulation in the organic substance is played by microorganisms

which actively participate in the formation of uroliths [25, 45].

In urate stones, zinc was detected in microlayers and micrograins of four concrements out of eight where its content varied from 0.05 to 0.35 % (see Table 2). Analysis of zinc reflexes shows that its distribution along the surface studied coincides with those of calcium and phosphorus. Taking into account the considerable prevalence of calcium content over that of phosphorus, one may suppose that zinc is preferentially included in the composition of oxalates, and then in that of phosphates. However, it is noteworthy that in specimen No. 817, along the line of analysis, several relatively strong zinc reflexes were found which coincided with those of phosphorus. It is not ruled out that in this case several micrograins of independent zinc phase – mineral hopeite, are present at the nanolevel, although, possibly, it is included also in an organophosphorous compound.

In the cystine stone, zinc was not found.

Comparing our data with the results of studies of other authors, one may conclude that, depending on the parameters of concrement formation environment, zinc will in some cases prefer oxalates, and in other cases prefer phosphates (apatite and sreurvite).

Mercury

We have not come across any information about quicksilver content of uroliths.

Mercury was found in seven of fourteen uroliths studied. Its content of white and gray microlayers of five concrements varied within the limits of 0.5–0.85 %, in specimen No. 877 it was 0.15–0.5 %, and in concrement 810 it varied from vestigial amount to 0.01 % (see Table 2).

A study of the distribution of the metal in white and gray microlayers and micrograins along the whole surface has demonstrated that in five oxalate-phosphate uroliths (specimens No. 824, 810, 887 and 772) mercury reflexes having different intensity were distributed non-uniformly. In the microlayer of specimen No. 877, on one edge the trace element content was much higher than on the opposite one (see Fig. 3), and sometimes, *e. g.* in specimen No. 891,

there was a uniform distribution of mercury within the limits of the whole field of study. Bearing in mind that the distribution pattern of mercury reflexes does not practically coincide with that of Ca and P, and the presence of chlorine ion in the urine (in healthy people its content is 0.4–0.6 % [52]), one may hypothesize that this trace element either forms nanograins of calomel, or is contained in the organic substance. The mineral's distribution in grains and microlayers of the stones studied is usually non-uniform; however, sometimes it can be uniformly scattered. Information about the quicksilver content of phosphorites, including marine ones, in the amount of 0.005–0.0055 % has been available only in two publications [53, 54].

In the brushite stone, the trace element content does not exceed 0.01 %. The character of mercury reflex distribution is the same as in oxalate-phosphate stones. Probable is either the existence of an independent phase – calomel, or its being included in the organic substance.

In urate stones, the heavy metal was detected in five specimens out of eight. In microlayers and micrograins of specimens No. 879, 883 and 885, quicksilver is present at the level of 0.1–0.2 %, in specimen No. 807₂ within the range of 0.1–0.3 %, and in stone 817 its proportion varies from 0.1 to 0.5 % (see Table 2). In three stones studied, quicksilver is characterized by a uniform distribution, and in two by a non-uniform one. It is possible that it either forms a separate independent phase, or is contained in the organic substance.

Iron

According to Table 1, the highest level of this trace element has been found in the stones of patients from the Khabarovsk Region where it amounts to 0.01–1.0 % at an occurrence of 90.5 % [17]. According to [19], the proportion of iron in concrements of patients from Kazakhstan may vary within a wide range of 0.0003 to 0.3 % at the occurrence of 98.9 %. Relatively low is the iron content of uroliths from patients from the Chelyabinsk Region [9], where its proportion is (0.017 ± 0.0007) %. In urine bladder stones, this trace element has also been

detected at a relatively low level (vestigial to 0.04 % [20]). One may hypothesize that there is a tendency to decrease of iron content in urine bladder stones.

The occurrence of iron is mostly rather high (82.0–100 %); however, according to L. I. Kuzmenko [55], it may sometimes fall down to 46.1 %. The occurrence of iron depends on its content of stones. According to [23], the proportion of this trace element in concrements of patients from Uzbekistan amounts to 0.001 and 0.01% at the occurrence of 54.35 and 36.96 %, respectively, *i. e.*, as the content increases, the occurrence decreases.

According to [24], iron content of stones from patients from Dagestan is very low, but even in this case, as it increases from 0.001–0.003 to 0.003–0.01 %, the occurrence decreases from 66.67 to 16.7 %.

Attempts to estimate the trace element content depending on the mineral composition of stones have been made. For example, according to [25], iron in oxalate stones has been detected at the level of 0.00045–0.001, 0.001–0.01 and 0.01–0.05 % at respective occurrence of 7.7, 84.6 and 7.7 %. In phosphate stones, the trace element was detected within the range of 0.001–0.01 % at the occurrence of 100 %. Finally, in urates iron was detected within the ranges of 0.0001–0.001 and 0.001–0.01 % at the occurrence of 33.3 and 50.0 %. The author of [19] also reported data on iron content of stones from patients from Kazakhstan taking into account their mineral composition. Its amount in the series phosphates – phosphates + oxalates – oxalates – urates diminishes respectively: 0.034 – 0.027 – 0.013 – 0.014 %. In the case of oxalates and especially urates, one may hypothesize that the trace element is contained as an admixture in the composition of phosphates which, as witnessed by our microscopic studies, is very often present in such stones.

Iron has been assayed also in incinerated residue of concrements from patients from the Kuznetsk Basin where its content amounted to 0.01–0.5 % [28]. According to [31], the trace element content of the ash of uroliths from patients from Germany depends on their mineral composition. The following series seems to exist: oxalates – oxalates + phosphates – phos-

phates – urates, which corresponds to iron content levels of 0.0191 – 0.0121 – 0.0084 and 0.0098 %, *i. e.* a diminution of the proportion of iron seems to take place from oxalates to urates. However, it is noteworthy that at a low trace element content (0.001–0.01 %), as it can be seen on the example of stones from patients from Hungary, it is not always possible to follow up the dependence of the content on the mineral composition, especially if one takes into account the resolution capacity of spectral analysis. On the whole, proceeding from what was told above, one may hypothesize that iron is isomorphically included in the composition of phosphates, and then oxalates.

In the oxalate-phosphate stones studied by us, the trace element was assayed in twelve specimens out of fourteen. The highest iron content (0.5–1.2 %) was recorded in gray microlayers of specimen No. 884. In eight specimens, the amount of the trace element varied from vestigial level to 0.5 %. In separate grains of specimens No. 872 and 891 the iron content attained 0.5 %, while the lowest level (from traces to 0.01 and from traces to 0.05 %) was recorded in white spherical formations of specimens No. 724 and 869.

Considering the distribution of iron reflexes along the surface studied, we came to the conclusion that reflexes of this trace element coincided with those of calcium and phosphorus, *i. e.* apatite; this can be observed especially clearly in micrograins and microlayers of specimens No. 881, 724, 824. In concrement 861, reflexes of iron coincided with those of apatite (Ca, P) and oxalate (Ca). In urolith 884, reflexes of iron and calcium (oxalate) coincided, however, bearing in mind the considerable intensity of reflexes of the former and the insignificant one of the latter, as one can see in Fig. 1, one may hypothesize that in this case the presence of a separate phase of humboldtine type is possible. In dark grains of specimen No. 810, reflexes of this trace element are not in accordance with reflexes of calcium. A conclusion comes to the mind that in this stone there is either a separate phase – humboldtine, or iron is present in the amorphous organic substance, since they are of dark color.

In separate grains of brushite stone of dark color, iron is contained within the range of

traces – 0.01 %. Its reflexes along the whole surface of the urolith are associated with the amorphous organic substance where the trace element is in a scattered state.

In urate concrements, iron was detected in seven specimens out of eight. Its content of specimens No. 817 and 807₁ varies from traces to 0.01 %, and in stone 890 it is 0.2 %. However, in specimen No. 807₂, its level is higher and attains 0.5 % (see Table 2). Reflexes of the trace element in grains and microlayers of specimens No. 807₂, 879 and 890 coincide with reflexes of phosphorus, *i. e.* iron is isomorphically included in the composition of apatite, which is confirmed by the data of many researchers who have studied apatites of both biogenic [37, 38, 49] and geological [56–59] objects. In micrograins of white color of specimen No. 817, reflexes of iron coincide with those of calcium, *i. e.* in this case one may suppose that it is included in oxalates. In stone 817, reflexes of iron along the whole surface analyzed coincide with those of either only Ca or Ca with P. This gives reasons to hypothesize its being included in the structure of oxalates and phosphates. In concrement 807₁, iron is probably contained in amorphous organic substance and partially in apatite whose presence is confirmed by insignificant reflexes of phosphorus. In urolith 813, this trace element is characterized by single rather large reflexes, which witnesses most probably to the presence of a separate humboldtine phase. However, we are not ruling out the presence of iron also in the amorphous organic substance.

In the cystine stone, the trace element has been detected (from traces to 0.01 %) in microlayers of amorphous organic substance where it is in a scattered condition.

Manganese

The level of content of this trace element, according to publications, is somewhat lower than that of iron. Its relatively high content (0.001–0.01 %) has been detected in stones from patients from the Khabarovsk Region [17, 22]. According to A. V. Golubchanskaya [18], the manganese content of stones from patients from the Novosibirsk Region is some what lower and

amounts to 0.001–0.005 %. In all the other collections, its proportion is by an order lower and varies from 0.0001 to 0.003 % or from 0.0001 to 0.07 %. Therein, there is a tendency to decrease of manganese content of urine bladder stones (see Table 1).

The occurrence of this trace element in the cases described is usually lower than that of iron (see Table 1). However, according to M. M. Kovalev [60], it may be high and amount to 97.4 %. The occurrence can depend also on the trace element content. For example, at the magnesium content of concrements from patients of Uzbekistan of about 0.001 and 0.01 %, its occurrence is 17.39 and 6.52 % [23]. In stones from patients from Dagestan, the proportion of manganese is 0.001–0.003 and 0.003–0.01 %; however, in both cases, the occurrence is 8.33 % [24], *i. e.* the indicated dependence is not observed here.

There is information about the manganese content of stones with various mineral composition. For example, according to [25], the proportion of this trace element in oxalate stones amounts to 0.001–0.01 % at the occurrence of 7.7 %, whereas in phosphate and urate concrements it is not found. According to [1], manganese content has been estimated in a phosphate and an oxalate stones at 0.5 %. According to [19], in concrements from patients from Kazakhstan with different mineral composition, its content is 0.0001–0.0003 %. In this way, it follows from what has been told that manganese is most probably isomorphically included in the composition of oxalates and phosphates.

This trace element has also been assayed in the ash of uroliths. For example, in incinerated residues of stones from patients from Kirghizstan, it has been found at the level of traces to 0.0003 %, with an occurrence of 3.3 % [27]. The level of its content is by an order higher in the ash of stones from patients from the Kuznetsk Basin (0.001–0.01 %) [28]. According to [31], there is a tendency to diminution of the proportion of manganese in the ash of the following series of uroliths: oxalates – oxalates + phosphates – phosphates – urates, which corresponds to the content of 0.00201, 0.00113, 0.00112 and 0.00056 %. Hence it follows that manganese is first of all included in the composition of oxalates.

In the uroliths studied by us this trace element turned out to be one of the most widespread ones. It has been found in twelve oxalate-phosphate stones out of fourteen. In micrograins and microlayers of three specimens, the proportion of manganese did not exceed 0.01 %, and in five specimens this trace element content amounted to 0.1–0.3 %. Relatively high (1.0–1.5 %) is its content in microfragments of specimens No. 887, 877 and 884, and finally, in 891 its content was 0.5–2.0 % (see Table 2). In specimens No. 824, 887 and 884, the distribution of manganese in grains and microlayers coincides with that of calcium, *i. e.* the trace element most probably is isomorphically included in the composition of oxalates. In micrograins and microlayers of specimens No. 724, 891, 877, 872, 861 and 870, reflexes of manganese along the whole surface studied partially coincide with those of only calcium or of phosphorus + calcium. This can be seen on the example of specimen No. 877 (see Fig. 3). One may hypothesize that this microelement is isomorphically included both in oxalates and in phosphates. In specimens No. 881 and 772, the distribution of reflexes of manganese coincides with that of calcium and phosphorus, which witnesses to its being included in the structure of apatite. It is known that manganese may occur in apatite as ions Mn^{2+} , Mn^{3+} , Mn^{7+} [44]. It has been detected in apatites of both biological [37, 38, 49, 61] and geological [59, 60, 62, 63] objects. In this way, manganese in uroliths may be found in the composition of both oxalates and phosphates.

In specimen No. 810, grains of dark color where reflexes of manganese partially coincide with those of calcium have been found, which suggests that this trace element is included not only in oxalates, but also in the accompanying amorphous organic substance. The manganese concentration in the organic substance may be determined by the life activity of microorganisms. In the brushite stone, it has not been found.

In the urate stones studied, manganese was found in six cases out of eight. The maximal content (1.0–1.5 %) was detected in micrograins of specimen No. 807₂, and in microlayers and in micrograins of specimens No. 879, 813 and 883 it was estimated at 0.3–1.0 %. In microlay-

ers of specimens No. 807₁ and 890, the proportion of manganese amounted to 0.25 and 1.0 %, respectively (see Table 2). In specimen No. 883, reflexes of manganese and calcium in light-gray layers coincided, *i. e.* the trace element was contained probably in oxalates. In specimens No. 807₁, 807₂ and 890, the distribution of reflexes of manganese along the whole surface studied was close to that of phosphorus, however, since reflexes of the latter were found only in certain sites of the surface, and its content is lower than that of calcium, one may suppose that manganese is first of all included in the composition of oxalates, and then in that of phosphates. In specimen No. 813, along the whole surface analyzed, reflexes of Ca and P have not been found, while those of manganese have. One may hypothesize that weak reflexes of the trace element witness to its being contained in the amorphous organic substance, whereas single relatively intense reflexes give reasons to suppose the presence of a separate phase of manganese carbonate contained in the form of scattered micrograins.

In the cystine stone (specimen No. 827), manganese content was estimated at the level from vestigial to 0.01 % and seems to be found in a scattered state in the amorphous organic substance.

CONCLUSIONS

Our study of the content of trace elements in uroliths and the comparison of the data obtained with those available in published sources demonstrate that the main carriers of heavy metals in concrements are oxalates and phosphates (apatite and struvite) and amorphous organic substance. The distribution of trace elements across the components of the concrements is complicated. The main carriers of copper, zinc, and manganese are oxalates; however, under certain conditions they may be included also in the composition of phosphates, mainly apatite. Characteristic of lead and iron is isomorphic inclusion in phosphates, first of all apatite followed by struvite. To a smaller degree they are contained in oxalates. Mercury, and partially lead, zinc, iron and manganese, may most probably form, at the

nanolevel, micrograins of separate phases – calomel, hopeite, cerussite, humboldtine and manganese carbonate scattered among other components. Finally, all the heavy metals may be partially contained in a scattered state in the amorphous organic substance, especially if this is formed as a result of life activity of microorganisms.

The study of trace element content of concrements from patients from the Donbas and piedmonts of the Carpathians region demonstrates that the occurrence frequencies of copper, zinc, iron, manganese and mercury in the uroliths studied almost coincide; only lead in stones of patients from the Donbas is found twice as much as in the piedmont of the Carpathians region.

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