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Special Review

THE USE OF THERMAL ANALYSIS IN MEDICAL SCIENCE WITH SPECIAL REFERENCE TO NEPHROLITHS

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The applications of thermal methods in medical science have been summarized, with special regard to kidney stones. Complex thermal analysis can be used successfully for examination of human and animal urinary calculi, bones, odontoliths biological tissues (proteins, skin, callus, nail) etc.

1. Human kidney stones. In recent years thermal analysis has been gaining ground progressively in the various fields of medical science. The first and most elaborated example in this subject was the thermal analysis of nephroliths [1 – 7]. This was suggested by the fact that in thermal analysis calcium oxalate is used as a standard, and this compound is the most frequent component of renal calculi. Other crystalline components of nephroliths fortunately show different thermal properties, and this provides an opportunity for the analysis of nephroliths containing several components (polyminerals) by thermal methods.

The compounds present in renal calculi (not only calculi formed in the kidneys, but also those developing in the urinary tract in general) can be listed according to frequency as follows:

calcium oxalate monohydrate,
calcium oxalate dihydrate,
ammonium magnesium phosphate hexahydrate,
carbonate and hydroxyapatite,
tricalcium phosphate,
uric acid,
uric acid dihydrate,
L-cystine,
sodium urate monohydrate,
ammonium urate,
calcium hydrogen phosphate dihydrate,
xanthine.

The compounds following uric acid in the above list are observed only rarely. Other components of calculi have been described in special cases.

From the analytical point of view the situation is simplified by our observation that there are one to three main components, and of the theoretically possible combinations only few varieties occur in practice.

The measurements were carried out with a Derivatograph (MOM, Budapest). In 1958 Philipsborn [8] recommended the DTA method for the identification of the components of calculi. In our experience the complex method is more useful, because it gives not only qualitative but also quantitative results.

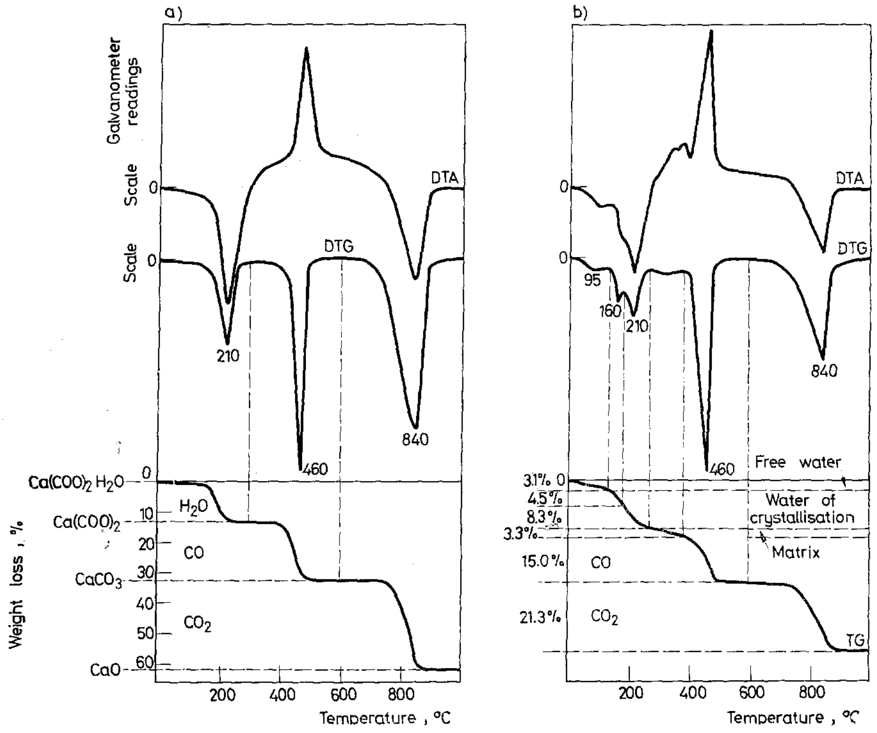

Fig. 1. Thermal analytical curves of *a)* calcium oxalate monohydrate, *b)* ureter stone containing calcium oxalates

Other instrumental analytical methods are used for the analysis of calculi, e.g. infrared spectroscopy and X-ray diffraction analysis. Because of the inhomogeneity of the stones the small amount of material required (one mg) is a drawback rather than an advantage.

Most small calculi discharged spontaneously weigh 20 to 50 mg; the determinations were carried out with samples of identical weight. Under our experimental conditions the efficiency of the thermal method is greater than that of the procedures mentioned above, because even a content of one to five per cent can be detected with certainty.

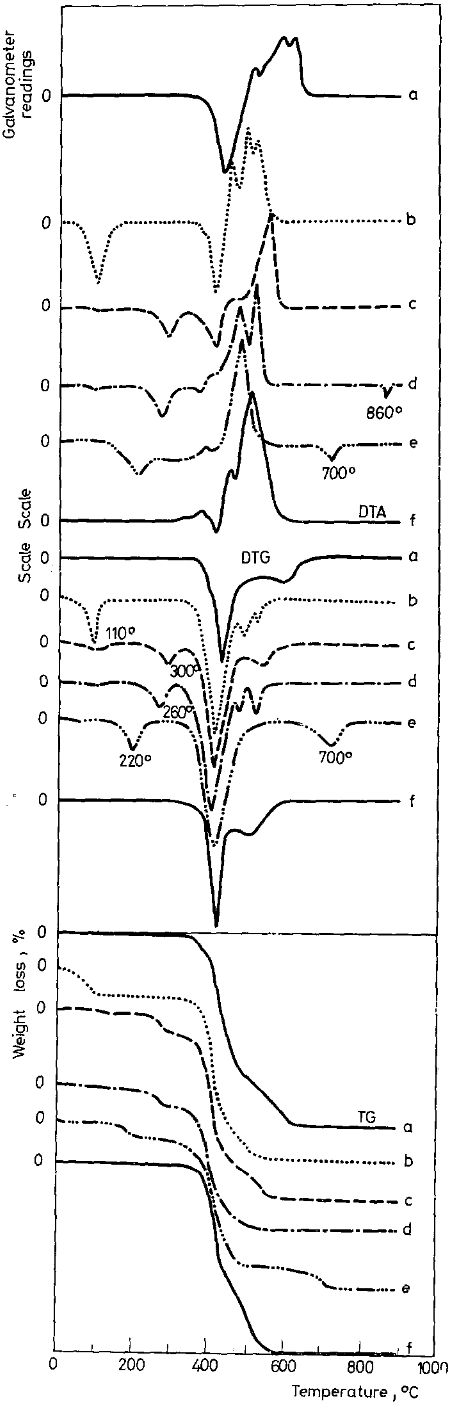

Fig. 2. Thermal analytical curves of *a)* uric acid, *b)* uric acid dihydrate, *c)* ammonium hydrogen urate, *d)* sodium hydrogen urate monohydrate, *e)* calcium urate, *f)* xanthine

In Fig. 1 are the thermal curves of pure $Ca(COO)_2 \cdot H_2O$ and of a ureter stone with three crystalline components, removed by operation. The diagram of the calculus differs at several positions from the well-known decomposition curves of the pure compounds (elimination of H_2O, CO and CO_2). During the first process the mechanically bound water always present in calculi is eliminated. According to the DTG and DTA curves, the loss of weight starting at 120° consists of two overlapping partial processes (II – III). First the more loosely bound water of crystallization of the dihydrate and at a higher temperature the water of crystallization of the monohydrate originally present and formed from the dihydrate are jointly eliminated. The calculi always contain non-crystalline organic material (matrix, globulins, cell fragments) generally in a quantity of one to five per cent; the exothermal decomposition of this is shown in process IV. A further difference can be seen in process V, in which not only carbon monoxide, but also the cracking products remaining from the organic matter are eliminated. The amount of the constant-weight residue exceeds that of the theoretical CaO, because calcium oxalate calculi always contain some calcium phosphate. The content of the latter can be calculated indirectly from the weight of the residue.

From the curves the quantities of the two forms of oxalate present in the calculus can be determined. This cannot be done using chemical methods, and only with limited certainty using other instrumental methods of analysis. As the conditions of formation and prognosis of the two kinds of calculi are different, this determination is of special significance in urological practice [9].

The growth of calculi containing mainly calcium oxalate monohydrate is slow: they attain the dimensions of spontaneous calculi only after several years, and are regenerated less frequently. The rate of growth of calculi composed of the dihydrate is greater, the needle-shaped crystals cause more complaints, their regeneration is rapid and their prognosis worse.

In Fig. 2 can be seen the thermoanalytical decomposition curves of the purine compounds involved. It is clear that the decomposition and oxidation of the purine structure proceed in nearly the same manner. Besides their similarities, there are also characteristic processes suitable for their differentiation (elimination of water of crystallization, ammonia, carbon dioxide; different weights and melting point of residues [6, 10]. Because of the considerable similarity of their decomposition curves, the differentiation of anhydrous uric acid and the extremely rare xanthine is uncertain, although Heide [11] did observe a difference using the micro-DTA technique.

The third group of common stone components are the phosphate calculi. The most frequently occurring member of this group is magnesium ammonium phosphate hexahydrate (struvite) in neutral or slightly alkaline urine; in nearly every case it forms a calculus together with carbonate apatite. The quantitative composition can be calculated from the process following the elimination of adsorbed water and from the total loss of weight. From acidic urine calcium hydrogen phosphate dihydrate may be formed, the derivatogram of which is entirely different from the above [3].

It can be seen in the diagrams presented that the difference in thermal decompositions offers an opportunity for the detection and determination of components. This is supported by the data available (1500 analyses of calculi), and the method has been used successfully in clinical practice for many years [12]. With the help of roentgenograms (calculus shadow) and utilization of the experience gained by thermal analysis, the in vivo analysis of calculi was rendered possible with adequate certainty, and this has a significant role in litholysis [13].

The efficiency and utilizability of the thermal analysis of nephroliths have been confirmed by several authors [14, 15]. It is one of the most efficient routine instrumental procedures: the method is quick and accurate, the evaluation is simple, the results are helpful for the physician, and it gives assistance in the revelation of stone imitations. It should be pointed out that the considerably greater rate of heating (20 to 50° per minute) than that used in ordinary thermoanalytical practice, has proved suitable for routine analysis.

2. Animal stones. The efficiency of the method encouraged us to analyse nephroliths of animal origin. In contrast to human calculi, calculi of horses and cattles are common [16]. The results obtained are of economic significance for stockbreeding: if the cause of calculus formation is the inappropriate composition of the food, the fattened animals may come to emergency slaughter in large numbers.

3. Odontoliths. Calculi can be formed in several parts of the human organism in addition to the urinary tract. Such are odontoliths, the most common components being the calcium phosphates, e.g. $CaHPO_4 \cdot 2H_2O$, which also occurs in nephroliths [17].

4. Enamel and dentin. In addition to the analysis of calculi, the thermoanalytical methods have also been used to study the properties of biological formations. For instance, examinations have been carried out using a complex thermoanalytical method for the determination of the most suitable temperature for the detection of the water, organic matter and ash content of enamel and dentin [18]. The TG curve has been used for the study of the properties of enamel and dentin by several authors [19].

5. Bones. The problem of the composition of various apatites occurs in medical science with reference to bones. From thermoanalytical measurements and IR-spectra it has been concluded that the inorganic substance of bones is a non-stoichiometric hydroxyapatite which also contains carbonate ions, the calcium ions being partly substituted by hydronium ions. Incidentally the composition changes with age and diseases [20].

The development of callus was also studied by thermoanalytical methods. It was found that during the development of callus $CaHPO_4$ appears first, and is transformed later into hydroxyapatite [21].

6. Proteins, protein complexes. The thermal method was used successfully for the study of glycosaminoglycane proteins and their lipid complexes present in biological tissues. On the basis of the thermal decomposition, the degree of sclerosis and the progression and change of the process with age can be followed. With this method it was possible to prove the presence of glycosaminoglycane-β-lipoproteid complexes in the atherosclerotic aorta [22—26].

The water-binding capacity of proteins, protein–lipid complexes or of biological tissues (human stratum corneum, nail, cortex, scale) can be studied with the help of DTA curves obtained in hydration and dehydration tests [27].

7. *Others*. The progression of silicosis can also be followed. The thermal method is suitable for the determination of the quartz content of an ashed lung specimen [28].

For determination of the percentage composition of dental materials (mixtures of waxes) thermogravimetry was successfully used [29]. Processes of dental cements during setting were investigated by the DTA method [30].

Without entering into details, it must be mentioned that the thermal study of other compact formations of the human organism is possible: substances of this kind are gallstones, salivary calculi, cartilage, etc.

With the above examples we have endeavoured (without aiming at completeness) to give a comprehensive picture of the results of practical and scientific significance which have been furnished to medical science by thermal analysis during its progressive spread.

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Résumé — Revue des applications des méthodes thermoanalytiques dans le domaine médical avec mention particulière pour les calculs rénaux. L'emploi des méthodes d'analyse thermique mixtes donnent de bons résultats pour l'examen des calculs rénaux animaux et humains, du tartre dentaire et des tissus biologiques (protéines, peau, ongles), etc.

Zusammenfassung — Es wurden die Anwendungen der Thermoanalyse auf medizinischem Gebiet unter besonderer Berücksichtigung von Nierensteinen zusammenfassend behandelt. Komplexe thermoanalytische Methoden eignen sich zur Prüfung von menschlichen und tierischen Harnsteinen, Knochen, Zahnstein, biologischem Gewebe (Proteine, Haut, Nägel, usw.)

Резюме — В статье обобщены результаты применения термического метода в области медицины со специальным воздействием на камни, находящиеся в почках. Успешно использован комплексный термический анализ для проверки мочевых камней, костей и биологических тканей (протеины, кожа, ногти, мозоль) человека и животных.