

Comparative Characterization of the Microelement Composition of Kidney Stones from Patients in the Novosibirsk and Omsk Regions

O. A. GOLOVANOVA¹, N. A. PALCHIK², N. V. MAKSIMOVA² and A. V. DAR'IN²

¹*Omsk State University,
Pr. Mira 55a, Omsk 644077 (Russia)*

E-mail: golovanoa2000@mail.ru

²*Institute of Geology and Mineralogy, Siberian Branch of the Russian Academy of Sciences,
Pr. Akademika Koptiyuga 3, Novosibirsk 630090 (Russia)*

(Received May 26, 2006)

Abstract

The microelement composition of kidney stones in patients from the Novosibirsk and Omsk Regions is investigated. It is shown that the concentrations of elements in kidney stones depends on the mineral phase. The common feature of the kidney stones in the regions under comparison is a broad range of detected elements. It was established by comparing the collections under investigation that heavy elements are dominant in the kidney stones from the Novosibirsk Region; different contents and distribution of microelements in samples are connected with the specific character of the region.

INTRODUCTION

Urolithiasis is a widespread disease; as a mean, every hundredth person in developed countries has calculi in the urinary system; they often cause no trouble *inter vivos* and are detected only during postmortem examination [1]. Systematic investigation of urinary calculi is carried out for several decades; knowledge on the features of the composition of urinary concretions over the regions with different natural and social factors taking into account the specificity of industry-related pollution promotes revelation of the reasons of disease in each specific case [2–7]. Successful treatment of urolithiasis is impossible without taking into account the factors depicting the physicochemical conditions of formation and development of the pathology. These factors are depicted in the phase and elemental composition of concretions and, as shown recently, in their structure, in particular in the distribution of phases and elements over the calculus volume, in

the composition of the central region and in the structure of separate crystals [8–12].

The frequency of their occurrence and compositional distribution are nonuniform over different territories of the planet. The affecting factors are the specificity of local conditions (water hardness, climate *etc.*), occupation, nutrition type, and finally the ecological status of a given region [1, 10]. Because of this, the studies carried out by researchers are not only replication of the data on the nature of definite solid formations in a human organism. The accumulation of the analytical material and its generalization taking into account local conditions and the state of environment help solving an important social task – prevention and efficient treatment of the corresponding diseases.

Omsk and Novosibirsk Regions are unfavourable regions in this respect. An increase in the number of urolithiasis cases is observed in these regions during the recent years (Figs. 1, 2) [13]. The highest frequency of disease is attributed to the regions with developed industrial poten-

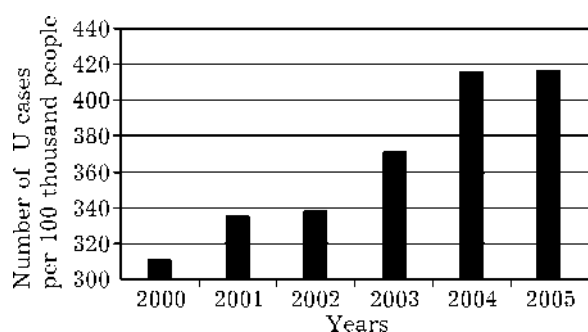


Fig. 1. Dynamics of an increase in urolithiasis (U) rate in the Omsk Region.

tial and the zones with poor quality of drinking water.

For instance, during a definite period of time, 43 patients from the industrial Leninskiy District of Novosibirsk with different localization of calculi in urinary organs were taken for treatment, while only 9 patients came from the ecologically more favourable Tsentralny District. A similar situation was also observed for the rural territory. The majority of patients suffering from urolithiasis came to the Novosibirsk Regional Hospital from ecologically unfavourable regions: Iskitim and Novosibirsk Rural Districts [9].

Omsk Region also belongs to the regions with the critical ecological situation. According to the data of the State Committee for Ecology for the years 2000–2003, Omsk belongs to the list of 33 cities with the highest level of atmospheric pollution and occupies the 7th place among the cities in the total amount of emissions from stationary sources and motor transport. Pollution of drinking water is also a problem for the Omsk Region.

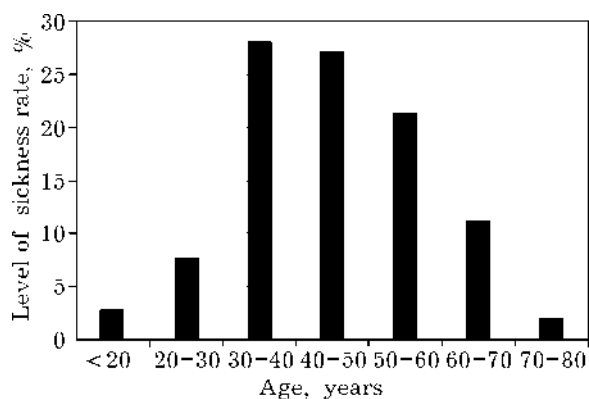


Fig. 2. Frequency of urolithiasis over age groups.

The worst situation arises in the rural regions of the Omsk Region. In public water supplies, 24.1 % of water samples do not meet the requirements of State Standard GOST 2874–82 in bacteriological indices and 42.7 % in chemical ones; in non-departmental water supplies the figures are 25.0 for bacteriological and 46.7 for chemical indices. On the basis of the data that were obtained by processing the information about the patients who were passing the course of remote lithotripsy in the Omsk Region Hospital, the regions with the highest rate of urolithiasis sickness were revealed. These regions are situated mainly in the southern part of the Omsk Region [14].

The application of the modern methods of matter investigation, including X-ray fluorescence analysis with the synchrotron radiation, provides the possibility to determine the concentrations of a number of chemical elements in the samples of biological matter with the high accuracy and to specify the features of the crystal chemistry of minerals that incorporate those elements. Examination of the composition of urinary calculi is also important for choosing the procedure of remote lithotripsy and for carrying out the prophylactics of relapses of calculi formation.

The goal of the work was the analysis of the microelement composition of the collections of urinary calculi from the patients in the Omsk and Novosibirsk Regions, and revelation of the structure of heavy metal (Sr, Hg *etc.*) carriers and the features of the distribution of the elements over the mineral phases.

SUBJECTS AND METHODS OF INVESTIGATION

The subjects of investigation were 146 samples of urinary calculi from the patients of the Novosibirsk Regional Hospital into which the majority of persons suffering from urolithiasis (according to the data of the surgeons of the urology department) came from the ecologically unfavourable regions, and 120 kidney stones from the patients living in the Omsk Region. In order to form a correct opinion on the complete phase composition of calculi and their quantitative relations, average samples were analysed. Large concretions were cleaved at the

TABLE 1

Features of the element composition of kidney stones of different mineral composition from the Omsk and Novosibirsk collections

Group	Elements with maximal content	Elements with minimal content
<i>Omsk Region</i>		
Phosphate	Mg, P, K, Sr, Cd, Zr, Sb, I, Ba, Si, F, Zn, Rb	Pb, Br
Oxalate	Ca, S, Fe, Cr, Cu	K, I, Al
Urate	Na, U, Mn, Cu, As, Se	Ca, Mg, P, Sr, Cd, Zr, Sb, Ba, Si, Cr, Zn
<i>Novosibirsk Region</i>		
Phosphate	K, Sr, Ti, Ni, Zn, V, Mo, Mn, Fe, Cu, Cd, I, Br, Rb	Cr, As, Ag
Oxalate	Ca, K, Zn, Sr, Fe, Ni, Cu, Ti, I	Ag, Sn, Mo
Urate	Ca, K, Br, Fe, Ti, Mn, Zn, I, Cu	Sr, Cd, Mo, Rb, Ag, Cr, As

geometric centre, and the material from the entire surface was sampled. The small-sized calculi and sand were examined as a whole. For a number of calculi, we studied the substance sampled in the centre, at the periphery and from the surface (fragmentary analysis). Energy dispersion X-ray fluorescence element analysis of the samples was carried out at the station for element analysis of the Centre for SR VEPP-3 of the Budker Institute of Nuclear Physics, SB RAS (Novosibirsk). Emission spectra of the samples under investigation were excited with the beam of monochromatic radiation with the energy of 25 keV. The samples were prepared by pressing the powder in tablets 30 mg in mass and 6 mm in diameter. Emission spectra were treated with the special software Axil [15]. Calculations of element content were carried out using the external standard procedure. The reference samples were the rock standards: ST-1a (trap), SA-1 (siltstone), SG-1 (granite), SI-1 (limestone), BCR-32 (phosphorite). Normalization factors for calculating the concentrations of elements not certified in the indicated standards were obtained by interpolating the corresponding values for the neighbouring groups of elements. Detection limits for the elements under loading the spectrometric

tract with the frequency of 10 kHz and measurement time 1000 s are listed in Table 1. The error of element determination was within the limits 2–10 rel. %.

To study the changes in the element composition from the centre to periphery of a kidney stones of the phosphate-oxalate type from the Omsk collection (Fig. 3), we used emission spectral analysis according to the procedure described in [16]. The error of determination of all the elements was within the limits 2–3 rel. %. In

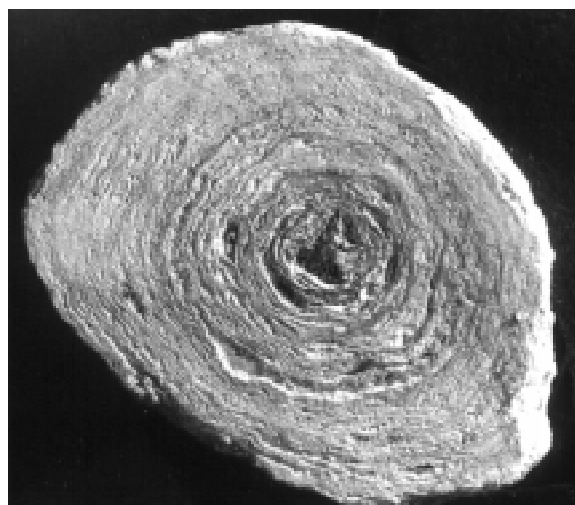


Fig. 3. Cross-section of a phosphate-oxalate calculi from the Omsk collection.

addition, this method was used to broaden the range of elements (such as Mg and Al) incorporated in the nephroliths from the Omsk collection.

RESULTS AND DISCUSSION

The microelement homeostasis of population (homeostasis is a feature of an organism consisting in the ability to resist changes and conserve relatively constant composition and properties during the lifetime) is due to the biological evolution factors under specific geochemical conditions. In this sense, the homeostasis directly depicts the effect of environments [17]. Momentary (from the geological and evolution viewpoints) changes in the element composition of the environment should be exhibited overcoming homeostasis.

We investigate urinary calculi as integral accumulators of the information about the external action and protective functions of an organism. The analysis of the microelement composition of calculi of the patients from different regions of Russia comprised by identical and different phases allowed us to establish some regularities.

According to the accepted practice, on the basis of the major component, urinary calculi are divided into oxalate, phosphate and urate groups; cystine, quartz and protein ones are less frequent. The results on the element composition of kidney stones from the Omsk and Novosibirsk Regions according to the data of XPA-SR are presented in Table 1 as an example. The data on the element composition of pathogenic minerals were processed by means of cluster analysis.

The results showed that three groups (clusters) of kidney stones (oxalate, phosphate and urate) differ both in number and in element content. The groups of elements with the maximal (31 to 0.4 mass %) and minimal (0.05 to 0.0005 mass %) content in different mineral phases can be distinguished (see Table 1). Such a distribution of the elements over different mineral groups is likely to be connected with the features of isomorphism of the minerals of kidney stones, which has not been investigated yet.

Comparing the elemental composition of the collections of kidney stones from the Omsk and Novosibirsk Regions (see Table 1) one can see

that a broader element range is characteristic of the latter. This is especially clearly observed in the set of heavy metals incorporated in the calculi from the Novosibirsk collection: the phosphate group – Ti, Ni, Zn, V, and Mo; the oxalate group – Zn, Sr, Ni, and Ti; the urate group – Fe, Ti, and Zn. It is likely that the presence of such elements as Ti, Ni, and Zn in the major phases of kidney stones is characteristic of this region; it is these elements that affect the interrelations of humans with the environment causing homeostasis disorder.

The difference of the calculi of the Omsk collection is that the oxalate group is characterized by the high sulphur content (0.4 to 0.7 mass %), in the rest less than 0.07 mass %. This fact can be explained by the higher concentration of sulphur-containing compounds of protein nature in the calculi of oxalate nature [18–19]. The concentrations of P, K, F, Sr, Zn, Ba, Zr, Sb, and Rb are maximal in the phosphate group and minimal in the urate group of kidney stones. It turned out that the higher concentrations of Na, Br are characteristic of urate calculi in comparison with oxalate and phosphate ones.

Some elements are present in both collections of kidney stones (phosphate group: Sr, Cd, and Zn; oxalate group: Fe, and Cu; urate group: Mn, Cu, and Br). The largest number of elements is detected in the calculi of the phosphate type, both for Omsk and for Novosibirsk (see Table 1).

Phosphate calculi, which are usually believed to originate due to infectious processes in the urinary system [5], are represented by hydroxylapatite $\text{Ca}_5(\text{PO}_4)_3(\text{OH})$ and struvite $\text{MgNH}_4\text{PO}_4 \cdot 6\text{H}_2\text{O}$ and account for about 1/5 of all the concretions under investigation. Each twentieth of them has the only mineral component – carbonate-hydroxylapatite. Apatite calculi contain larger amount of heavy microelements: for example, Sr is found in them in the maximal amount (see Table 1). As far as the second phosphate ingredient struvite is concerned, it occurs as the sole mineral component rather rarely in the Novosibirsk collection; most frequently it is found with a small admixture of apatite. The simultaneous presence of apatite and struvite in the urinary calculi is determined by the closeness of their lattice param-

eters: for apatite, $c = 6.878 \text{ \AA}$, and for struvite $a = 6.941 \text{ \AA}$, which ensures the epitaxial interaction between these crystal phases. Struvite calculi contain higher concentrations of Rb than the samples of other compositions do; this element substitutes NH_4 . Also a substantial amount of Sr is observed. The most likely carrier of this element in these samples is weakly crystallized apatite that often accompanies struvite.

One of the struvite calculi from the Novosibirsk collection was investigated fragmentarily from the centre to periphery. This concretion, with the maximal size along the section 65 mm, was composed of different types of layers: a brown crust, yellow loose layers and white dense ones. According to the data of X-ray phase analysis, all the layers are represented by struvite; only the yellow layer contained a small amount of carbonate-hydroxylapatite. By means of IR spectroscopy, an additional phase (newburyte) was revealed almost in all the samples; the content of this phase is maximal in the brown crust, which is an evidence of a decrease of the ammonium component on the surface of the urinary calculi [19]. The microelement composition was also different from one layer to another: Mn and a significant amount of Fe were detected only in the brown sample; the white and yellow samples contained no Mn at all, while the concentration of Fe in the white layer was an order of magnitude lower and in the white layer by two orders of magnitude lower than in the brown one. In all the regions of the calculus, Sr, Ag, B, Pb, Zn *etc.* were detected; their concentrations were <0.05 mass %. For another investigated kidney stone, the mineral component of which was composed of struvite and apatite, anomalously high concentrations

of some elements were detected. Analysis of the structure of this concretion revealed metal pieces in its centre. The size of one of them was sufficient to carry out its X-ray diffraction analysis. It was established that this was an alloy of titanium and nickel introduced into the organism of this patient during a surgical procedure; it has been a prosthesis previously (according to the data of the surgeon of the urology department); as a result, this piece turned out to be the centre of calculus formation. According to the data of elemental analysis of the middle sample of this calculus, it was discovered that along with Ti and Ni this prosthetic alloy contained rather high concentrations of such elements as V, Sr, Nb, Mo, and Cd. As a matter of principle, the positions of Mg in struvite can be occupied by Cu, Zn, Ni, and Fe^{2+} ions and more complicated groups. This fact provides evidence of the broad possibilities of isomorphous substitutions in struvite in all the positions similarly to apatite [20]; this is due to its structural features. This is why many different microelements are present in struvite urinary calculi; a higher Rb concentration than that in the apatite samples along with almost the same amount of Sr as that in the apatite samples was observed.

The data on the microelement composition of the sample of phosphate-oxalate type from the Omsk collection (Table 2) confirm this regularity. An increase in the number of the phosphate component from the centre to the periphery from zone 1 to zone 2 is accompanied by an increase in the number of elements and their concentrations.

Oxalates, whewellite $\text{CaC}_2\text{O}_4 \cdot \text{H}_2\text{O}$ and weddelite $\text{CaC}_2\text{O}_4 \cdot 2\text{H}_2\text{O}$, the most frequent components of urinary calculi, occur in the sam-

TABLE 2

Contents of elements in different zones of a kidney stone of the mixed type, mass %

Zone	Fe	Mg	Pb	Si	Mn	Ca	Ti	Al	Cu
1	0.006	3	0.006	0.004	0.004	22	—	0.0018	0.0016
2	0.014	4.2	0.0047	0.0012	0.0053	26	0.001	0.034	0.0021
3	0.026	6.6	0.011	0.029	0.049	38	0.0006	0.0028	0.0018

Notes. 1. Mineral composition: zone 1 - $\text{CaC}_2\text{O}_4 \cdot \text{H}_2\text{O}$ 70 %, $\text{Ca}_5(\text{PO}_4)_3\text{OH}$ 30 %; zone 2 - $\text{CaC}_2\text{O}_4 \cdot \text{H}_2\text{O}$ 50 %, $\text{Ca}_5(\text{PO}_4)_3\text{OH}$ 50 %; zone 3 - $\text{CaC}_2\text{O}_4 \cdot \text{H}_2\text{O}$ 30 %, $\text{Ca}_5(\text{PO}_4)_3\text{OH}$ 70 %. 2. Dash means the absence of data.

ples as the sole mineral component, in association with each other and with other inorganic and organic compounds [21]. A comparison of the structures of whewellite and weddellite showed that they are similar, and this explains why these two minerals so frequently get associated with each other and easily transform into each other. The structural representation of the compounds comprising urinary calculi is very important for the investigation of their growth and possible epitaxial connections between them [22]; it also allows one to understand the kinetics of the formation of these concretions. In the urinary calculi composed of calcium oxalates, in spite of their perfect crystal structure and limited capacity for isomorphous substitutions, a substantial number of various microelements was detected (see Table 1).

According to the observations of clinicians, urate urolithiasis accounts for about 12 % of the whole number of patients [7] in the absence of any extremal conditions causing exactly this type of urolithiasis. Approximately the same number characterizes the calculi of patients in Novosibirsk: 11.3 % samples contained uric acid of both forms (anhydrous $C_5H_4N_4O_3$ and hydrated $C_5H_4N_4O_3 \cdot 2H_2O$); 8.3 % of them were monophasic according to the X-ray diffraction studies. Ammonium urate $C_5H_2N_4O_3(NH_4)_2$ was found only in two calculi. Somewhat increased concentration of urate calculi (15.7 %) is characteristic of the Omsk collection; the fraction of anhydrous $C_5H_4N_4O_3$ is 14 %, the rest amount falls at the hydrated form $C_5H_4N_4O_3 \cdot 2H_2O$.

In the urate concretions, the lowest Sr concentration was observed; however, large amounts of K, Ca, Na, and Ti, sometimes V, Cu, Fe *etc.* were observed, which is likely to be due to the geochemical features of the environment in which the patients live (see Table 1). An order of magnitude higher iodine concentration was detected in one of the samples; this may be connected with taking iodine-containing preparations by that patient.

Comparing the mean concentrations of microelements in the urine of a healthy adult average statistical person (Na > K > S > Si > Br > Fe > Zn > Ni > Mn > I > Cu, Se > Pb > As [23]) and in kidney stones of the inhabitants of the Omsk (Na > K > S > Si > Fe > Zn

> I > Pb > Br > Ni, Cu > Mn > As > Se) and Novosibirsk (K > Zn > Sr > Fe > Mn > Cu > Ni > Br > Ti > I > Mo >> Ba) regions, we established that the concentrations of such microelements as Fe, Zn, Cu, Ni, Mn, and As and especially Sr, I, and Pb in kidney stones are higher than in urine, which is the evidence of selective accumulation of these elements during the pathogenic mineral formation processes. It is important to stress that the rows of heavy element concentrations in the samples under investigation differ for different regions. For the collections from Omsk (Fe > Zn > Pb) and Novosibirsk (Zn > Sr > Fe > Mn), different concentrations and distributions of microelements in the uroliths from different geographic regions is likely to be explained by the specific features of the regions. The data reported in [24–26] provide evidence in favour of this assumption, as the presence of elevated concentrations of microelements in kidney stones of the inhabitants of biogeochemical provinces and industry affected regions is connected with the permanently acting etiological factor of the formation of pathogenic aggregates in human organism.

CONCLUSIONS

Thus, the analysis of the element composition of urinary calculi was carried out; the interconnection with the substance composition was investigated. It was shown that the basic factors determining the variety and number of microelements in urinary calculi are the features of the mineral composition and the effect of the regional geochemical background (natural and industry related), and also the specificity of exchange processes in a patient's organism. One of the possible reasons of the formation of urinary calculi is the intake of increased amounts of some microelements in a human organism. A comparison of the element composition of calculi composed of the same phases allows one to approach better understanding of the specific characteristics of the external action on a human organism.

REFERENCES

- 1 A. A. Korago, *Vvedeniye v biomineralogiyu*, Nedra, St. Petersburg, 1992.

- 2 L. C. Herring, *J. Urol.*, 88 (1962) 545.
- 3 K. Lonsdale, D. Sutor, *Kristallogr.*, 16 (1971) 1210.
- 4 A. V. Golubchanskaya, *Urol. and Nefrol.*, 3 (1976) 43.
- 5 M. Mebel, G. Brin, G. Schubert, *Nauka i chelovechestvo, Znaniye*, Moscow, 1988.
- 6 M. T. Tynaliyev, B. I. Imanakunov, L. J. Bokonbaev *et al.*, *Izv. AN KirgSSR. Ser. Khim.-Tekhnol. i Biol. Nauk*, 4 (1991) 79.
- 7 V. I. Katkova, *Mochevye kamni: mineralogiya i genesis*, Syktyvkar, 1996.
- 8 A. K. Polienko, G. V. Shubin, V. A. Ermolaev, *Ontogeniya urolitov*, Tomsk, 1997.
- 9 N. A. Palchik, V. N. Stolpovskaya, I. V. Leonova *et al.*, in: *Mineralogiya tekhnogeneza*, Miass, 2001, p. 99.
- 10 G. Schubert, M. V. Chudnovskaya, G. Brin *et al.*, *Urol. and Nefrol.*, 5 (1990) 49.
- 11 H. A. Lowenstam, Sh. Weiner, *On the Biomineralization*, Oxford Univ. Press, New York, 1989.
- 12 E. V. Sokol, E. N. Nigmatulina, N. V. Maksimova, A. Yu. Chiglintsev, *Chem. Sust. Dev.*, 11, 3 (2003) 535. <http://www.sibran.ru/English/csde.htm>
- 13 O. A. Golovanova, V. F. Borbat, *Pochechnye kamni*, Med. kniga, Moscow, 2005.
- 14 O. A. Golovanova, P. A. Kachesova (Pyatanova), *Izv. Vuzov. Khim. i Khim. Tekhnol.*, 45, 2 (2002) 136.
- 15 V. B. Baryshev, G. N. Kulipanov and A. N. Skrinsky, *Handbook on Synchrotron Radiation*, Elsevier, Amsterdam, 1991, vol. 3, p. 639.
- 16 O. A. Golovanova, P. A. Pyatanova, N. N. Strunina, B. T. Baysova, *Zh. Prikl. Spektrosc.*, 70, 3 (2003) 432.
- 17 A. P. Avtsyn, A. A. Zhavoronkov, A. Rish, L. S. Stochkova, *Mikroelementozy cheloveka*, Meditsina, Moscow, 1991.
- 18 O. A. Golovanova, P. A. Pyatanova, E. V. Rosseva, 1 Ros. soveshch. po organicheskoy mineralogii (Proceedings), St. Petersburg, 2002, pp. 36–37.
- 19 N. A. Palchik, T. N. Grigorieva, T. A. Korneva *et al.*, *Khim. Ust. Razv.*, 7, 5 (1999) 541.
- 20 T. A. Shippey, *J. Mol. Struct.*, 63 (1980) 157.
- 21 V. N. Stolpovskaya, N. A. Palchik, S. S. Shkuratov, I. V. Leonova, *Chem. Sust. Dev.*, 10, 4 (2002) 467. <http://www.sibran.ru/English/csde.htm>
- 22 M. Tazzoli, Ch. Djmeneghetti, *Amer. Mineral.*, 65 (1980) 327.
- 23 E. A. Borodin, *Biokhimicheskiy diagnoz*, part 1, Blagoveshchensk, 1989.
- 24 S. V. Kadurin, A. V. Chepizhko, *ZVMO*, 4 (2001) 54.
- 25 N. V. Maksimova, A. V. Dar'in, E. V. Sokol *et al.*, 1 Mezhdunar. simp. "Biokosnye vzaimodeystviya: zhizn' i kamen" (Proceedings), St. Petersburg, 2002, pp. 169–170.
- 26 A. Yu. Chiglintsev, V. N. Udachin, S. S. Potapov, in: *Mineralogiya tekhnogeneza*, Miass, 2001, p. 130–137.