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# COMPLEX DETERMINATION OF THE IDENTIFICATION OF URINARY STONES IN PATIENTS RESIDENTS OF THE INDUSTRIAL REGION

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**Summary.** *Physico-chemical, biological and biochemical processes that occur during the formation of urinary stones determine the peculiarities of their composition and structure, as evidenced by modern methods of analysis: spectral, X-ray, polarization, optical, immersion, infrared spectrometry, etc. Modern Fourier Transform Infrared (FTIR) spectroscopy is a powerful instrument for identifying organic and inorganic substances by measuring the infrared (IR) absorption spectrum. It provides qualitative information about the molecular composition of the target material. The analysis of the results of the identification of urinary stones of patients, residents of the industrial region by the Mid-FTIR Spectroscopy method showed advantages among similar methods of studying urinary stones and proved the feasibility of its use in the complex examination of patients with urolithiasis. Accurate analysis of the primary and secondary chemical composition*

*and spatial distribution of stone components will lead to an understanding of the physicochemical processes that form the basis of the pathogenesis of stone formation. Spectral monitoring of the chemical composition of urine is important for early diagnosis, effective personalized treatment and prevention of stone recurrence in patients with urolithiasis.*

**Key words:** *urinary stones, petrography, infrared spectrometry, spectral monitoring.*

**Introduction.** Urinary stone disease is one of the most difficult problems of modern urology in the world. It has a prevalence of 2-3% among the population. Urinary stone disease affects people of working age, often has a sudden acute onset, the course of which often depends on the urgency of adequate care, high-quality timely diagnosis, effective treatment and elimination of obstructions to urination [1]. In addition, the development of complications of the disease can become the cause of disability in up to 20% of patients and even lead to death. The disease has a polyetiological basis, which has been sufficiently studied today, and the main mechanisms of stone formation have been determined. However, the high percentage of recurrence of stone formation indicates the presence of a problem of metaphylaxis of this disease. The gentle operative and instrumental methods of removing urinary stones developed today do not have a one hundred percent long-term effect, due to a sufficiently high frequency of disease recurrences and are not without possible complications [2]. The developed methods of metaphylaxis of relapses of stone formation also do not have a full effect and need to be improved. Therefore, a perfect study of the mechanism of stone formation in the urinary system, the search and development of perfect methods of their controlled litholysis, preliminary influence on the strength of the characteristics before the foundation of lithotripsy, as well as the determination of individual schemes of metaphylaxis of urolithiasis is quite relevant, has a certain practical significance and conditions the implementation of the proposed research. Urolithiasis is a complex multifactorial disease that occurs as a result of interaction between environmental and genetic factors [3, 5]. Epidemiological studies have shown that there is a close relationship between it and a number of lifestyle-related diseases, including cardiovascular diseases, arterial hypertension, chronic kidney disease, diabetes, and metabolic disorders [3, 4]. Physico-chemical, biological and biochemical processes that occur during the formation of urinary stones determine the peculiarities of their composition and structure, as evidenced by modern methods of analysis: spectral, X-ray, polarization, optical, immersion, infrared spectrometry, etc. [6, 8]. Determining the mechanisms that underlie the formation of urinary stones will allow the development of new preventive measures. Timely data on the chemical composition of a urinary stone, or more precisely, on its metabolic type, are of great importance for the selection of both methods of treatment of urolithiasis and methods of prevention of repeated stone formation. One of the directions of this search is a comprehensive analysis of lithogenic metabolic factors, the long-term action of which leads to the formation of urinary stones [7, 8].

Modern Fourier Transform Infrared (FTIR) spectroscopy is a powerful instrument for identifying organic and inorganic substances by measuring the infrared (IR) absorption spectrum. It provides qualitative information about the molecular composition of the target material. For quantitative analysis, it is possible

to use appropriate standards [8, 9]. FTIR spectroscopy has a reliable ability to analyze stones in the kidneys and gall bladder. FTIR spectroscopy measurements are non-destructive in nature and reveal high specificity, responsiveness and accuracy. This method can be used to analyze a wide range of materials: powders, liquids, gases, surfaces of solids, thin films, pastes, etc.

**The aim of the study.** To determine the possibilities and improve the results of identification of urinary stones of patients, residents of the industrial region by the method of Mid-FTIR Spectroscopy.

**Materials and methods.** To carry out the work, a comparative analysis of the chemical composition, morphology and structural features of 85 urinary stones of patients, residents of the Dnipropetrovsk region, was carried out. The age of the patients is from 18 to 70 years. By gender: there were 34 women, 51 men. The study was conducted of stones that came out on their own during conservative treatment, after contact or non-contact lithotripsy, and were removed as a result of surgery. The sizes of the studied stones were from 5 mm to 67 mm in length, from 4 mm to 54 mm in width, from 3 mm to 31 mm in thickness. Some stones were larger. The shape of the stones was varied. The morphology of uroliths was studied using a stereoscopic binocular microscope MBS-9. Microscopic examination of sections of uroliths was performed using an optical polarizing microscope MIN-8. The analysis of the mineral composition of all urinary stones was carried out by a hardware and software complex that combined a Nicolet iS10 FTIR spectrometer and  $\mu$ -FTIR Continuum microscope from the American company Thermo Scientific, ATR-Smart Golden Gate prefix with a diamond crystal from the English company Specac, OMNIC FTIR Software and Spectral Library NICODOM IR Kidney Stones, which contains 1668 transmission spectra.

**Research results and their discussion.** It is known that solid bodies differ from each other not only in mineral composition, but also in structure and texture. The construction of a solid body, which is a urinary stone, is characterized by structural and textural features due to its origin and subsequent transformation (genesis). Structure and texture determine the structure of matter at different levels. Texture is the composition of a sedimentary rock, determined by the orientation, relative arrangement of constituent parts, and the manner of filling the space. Texture is mainly a macroscopic feature, the study of which is carried out on rock samples (on dissections of stones, on the surface of anschliffe). Structure - the structure of the rock, which is determined by the size, shape, orientation of the particles and the degree of preservation of the organic residue (microscopic feature). The structure of rocks of chemical origin, including urinary stones, is characterized by the degree of crystallinity and the size (sizes) of grains.

The structure is of great importance in the strength of the urinary stone. The most durable and resistant to destruction are stones that have a fully crystalline equally medium-grained or fine-grained structure. Large-grained, coarse-grained, giant-grained formations are more prone to destruction, both under conditions of mechanical impact and under conditions of significant temperature changes, because large crystals with significantly pronounced adhesion in large-grained formations easily split and break. Vitreous stones quickly split under conditions of sudden temperature changes. Stones are characterized by the presence of cavities,

such as cracks and caverns. Cavities are different in shape - bubbly, channel-like, fissure-like, branched, etc. The shape and degree of hollowness of the stone determine its properties such as density, strength, and susceptibility to destruction.

Urinary stone spherulites, as a rule, are heterogeneous. Several zones are usually distinguished in their structure. The zonal structure is formed by the alternation of essentially mineral and mainly organic layers, as well as mineral layers of different composition. Layering can be observed at different levels of research — during the visual study of samples of large stones, and in the process of studying some areas of the samples. The layered structure in urinary stones of the spherulite type is recorded most clearly, somewhat worse - in granular aggregates. The central ("nuclear") part of such uroliths is most often represented by an accumulation of organic matter, which plays the role of a kind of "seed". In this case, the spherulite first forms as a polycrystalline aggregate of several split individuals. The sub-individuals that make up the spherulite have a conical shape, but in the process of increasing the splitting intensity, they interact with each other, obeying the law of geometric selection. Optimally oriented individuals, the elongation of which coincides with the radius of the future spherulite, will later transform into the thinnest fibers. The peculiarities of crystallization phenomena in the kidney are largely determined by the fact that the mineral-forming medium (urine) is characterized by transient supersaturations and is not an ionic but a colloidal solution. Under normal physiological conditions, this supersaturated solution retains its homogeneity and exists without crystallization phenomena. The mechanism of inhibition (prevention) of the growth of mineral phases in the urinary system is based on the process of keeping cations and anions in a dissolved state, thanks to the transition of their chemically active ionic forms into complex compounds.

Only thermogravimetry and polarization microscopy, which have significant limitations, compete with FTIR spectroscopy in terms of assessment reliability. The first method requires destruction of the sample during the study and requires a relatively large amount of material to obtain optimal resolution. The second method is characterized by the duration of preparation of preparations, it is not possible to identify a small amount of transparent materials in mixtures, and the results depend on the subjective experience of the expert.

Another widespread physical method of structural studies of solids, powder X-ray diffraction, showed a low recognition accuracy of less than 60% (ie, lower than wet chemical analysis). The reason lies in the peculiarities of the absorption of X-ray radiation by the crystalline structure of urinary stones.

The vast majority of urinary stones contain calcium oxalate in its pure form or in combination with phosphates and uric acid. Calcium oxalate can crystallize in two different chemical and crystallographic forms: monohydrate  $\text{CaC}_2\text{O}_4 \cdot \text{H}_2\text{O}$  (whewellite) and dihydrate  $\text{CaC}_2\text{O}_4 \cdot 2\text{H}_2\text{O}$  (weddelite). These types of stones are opaque to X-rays. At the same time, crystals of uric acid, urates, as well as amorphous calcium phosphate and organic substances such as proteins are X-ray transparent.

In FTIR spectroscopy, these limitations are absent. It is suitable for determining all crystalline, amorphous or poorly crystallized components, mineral and organic molecules. This is quite important for the analysis of the molecular composition of stones, in the formation of which both inorganic and organic substances participate.

Changes in the molecule's own dipole moment during the process of oscillation of its atoms leads to the absorption of the substance in the mid-IR range. At the same time, 3 main types of vibrations are possible: valence (changes in bond length), planar and out-of-planar deformation (changes in the bond angle), as well as multiple variations of them. These types of vibrations are distributed according to the wavelength of the electromagnetic scale and form the corresponding IR spectrum. For heteronuclear bonds, the symmetry ban is removed, so they are active in the mid-IR region. Urinary stones are characterized by bonds of OH, NH, CH, CO, CN, PO, CS, SO, SiO, etc., which are part of mineral and organic components. The simultaneous presence of several types of vibrations in a molecule helps to identify its functional groups.

Registration of IR spectra is possible in transmitted light, attenuated total internal reflection (ATR) and diffuse reflection (DRIFT) using appropriate spectrometer attachments. Each method has its pros and cons. The advantages of research in transmitted light are a sufficiently small amount of analyte and compliance with the Bouguer-Lambert-Beer law of linear dependence of the optical density on the concentration of the substance, which is important for quantitative analysis. Disadvantages include the length of the procedure for making a KBr (potassium bromide) tablet that is transparent in the mid-IR range.

The main advantage of the DRIFT method is the ability to determine the spectrum of finely dispersed urinary stone powder without diluting it with potassium bromide with a positive signal/noise ratio. The limitations are a relatively large amount of material, difficulties with quantitative analysis, and the possible presence of characteristic changes in individual spectral bands. These artifacts carry additional information, but make it impossible to search for matches in spectral libraries (Fig. 1.).

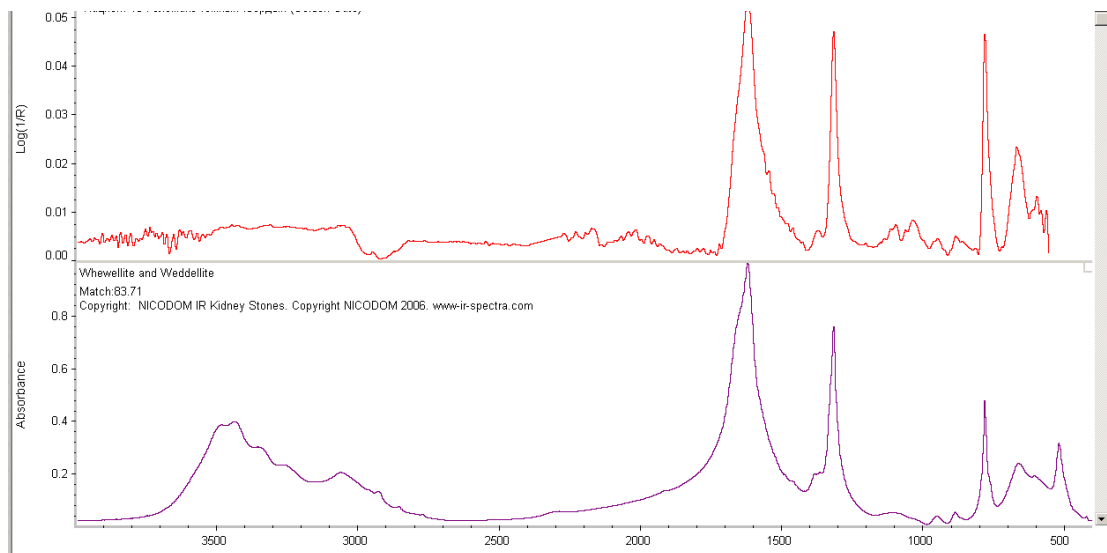


Fig. 1. Results of stone determination using the NICODOM database. The 3 most matching spectra by decay state are given, where the Match parameter is the correlation coefficient in %. Patient G. 51 years old

ATR-FTIR spectroscopy is most optimal for analyzing the molecular composition of stones. Which combines the low weight of the substance under investigation, the identity of the ATR spectrum with the transmission spectra, and the

possibility of quantitative analysis. The only drawback of this method is that there is a shift of the low-frequency limit of the mid-IR range from 400 to 650 cm<sup>-1</sup> (inverse centimeters). This limitation is due to the presence of focusing lenses made of non-hygroscopic IR transparent materials. However, the practice of measurements proved that the real limit corresponds to 500 cm<sup>-1</sup>. This is sufficient for the exact identification of all test stones because there are no intense characteristic bands at long wavelengths.

According to the results of the analysis, most of the stones in 48% of the patients were oxalates, 43% of the stones belonged to the oxalate-containing mixed type (Table 1.).

Table 1

Statistics of the identification of urinary stones according to the NICODOM database

Components of urinary stones	%
Wevelite and wedelite	48%
Wevelite, wedelite, carbonate apatite and struvite	25%
Wevelite, wedelite, carbonate apatite, struvite, uric acid	10%
Wevelite, wedelite, uric acid	8%
Uric acid	5%
Carbonate apatite and struvite	4%

Conditionally pure urate and phosphate stones were 4% and 5%, respectively. The registered spectra generally showed a satisfactory agreement with the library analogues. The average correlation coefficient of  $82.7 \pm 5.3\%$  could be slightly higher due to the fact that in the process of working out the measurement technique and spectrum processing, the first samples gave a more noisy signal, but this did not affect the accuracy of identification. This was manifested in a local maximum on the histogram centered at 74%. The search for matches using the spectral base shows that 55% of the stones have a semi-quantitative composition, while the rest only have a qualitative composition (Fig. 2).

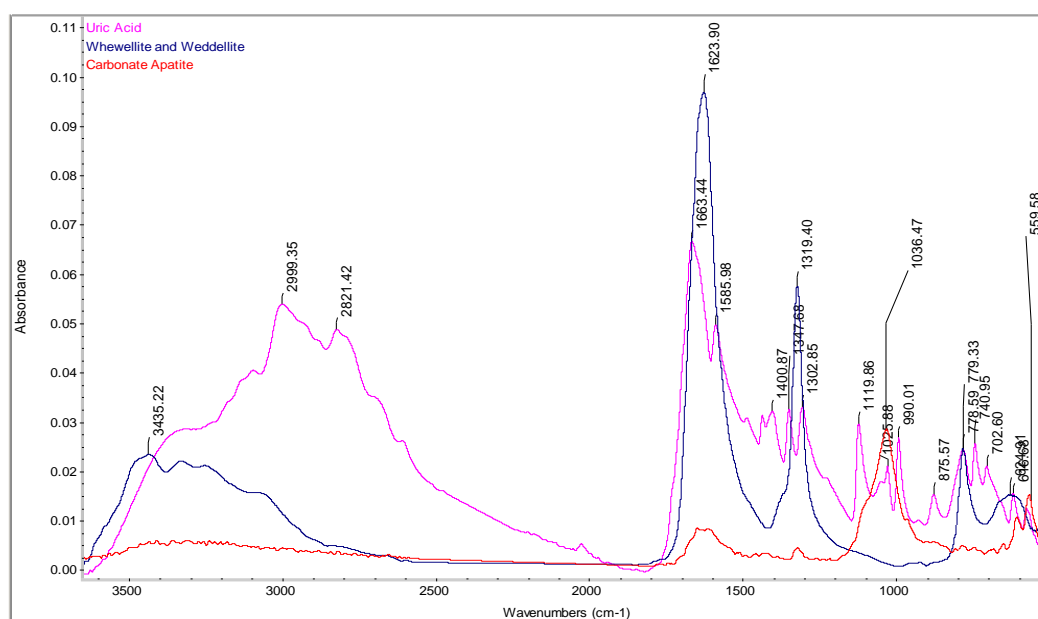


Fig. 2. ATR-FTIR spectra of conditionally pure oxalate, phosphate and urate stones

Comparison of ATR-FTIR spectra of patients with conditionally clean oxalate, phosphate and urate stones in a single scale showed that the long-wave part of the spectrum is lower than 1800 cm<sup>-1</sup> and more saturated with characteristic peaks. But, the maximum values of all the peaks are different, in a mixture they will overlap each other, potentially leading to false identification. Bands of the dominant mineral can mask the characteristic peaks of impurities. To eliminate this problem, along with determining the correlation, an additional analysis of the shape of the spectral bands is required.

However, the evaluation of the obtained results requires careful study. We give an example of an error in the automatic identification of the spectrum of a stone with a mixed composition using a spectral library.

A database search showed a maximum match with Whewellite + Weddellite in equal proportion. A formal comparison of the spectral curves led to the fact that the strong shaded band characteristic of apatite carbonate became less important than the similarity of the shape of the diffuse peak of the valence vibrations of protons at 2700-3700 cm<sup>-1</sup>. This strip is more informative for urate stones than for oxalates. Only in the 8th place according to the match rating was the spectrum of the stone of the corresponding composition, where the proportion of carbonate apatite was more than 50% of the compositional content.

The capabilities of the hardware and software complex are not limited to the measurement of the FTIR spectrum. For whole stones not split during destruction, it is advisable to use the methods of micro-scale  $\mu$ -FTIR analysis. This makes it possible to map and visualize the spatial distribution of organic substances and minerals in rock samples. The  $\mu$ -FTIR method makes it possible to reasonably understand the cause of the microstructural heterogeneity of stones and the triggering mechanism of the layer-by-layer deposition of constituent substances during the growth of the stone mass.

The given example shows the  $\mu$ -FTIR map of inhomogeneity of the spatial redistribution of organic CH groups, which probably belong to proteins on the surface of the urinary stone.

Therefore, it is the complex of various-scale studies that combines the morphological analysis of the sample and its petrographic study, aimed at identifying the structural features and mineral composition of urolith, that makes it possible to confidently establish the main regularities of its ontogenesis and to determine an adequate and unambiguous decision in the choice of methods and methods of prevention of this disease. The accumulation of analytical material on the ontogenesis of uroliths and its generalization, taking into account local conditions and the state of the environment, contributes to solving an important social task - preventing the spread and ensuring effective treatment of urolithiasis.

**Conclusion.** The analysis of the results of the identification of urinary stones of patients, residents of the industrial region by the Mid-FTIR Spectroscopy method showed advantages among similar methods of studying urinary stones and proved the feasibility of its use in the complex examination of patients with urolithiasis. Accurate analysis of the primary and secondary chemical composition and spatial distribution of stone components will lead to an understanding of the physicochemical processes that form the basis of the pathogenesis of stone

formation. Spectral monitoring of the chemical composition of urine is important for early diagnosis, effective personalized treatment and prevention of stone recurrence in patients with urolithiasis.

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